

From the Editor-in-Chief

A FEATURE OF OUR JOURNAL OVER RECENT YEARS has been the publication within its pages of the content of the Mannheim Lecture given at the annual meeting of the Association for European Paediatric Cardiology. The lecture is given in honour of Edgar Marinheimer, the “father” of Swedish paediatric cardiology. In an earlier issue, we also published an excellent review by Carlgren of the multiple contributions of Dr Marinheimer.¹ Not least of Mannheim’s achievements was the publication, along with his colleagues Kjellberg Rudhe and Jonsson, of a quite superb textbook detailing the angiographic investigation of congenital cardiac malformations.² To an extent, this book was well ahead of its time, and the content still provides much food for thought. In this issue of the journal, however, we are pleased to be able to publish the latest Mannheim lecture.³ This was given by Adriana Gittenberger-de Groot, in Porto in May of 2002, and was devoted to the development of the heart. An integral part of Adriana’s presentation was the superb series of animations, or “morphings”, that provided three-dimensional overviews of the crucial stages of cardiac development. The difficulties inherent in describing these four-dimensional events in simple and straightforward fashion is well recognised, and the animations go a long way to providing the necessary comprehension. It is clearly impossible to reproduce these sequences on the printed page, but Adriana has made a series of videoclips that contain the highlights of her animations. These are available for study on our website at www.greenwich-medical.co.uk, and provide the additional dimensions that make the morphogenetic processes so much easier to understand.

There is a huge amount of information contained within the review that will be of interest to clinicians working in the field of congenital heart disease. Those working in this area have always tended to be fascinated by the development of the heart. Indeed, in the past, it was almost “de rigeur” to include a short section devoted to the presumed morphogenesis of described malformations. The problem with this approach was that, in most instances, these reviews of morphogenetic events were collated from the arm-chair rather than the workbench. Furthermore, the speculations concerning abnormal mechanisms were usually extrapolated from interpretations of normal development. I was not averse, however, from making such speculations myself. One of my earliest

papers was concerned with the “morphogenesis of bulboventricular malformations”.⁴ When I return to this text now, I have difficulty understanding precisely what I was trying to say, but it all seemed very sensible at the time. Subsequent to this early experience, under the significant influence of my clinical colleagues in London, I veered away from speculations designed on presumed normal events. Anton Becker and I, together, went so far as to write a forceful chapter in which we questioned whether the embryological theories available at the time were a help or hindrance in understanding the malformed heart.⁵

Much has changed since we wrote that chapter, and the essence of the change is encapsulated in this year’s Mannheim lecture. As is emphasised, much of the evidence now comes from detailed studies in avian and rodent embryos, coupled with the most exquisite experimental techniques that hone down development to genetic and molecular levels. In this respect, our current issue carries another article showing the huge advances that have been made in the study of the developing heart. In a superbly illustrated contribution, Jorg Manner and Franziska Heinicke⁶ show how the chick can be used as a model for human cardiac malformations, in this case leftward juxtaposition of the morphologically right atrial appendage. Returning to the Mannheim lecture, as shown by Professor Gittenberger-de Groot, the quintessence of cardiac development is the contribution made to the growing heart by cells originating from extracardiac sources. Clinicians are well aware of the importance of the ingrowth of the population derived from the neural crest. Professor Gittenberger-de Groot now emphasises that this population grows into the heart not only through the arterial pole, but also through the venous pole. She also focuses our attention on the significant population of cells derived from the proepicardial organ. It should not be presumed, however, that all is now fully understood. There are several areas of development that remain contentious, not least the extent of the embryonic “sinus venosus”. As will be seen from Figure 4 of the Mannheim Lecture (page 178), and from the animated sequence that illustrates this aspect, the Leiden group remain convinced that part of the morphologically left atrium is derived from the embryonic venous sinus. My colleagues and I remain equally convinced that this is not the case. In our opinion, the pulmonary vein is a new structure that canalises in the medlastinal tissues behind the

developing heart, having nothing to do with the systemic venous sinus. Instead, it uses the dorsal mesocardium to gain its entrance directly to the left side of the primary atrial component of the heart tube. We presented our own evidence for these events in several instalments, following our studies of cardiac development in mice,⁷ chick,⁸ and man,⁹ the last investigation published in *Cardiology in the Young*. In this issue of the Journal, we recapitulate some of these findings. Together with Geoffrey Sharratt and Sandra Webb, we present what we hope will be the first of a series of clinico-anatomico-embryologic correlations, starting with a defect of the atrial septum that I had not seen before Geoff Sharratt brought it to my attention.¹⁰ You, the readers, will then be free to make your own minds up concerning the controversial areas concerning development. As always, we are interested to hear your comments, and we are ready to review, and hopefully publish, similar correlative offerings bringing together our understanding of morphology and development.

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References

1. Carlgren L-E. The Edgar Mannheimer Memorial Lecture. *Cardiol Young* 1998; 8: 3–5.
2. Kjellberg SR, Mannheimer E, Rudhe U, Jonsson B. *Diagnosis of Congenital Heart Disease 2nd Edition*. Chicago, Year Book Medical Publishers. 1959.
3. Gittenberger-de Groot AC. The quintessence of the making of the heart. *Cardiol Young* 2003; 13(2): 175–183
4. Anderson RH, Wilkinson JL, Arnold RA, Lubkiewicz K. Morphogenesis of bulboventricular malformations. 1: Consideration of embryogenesis in the normal heart. *Br Heart J* 1974; 36: 242–255.
5. Becker AE, Anderson RH. Cardiac embryology: a help or hindrance in understanding congenital heart disease? In: Nora JJ, Takao A (eds). *Congenital Heart Disease: Causes and Processes*. Mount Kisco, New York: Futura Publishing Co. 1984; 339–358.
6. Manner J, Heinicke F. A model for left juxtaposition of the atrial appendages in the chick. *Cardiol Young* 2003; 13(2): 152–160.
7. Webb S, Brown NA, Wessels A, Anderson RH. Development of the murine pulmonary vein and its relationship to the embryonic venous sinus. *Anat Rec* 1998; 250: 325–334.
8. Webb S, Brown NA, Anderson RH, Richardson MK. Relationship in the chick of the developing pulmonary vein to the embryonic systemic venous sinus. *Anat Rec* 2000; 259: 67–75.
9. Webb S, Kanam M, Anderson RE, Richardson MK, Brown NA. Development of the human pulmonary vein and its incorporation in the morphologically left atrium. *Cardiol Young* 2001; 11: 632–642.
10. Sharratt G, Webb S, Anderson RH. The vestibular defect: an interatrial communication due to a deficiency in the atrial septal component derived from the vestibular spine. *Cardiol Young* 2003; 13(2): 184–190.