Pathology of Congenital Heart Disease

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Foreword by Sir Theo Crawford

It is, I think, true to say that most pathologists find the subject of congenital heart disease a difficult one. In the past many of us have been content to learn the main anatomical features of the half-dozen or so more common varieties and to allocate the post-mortem examples that came our way to the 'nearest fit' amongst the half-dozen. In the days when treatment was entirely expectant or symptomatic this attitude was perhaps excusable; but today, when every case is a potential candidate for ameliorative or even curative surgery, pathologists must be prepared to work in collaboration with surgeons who have the right to expect a detailed assessment of material passing into the pathologist's hands. A surgeon may even hope to benefit from discussing the likely morbid anatomy of his cases with the pathologist before he plans his operative intervention.

The present volume in the Postgraduate Pathology Series is designed to supply both the pathologist in training and the hospital consultant with the basic information necessary to become expert in the field. In addition, this gathering of detailed material in a single volume will, we hope, prove a valuable source of instruction and reference for all members of the cardiological team.

Foreword by Jesse E. Edwards

The states that come under the heading of congenital heart disease have diverse morphological and functional characteristics. What initially may seem complex and confusing need not be so. The dominant issue in any given case is whether the course of the circulation is normal or abnormal. Additional factors are whether or not there are obstructive sites, competent valves and adequate myocardial contraction.

Doctors Becker and Anderson are to be congratulated for having put this book together in such a fashion as to simplify the analysis of cases either with or suspected of having congenital heart disease. The analysis is presented from the viewpoint of the pathologist but has appropriate application for all who deal with structural abnormalities of the heart, including the paediatric cardiologist, the radiologist, the echocardiographer and the cardiac surgeon.

The book is based on the principal that three features apply in analysis of any case. These are *morphology* of chambers, *connections* between chambers and between chambers and great vessels and *relations* of chambers and vessels to each other. Step-by-step analysis leads to simplicity of morphologic definition and of an answer to the question as to whether the course and character of the circulation are normal or abnormal.

Additionally, a chapter that will prove eminently useful is that dealing with developmental syndromes of which congenital heart disease forms a part.

Among the various chapters the authors are not always in agreement with others, both as to observations and classifications. They are secure in their disagreements. The straightforward and courageous manner in which they handle such matters is exemplary both as to their manner of expression and their identifying issues yet unresolved. They leave no doubt as to their own positions regarding controversial subjects.

This book brings the subject of pathology of congenital heart disease up to date and in simple language superbly supported by illustrations. It will have a telling effect upon the field.

It is with deep respect for the qualifications both personal and professional of the authors that warmly I present this foreword.

Preface

Within the last decade the morphological approach to congenital heart disease has evolved from a stage of eponyms and 'spot-light' classifications with heavy embryological ties to a stage of more pragmatic and systematic step-by-step analysis of the various 'building blocks' of the heart. It is on the latter basis that we consider the pathology of congenital heart disease as a relatively simple subject, particularly regarding gross abnormalities. Yet numerous clinical practitioners and pathologists seem to believe that this is far from the case. When asked to recommend a suitable text to prove our point, we were hamstrung, since no such text existed. The answer was obvious. Write one! This, therefore, is our attempt to make congenital heart disease simple.

We are grateful to Sir Theo Crawford for giving us the opportunity to publish our concept in his series devoted to Postgraduate Pathology. We are also indebted to our numerous clinical colleagues who have collaborated with us, and indeed in many instances have been instrumental in formulating the concepts expressed herein. We particularly thank Dr Bob Freedom of the Hospital for Sick Children, Toronto; Dr Leon Gerlis of Killingbeck Hospital, Leeds; Professor Tom Losekoot of the Binnengasthuis, Amsterdam; Professor Fergus Macartney of the Hospital for Sick Children, London; Dr Carlo Marcelletti of the Binnengasthuis, Amsterdam; Dr Manuel Quero-Jimenez of Centro Ramon y Cajal, Madrid; Dr Elliot Shinebourne of Brompton Hospital, London; Dr Michael Tynan of Guy's Hospital, London; Dr Bob Van Mierop of the J. Hillis Miller Health Center, Gainesville; Dr James Wilkinson of the Royal Liverpool Children's Hospital and Dr James Zuberbuhler of the Children's Hospital, Pittsburgh.

We are much obliged to Dr N.J. Leschot, Department of Anthropogenetics of the University of Amsterdam, for his invaluable support in compiling a chapter as complicated as the one on inherited cardiovascular disorders. Likewise, we thank Professor C.A. Wagenvoort for his expert advice regarding Chapter 35.

We are also indebted to the numerous fellows who worked with us, and friends who have contributed specimens to our collections and, thus, have helped in the development of the concepts described within these pages.

We thank Professor C. A. Wagenvoort further, together with Dr M.C. Joseph for so readily putting whatever facilities we required at our disposal.

We were also helped beyond measure in the preparation of illustrative material for the book by Christine Anderson, Ineke Dijk, Ernst M.E. Heeren, Siew Yen Ho, Marinus J. Klaver, Wilfried P. Meun and Audrey Smith. The book itself would not have been possible without the continual immaculate secretarial support of Marsha Schenker. Equally, we are indebted to our publishers for their encouragement, support and speed during the processing of an often untidy manuscript.

But, if there are any deficiencies within the book, which undoubtedly there will be, they in no way reflect upon our collaborators or publishers, being our full responsibility.

Anton E. Becker
Robert H. Anderson
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I Basic Considerations

1

Basic Approach and Philosophy

INTRODUCTION

The series of volumes relating to postgraduage pathology are presumably intended to supplement facets of pathology which do not receive full coverage during basic training. Nowhere is this needed more than in the study of congenital heart disease. Congenital cardiac malformations are to us a paradox. It would seem that many pathologists consider them close to a mystery, and believe that provision of the label 'congenital heart disease' fulfils their responsibility with respect to diagnosis. Yet we are convinced that diagnosis of congenital cardiac anomalies is not difficult. Indeed, we believe it is open to all who can distinguish a right atrium from a left atrium, a right ventricle from a left ventricle or an aorta from a pulmonary trunk from a truncus arteriosus. In this volume we have the privilege of attempting to substantiate this claim. We will therefore attempt to show how, with the minimum of anatomic knowledge but with the maximum of patience and attention to detail, any who have the skill to become pathologists should find congenital cardiac morphology a simple and easily understood branch of cardiac pathology.

The key to the understanding of congenital cardiac malformations lies in the approach one takes. An approach based upon recognition of given patterns or complexes into which one places individual cases is doomed to failure by the very complexity of the subject. In order to diagnose accurately congenital lesions within the heart, which is after all the prime responsibility of the pathologist, it is necessary to have a system sufficiently flexible to cope with all the cases the pathologist may have seen previously, but above this to cope with any case he may possibly be confronted with. Indeed, the ideal system for pathological diagnosis would cope with any case he could possibly meet.

Fortunately, the heart and its known congenital malformations are constructed in such a way that they can be simply analyzed to provide the perfect system alluded to above. With reference to the heart it is called 'sequential chamber localization'. The system of sequential analysis has been developed over the past 15 years primarily by Van Praagh *et al.* (1964, 1966, 1968, 1972, 1977a, 1977b), with a very comparable system worked out over the same period by de la Cruz *et al.* (1972, 1976). The

system which we recommend for pathological use is based firmly upon these prototypes, yet is not a 'carbon-copy' of either. The major disadvantages of these systems as we see them are firstly placement of an undue emphasis on embryology, or rather presumed concepts of cardiac development, and secondly a failure to distinguish between connections, relations and morphology of the cardiac segments.

The study of the pathology of congenital heart disease has, to our minds, for too long been tethered by the constraints of cardiac embryology. Many of the apparent disagreements concerning congenital cardiac lesions relate not to the morphology of the defects themselves but to the presumed maldevelopment which underlies them. These disagreements are fuelled by many articles on morphology of congenital malformations which are not considered complete unless they possess a paragraph on presumed embryogenesis, presumably to give the work a veneer of academic respectability. We ourselves are by no means guiltless in this respect. But the system we now espouse offers universality, we believe, by now eschewing any considerations of morphogenesis, which of necessity are more or less speculative.

The pruning of morphogenetic considerations from a sequential system offers it the option of being purely descriptive. The important point then is to determine precisely which features of a congenitally malformed heart warrant description. It is our belief that the deficiencies of other systems advanced for diagnosis are a failure to distinguish which features warrant description, or else use of polyglot terms in an attempt to combine several features together in the interests of brevity. Alternatively, one feature of a heart is used to predict the arrangement of other features.

The basis of sequential chamber localization is that it recognizes the integrity of three segments of the heart, namely the atrial chambers, the ventricular chambers and the great arteries. It is possible to cater for additional segments, for example the great veins, but we do not believe this is necessary as unwanted complications are produced. In a system based upon recognition of cardiac chambers, three features demand description.

1. The morphological characteristics of the chambers themselves.
2. It is essential having identified the chambers to know which chambers are attached to each other.
3. It is necessary to know how each chamber lies in relation to the others, and how the heart itself is positioned within the body.

The system we advocate in this volume is based upon the recognition of these three features, namely morphology, connections and relations, but uses mutually exclusive terms for the description of each feature (Tynan *et al.*, 1979). Of course, in the majority of cases of congenital heart disease which confront the general pathologist, the cardiac chambers will be of normal morphology, will be connected to each other in usual fashion and will be normally related. The lesion will probably be a hole between two chambers, or else a narrowing within or between the chambers. Such a lesion is termed an associated lesion. In this case, it will have cost the pathologist nothing to have established the presence of normal morphology, connections and relations. Having established such normality, he can

then diagnose the associated malformation as the lesion with confidence. But, had there been abnormal morphology, connections or relations, they would have been identified, and described along with the associated lesion. In other words, use of a system of sequential analysis costs the pathologist little in those cases which turn out to be relatively normal. It is of inestimable value in complicated cases and indeed provides the platform for making such complex cases simple to understand, diagnose and describe.

THE BASIS OF SEQUENTIAL CHAMBER LOCALIZATION

Sequential chamber localization is a standardized system of examination of any heart and provides the facility for diagnosis of any lesion as yet known or unknown. Basically, it depends upon the establishment of atrial position, or situs, and then an analysis of the atrioventricular and ventriculoarterial junctions in terms of morphology of the ventricular chambers, connections of the segments and relationships of the segments. Finally, it demands a catalogue of all associated anomalies present, including the position of the heart itself within the thorax.

Atrial situs

Situs describes the arrangement of organs within the body. Since the arrangement of organs within different parts of the body does not always coincide, it is usual to speak of thoracoabdominal situs, of thoracic and abdominal situs separately and finally of situs of the atrial chambers themselves. Most frequently the situs of abdominal organs, thoracic organs and atria will correspond. For this reason the arrangement of the abdominal organs can be used to predict atrial situs with a high degree of accuracy. Two basic plans are recognized, situs solitus and situs inversus. Situs inversus is the mirror-image of situs solitus (*Figure 1.1*). Unfortunately for those concerned with congenital heart disease, all persons do not have situs solitus or situs inversus. The feature of these arrangements is lateralization of organs, there being a difference between organs found on the right and left side of the body. In situs solitus the trilobed lung, liver and gall-bladder are all found on the right and are called 'morphologically right' structures. In situs inversus, these 'morphologically right' organs are found on the left side of the body. The minority of people who have neither situs solitus or situs inversus have isomerism of organs, that is to say the organs on the right and left sides of the body have either morphologically right features on both sides, or else morphologically left characteristics. This arrangement was termed by Van Mierop, Gessner and Schiebler, (1972) 'situs ambiguus'. In several respects it is an unfortunate title, because the morphology is not ambiguous but isomeric. Nonetheless the term has widespread usage. However, we divide situs ambiguus into isomeric right and isomeric left forms (*Figure 1.2*). In the presence of atrial isomerism, abnormal organ arrangement is a far less reliable guide to the situs (Macartney *et al.*, 1978). The arrangement of bronchial anatomy is of far

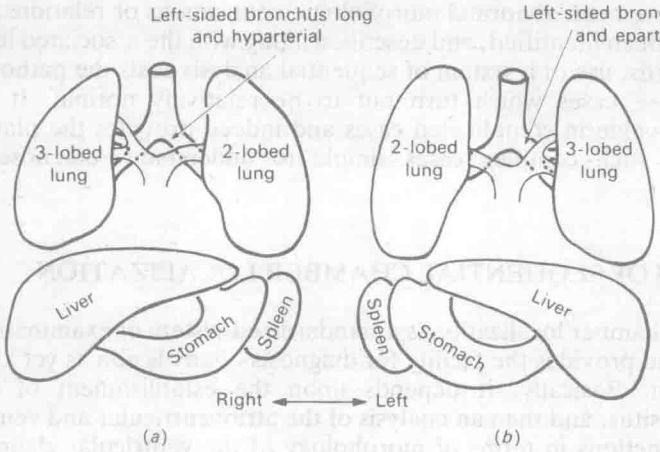

Figure 1.1 Diagram illustrating the features of the lateralized forms of body arrangement, namely (a) situs solitus and (b) situs inversus

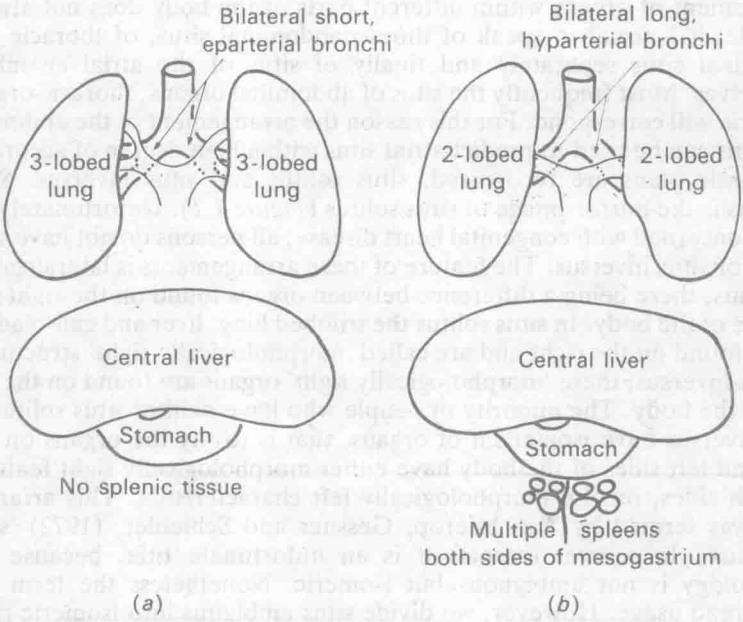

Figure 1.2 Diagram illustrating the features of the two isomeric varieties of body arrangement, frequently termed 'situs ambiguus', but best considered as right isomerism (a) and left isomerism (b)

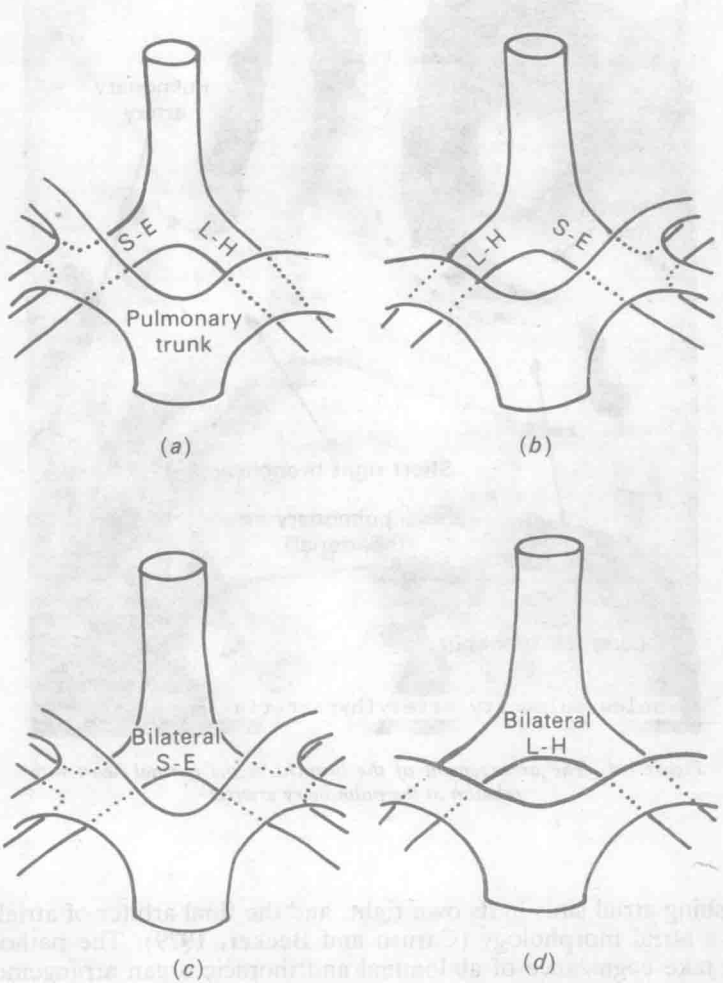

Figure 1.3 Diagram of bronchial anatomy as a guide to situs. (a) Situs solitus; (b) situs inversus; (c) right isomerism; (d) left isomerism. S–E: short and eparterial; L–H: long and hyparterial

greater value (*Figure 1.3*), and is of inestimable value in a clinical setting (Partridge *et al.*, 1976; Macartney *et al.*, 1978). Use is made of the fact that the morphologically right bronchus, by virtue of its branching pattern, is approximately half as long as the morphologically left bronchus. In relation to the pulmonary arteries, the first branch of the morphologically right bronchus is eparterial (above the artery extending to the lower lobes) whereas that of the morphologically left bronchus is hyparterial (below the artery, *see Figure 1.4*). Thus, the finding of two morphologically right or two morphologically left bronchi is evidence of right isomeric or left isomeric forms of thoracic 'situs ambiguus'. In the greater majority of cases, this will also indicate atrial situs, but not always. Here the pathologist comes into his own, because he always has the facility of

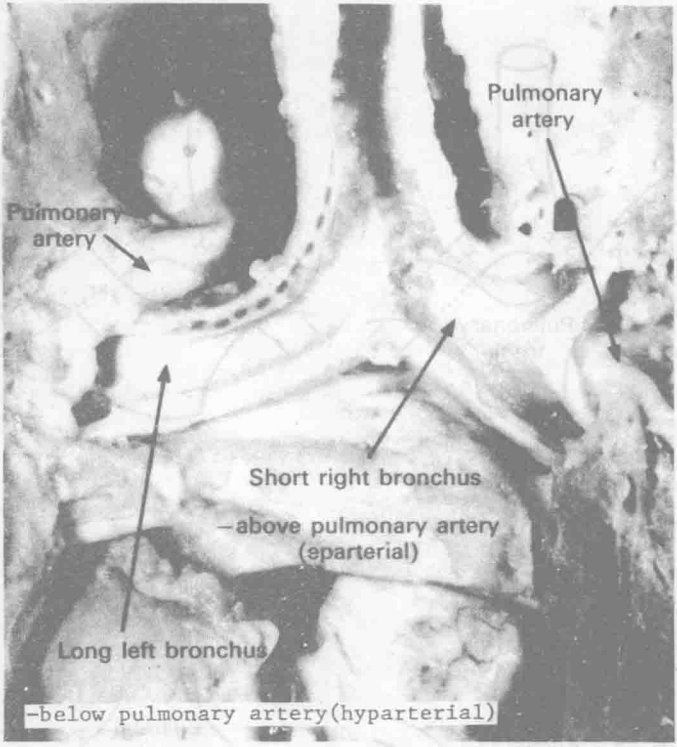

Figure 1.4 The arrangement of the bronchi in the normal heart with relation to the pulmonary arteries

establishing atrial situs in its own right, and the final arbiter of atrial situs must be atrial morphology (Caruso and Becker, 1979). The pathologist should take cognizance of abdominal and thoracic organ arrangement in any case of congenital heart disease, but should determine the arrangement of the atrial chambers by direct inspection. It is very easy for the morphologist to distinguish the morphologically right atrium from the morphologically left atrium (*Figure 1.5a*). The morphologically right atrium has a blunt atrial appendage which has a wide junction with the smooth walled part of the chamber. There is a prominent muscle bundle (crista terminalis) between the appendage and the smooth walled atrium (sinus venarum). The septal surface of the morphologically right atrium has the limbus of the fossa ovalis and remnants of the valves of the sinus venosus are found within this atrium. In contrast the morphologically left atrium (*Figure 1.5b*), has a hooked appendage which has a narrow junction with the smooth walled atrium. There is no crista terminalis between these components, the septal surface has the flap valve of the fossa ovalis and there are no remnants of valves of the sinus venosus. In atrial situs solitus the morphologically right atrium is to the right and the morphologically left atrium is to the left. In atrial situs inversus the mirror-image arrangement is