Heart Disease in Infants and Children

Edited by Gerald V. Graham

and Ettore Rossi

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Consultant-in-Charge, Clinical Physiology Department, The Hospital for Sick Children, Great Ormond Street and Clinical Physiology Laboratories, Institute of Child Health, University of London

and Ettore Rossi

Professor of Paediatrics and Medical Director of the University Children's Hospital, Berne.

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Contributors list

Robert H. Anderson
Joseph Levy Foundation Reader in Paediatric Cardiac Morphology, Cardiothoracic Institute, Brompton Hospital, London

Arnon Bentovim
Consultant Psychiatrist, The Hospital for Sick Children, Great Ormond Street, and The Tavistock Clinic, London

Kim M. Fox
Senior Registrar, Cardiovascular Research Unit, Hammersmith Hospital, London

Walter A. Fuchs
Professor of Radiology and Chairman, Department of Diagnostic Radiology, University Hospital, Berne, Switzerland

Gerald Graham
Consultant-in-Charge, Department of Clinical Physiology, The Hospital for Sick Children, Great Ormond Street, London

Hans Peter Gurtner
Professor of Medicine, Physician-in-Charge, Section of Cardiology, Department of Internal Medicine, Inselspital, Berne, Switzerland

David J. Hatch
Consultant Anaesthetist, The Hospital for Sick Children, Great Ormond Street, London

Sheila G. Haworth
Senior Lecturer, Department of Paediatric Cardiology, Institute of Child Health, University of London

Arthur Hollman
Consultant Cardiologist, University College Hospital, London and Honorary Consultant Cardiologist, The Hospital for Sick Children, Great Ormond Street, London

Rudolf König
Paediatrician, University Children's Hospital, Berne, Switzerland

Ralph Kuenzler
Consultant Paediatrician and Paediatric Cardiologist, Zurich, Switzerland

Marc de Leval
Consultant Cardiothoracic Surgeon, The Hospital for Sick Children, Great Ormond Street, London

Wedikund Lenz
Professor of Human Genetics, University of Westphalia, Münster, Germany

John Lind
Emeritus Professor of Paediatrics, Karolinska Hospital, Stockholm, Sweden

Fergus Macartney
Professor of Paediatric Cardiology, Institute of Child Health, University of London and Honorary Consultant in Paediatric Cardiology, The Hospital for Sick Children, Great Ormond Street, London

Celia Oakley
Consultant Cardiologist, Hammersmith Hospital, London and Honorary Senior Lecturer, Royal Postgraduate Medical School, London

William J. Rashkind
Director of the Cardiovascular Laboratories, Children's Hospital, Philadelphia and Professor of Paediatrics, University of Pennsylvania School of Medicine, USA

Franz J. P. Real
Director of Paediatric Cardiology, University Children's Hospital, Zurich, Switzerland

Ettore Rossi
Professor of Paediatrics and Medical Director, University Children's Hospital, Berne, Switzerland

Ursula Sauer
Paediatric Cardiologist, Deutsches Herzzentrum München, Munich, Germany

Leslie Shelton
Paediatric Cardiologist, University of South Carolina School of Medicine, USA

Eric D. Silove
Consultant Paediatric Cardiologist, The Children's Hospital, Birmingham and Senior Clinical Lecturer, The University of Birmingham

Franco P. Stocker
Paediatric Cardiologist, University Children's Hospital, Berne, Switzerland

James F. N. Taylor
Consultant Paediatric Cardiologist, The Hospital for Sick Children, Great Ormond Street, London

Georg Töndury
Professor of Anatomy, University of Zurich, Switzerland

Heinz Tschäppeler
Paediatric Radiologist, Department of Radiology, University Hospitals, Berne, Switzerland

Michael Tynan
Consultant Paediatric Cardiologist, Guy's Hospital, London

Colin H. M. Walker
Consultant Paediatrician, Tayside Health Board, Scotland and Honorary Senior Lecturer, Department of Child Health, University of Dundee. Formerly Director, Rheumatic Fever Center, Denver, USA

Jann W. Weber
Paediatric Cardiologist, University Children's Hospital, Berne, Switzerland

Bertrand G. Wells
Consultant Clinical Physiologist, The Hospital for Sick Children, Great Ormond Street, London

Felix Wyler
Associate Professor of Paediatrics, In Charge of Paediatric Cardiology, University Children's Hospital, Basel, Switzerland

Preface

When 25 years ago one of us (E.R.) wrote a book on congenital heart disease in infants, the era of its detailed diagnosis and surgical treatment was just beginning. Since then the advances in both these areas have been enormous. But a result of these new possibilities has also been a fragmentation of knowledge so that today heart disease in infants and children has largely moved away from being the domain of cardiologists and paediatricians to that of specialist paediatric cardiologists.

It is the aim of this book to inform and guide paediatricians, cardiologists and general physicians who may be the first to see a child with suspected heart disease. They need a more general approach and level of information which as far as possible avoids minutiae.

It was clear from the start that it would be best to enlist the help of colleagues with special experience in the various areas. Aware of the dangers and possible deficiencies of any multi-author book, we have tried to maintain a measure of uniformity by choosing as contributors, with only a few exceptions, those who have worked closely with one or other of the two editors. Editorial guidance was directed at a presentation which would be both reasonably comprehensive and succinct. At the same time, our contributors were urged not to avoid expressions of personal experience and opinion.

The arrangement of the book is such as to provide, in its general part, some of the basic information which bears on the later more detailed and systematic coverage of all important forms of heart disease in children—both congenital and acquired, the latter being given the full emphasis it deserves in view of its increasing incidence and recognition, as well as its importance to paediatricians in differential diagnosis.

The manner of reference citation has been kept flexible, leaving to the contributors whether they used the conventional way, as practised in articles, or suggested further reading, especially in the more general chapters.

The presentation as a whole has kept clinical problems and considerations at its centre. In addition, the growing importance of heart disease in infants has been fully taken into consideration.

We would like to thank our publisher, Edward Arnold, for coping so patiently and well with the many publishing and editing problems with which we confronted them.

Gerald Graham Ettore Rossi

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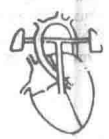
Abbreviations for end papers

ASD = atrial septal defect
BVH = biventricular hypertrophy
ICS = intercostal space
LA = left atrium
LAD = left axis deviation
LVH = left ventricular hypertrophy
PA = pulmonary artery
PDA = persistent ductus arteriosus
PS = pulmonary stenosis
RA = right atrium
RAD = right axis deviation
RVH = right ventricular hypertrophy
TGA = transposition of the great arteries
VSD = ventricular septal defect
W–P–W = Wolff–Parkinson–White syndrome

Congenital Heart Disease: Summary of differential diagnosis and other features of the more common forms (continued from front end papers)

Diagnosis	Percentage incidence (among all cases of CHD)	Schematic diagrams	Cyanosis	Clinical features	Sounds and murmurs	Electrocardiogram	Chest X-Ray	Complications	Operability	Prognosis
12 Aortic stenosis, valvar	3-5%		–	Rarely, sudden and short loss of consciousness	Murmur and thrill 2-3 ICS, right; A_2 decreased; radiation into the neck	Normal or LVH. Rarely S-T abnormalities. ECG poorly correlated with severity of stenosis	Normal or enlargement to left. Post-stenotic dilation of the aorta	Endocarditis; left-heart failure	Correction, if severe symptoms or high pressure gradient	Not operated: variable long-term prognosis; high mortality rate in early adulthood, but sudden death even in childhood not rare. Operated: depending on severity (long-term results uncertain)
13 Aortic stenosis, subvalvar			–	As in 9	As in 9, but normal A_2	As in 9	As in 9, without aortic dilitation	As in 9	As in 9	As in 9
14 Aortic stenosis, supravalvar			–	Sometimes characteristic facies. Possibly hypercalcaemia	As in 9, but much accentuated in A_2	As in 9	Normal or high aortic dilitation	As in 9, with early coronary arteriosclerosis	As in 9	As in 9, but perhaps better since valve often normal.
15 Fallot's tetralogy	5–10%		+/++ (rarely acyntotic)	Usually moderate cyanosis. Hypercyanotic spells, squatting; clubbed fingers and toes	Systolic murmur in 3-4 ICS; diminished P_2. Soft, short sytolic murmur over pulmonary area	P-pulmonale; RVH	Small or normal heart with upward tilt; boot-shaped or egg-shaped heart. Normal or even diminished pulmonary vascularity	Hypercyanotic spells with acidaemia and cerebral thrombosis; brain abscess	Total correction preferred, if necessary in infancy; otherwise, palliative shunt procedure	Not operated: life expectancy depends on severity: survival beyond puberty rare. Operated: markedly better, often seemingly normal, but long-term results still highly variable and uncertain
16 Pulmonary atresia with VSD	1% or less		+/++	As in 12, but more marked	Occasionally, systolic-diastolic murmur in 2, ICS right or left (PDA or bronchial arteries); otherwise as in 12. Absent pulmonary murmur, single second sound	As in 12	As in 12, but more marked	As in 12	As in 12, but palliative operation more frequent	As in 12
17 Tricuspid atresia	1–3%		++	Early cyanosis and dyspnoea. After infancy, strong liver and jugular venous pulsation possible. Characteristic ECG	Atypical systolic murmurs	LVH; LAD or RAD	If additional PS, similar to 12, otherwise as in 16, but small heart. Occasionally, prominent left ventricular contour	As in 12	Various shunt operations, followed by RA-PA connection (in later childhood). PA banding, if increased pulmonary blood flow	Not operated: months, rarely a few years Operated: after palliative operation, worse than expected with Fallot's. After radical operation improved; but long-term results still uncertain.
18 Transposition of the great arteries (+/– PDA; +/– VSD; +/– ASD)	5–15%		++/+++	Cyanosis from birth, often severe; dyspnoea; heart failure. Normal birth weight	At birth, often without murmur. If additional VSD, like 2. If pulmonary stenosis, similar to 12, but P_2 often increased	Maybe normal at birth; otherwise RVH	At birth, normal or enlarged heart. Absent pulmonary segment. Normal or increased pulmonary vascularity. If additional PS, as in 12	Heart failure; brain abscess, cerebral thrombosis	Isolated balloon atrioseptostomy or surgical atrioseptostomy during neonatal period, followed by radical operation. If additional VSD: septostomy followed by PA banding or radical operation with primary VSD closure. If plus VSD and PS: palliative shunt operation, followed by radical operation as necessary (optimally aged 5–7 years)	Not operated: 90% die in infancy. Operated: markedly improved since balloon septostomy. Radical operation: low operative mortality; reasonably good life expectancy, although long-term results (over 10 years) uncertain
19 'Corrected' transposition of the great arteries	Less than 1%		–, unless due to additional cardiac anomalies	Asymptomatic, except if additional other CHD	Atypical	Normal, or absent Q in left-precordial leads	Prominent left aortic arch. Pulmonary vascularity according to additional anomalies	Complete heart block; otherwise, depending on additional anomalies	No operation or depending on additional CHD	Depends on additional anomalies, including A-V block
20 Univentricular heart (primitive or single ventricle)	1–2%		+/+++	As in VSD (without cyanosis) or transposition (mild to moderate cyanosis)	As in TGA or atypical	Often LVH with broad transition zone. Absent precordial Q wave common	Cardiomegaly. Pulmonary vascularity according to additional anomalies	As in 12 or 16	Palliative operation, later radical operation(possible only in some forms)	Depends on additional anomalies, in general, poor
21 Ebstein's anomaly	Less than 1%		–/+++	Usually asymptomatic, but maybe severely cyanotic. Not rarely paroxysmal tachycardias. W-P-W syndrome	Often weak systolic and loud diastolic murmur. Gallop rythm. Heart sounds often diminished.	Very marked P-pulmonale; often RBBB with low voltage in right precordial leads; or W-P-W syndrome	Only in infancy normal or slightly enlarged heart. Vascularity increased; pulmonary oedema	Tachycardia; heart failure. Otherwise as in 12	Tricuspid valve replacement, if severe heart failure and/or interatrial right to left shunt	Not operated: depends on severity, may even be nearly normal. Operated: good, but long-term results uncertain
22 Hypoplastic left heart syndrome	1–2%		–/+	Severe dyspnoea; heart failure without corresponding cyanosis	Systolic-diastolic murmur as in PDA. Single P_2	Usually atypical RVH	Only in infancy Normal to slightly enlarged heart size. Pulmonary vascularity normal or increased; pulmonary oedema	Heart failure; arterial hypotension	Not operable, although certain palliative operations proposed	Not operated: almost 100% in neonatal period, occasionally survival for a few months

Congenital Heart Disease: Summary of differential diagnosis and other features of the more common forms For abbreviations see Contents, p. xiv

	Diagnosis	Percentage incidence (among all cases of CHD)	Schematic diagrams	Cyanosis	Clinical features	Sounds and murmurs	Electrocardiogram	Chest X-Ray	Complications	Operability	Prognosis
1	Persistent ductus arteriosus (PDA)	10–15%		Only in late stage (after puberty), if pulmonary artery pressure high	Infants: anorexia, poor weight gain, recurrent bronchitis or pneumonia. Possibly heart failure (tachycardia, hepatomegaly). later: upper respiratory infections. But often asympyomatic	Continuous systolic-diastolic (diastolic component often absent in early infancy) P_2 ++ in 2 ICS, radiating to left shoulder and back Maximal in 2–3 ICS, with wide radiation, also into neck	Mild LVH (In infants often BVH)	Cardiac silhouette normal- or, especially in infants, enlarged. Prominent left pulmonary segment. Increased pulmonary vascularity	Endocarditis; heart failure	Ligation (before school age; sometimes already in infancy)	Unoperated: complications in adulthood (in 70–80% of cases after 30 years of age) Operated: normal
2	Ventricular septal defect (VSD)	10–20%		Only in late stage (after puberty), if high RV pressure (Einsenmenger syndrome)	As in 1	P_2 ++. If large VSD, protodiastolic flow-murmur	In infancy BVH; later LVH	As in 1. Pulmonary segment, prominent bilaterally. Increased pulmonary vascularity	Endocarditis; bronchitis; pnumonia; heart failure	Closure: age of operation according to haemodynamics, since spontaneous closure frequent, PA banding only exceptionally (e.g. multiple defects)	Not operated: shortened life expectancy (average age 35 years); significant mortality even in infancy. Operated: normal
3	Atrial septal defect (secundum type) (ASD)	5–15%		Only in late stage (after puberty), if increased RA pressure due to secondary pulmonary hypertension	As in 1; often asymptomatic	No thrill; soft systolic murmur in 2–3 ICS; P_2 +, with fixed splitting	Incomplete RBBB	RA may be enlarged; otherwise as in 2	As in 2	Closure preferably before school age	Not operated: shortened life expectancy (50% die before aged 40 years) Operated: normal
4	Atrial septal defect (primum type)	1–3%		As in 3	As in 1; often severe and early symptoms	As in 3, often combined with loud systolic murmur of mitral regurgitation	Incomplete RBBB and LAD	As in 3, but LA may be enlarged (lateral view)	As in 2	As in 3 but timing of operation dependent on mitral valve involvement	Not operated: markedly shortened life expectancy. Operated: normal or depending on degree of postoperative mitral valve function
5	Atrioventricular canal (complete)			None or mild	As in 1; but onset in early infancy, often with mild cyanosis	Signs as in large VSD, but diastolic component more marked	As in 4, but often also RVH	As in 2, but more marked	As in 2	Total correction, but if possible after infancy (because of associated often severe valvar anomalies)	Not operated: 50% die in infancy; 10% survive to 30 years. Operated: high operative mortality, but late results satisfactory, depending on degree of A-V valve regurgitation
6	Total anomalous pulmonary venous drainage	1–2%		Mild	Often non-characteristic: mild dyspnoea; respiratory infections; mild heart failure. May be practically asymptomatic for weeks/months after birth, depending on type	Soft murmur in 2 ICS; increased, sometimes split, P_2	P-pulmonale; RVH	Cardiomegaly; increased pulmonary vascularity. Broad mediastinum after first few months, if to SVC ('showman')	Heart failure. Frequent pulmonary infections	Operation: anastomosis of pulmonary venous trunk to LA, as soon as serious symptoms appear. Otherwise, soon after diagnosis made	Operated: practically normal life expectancy, if lungs undamaged
7	Pulmonary stenosis (valvar)	5–10%		– or + later	Often asymptomatic. If severe, marked dyspnoea without cyanosis. Late-onset cyanosis possible. Short cyanotic episodes possible in infancy	Rough and loud systolic murmur in 2 ICS, with diminished P_2	RVH: severity correlates well with RV pressure	Normal or small heart. Prominent pulmonary segment, but vascularity normal or diminished	Endocarditis; cerebral thrombosis or abscess (paradoxical embolism); right-heart failure (late)	Valvotomy: time of operation dependent on severity	Not operated: depends on severity, but almost normal if mild stenosis; markedly shortened life expectancy if severe (average survival 20 years). Operated: probably normal, if early operation
8	Coarctation of the aorta, preductal	2–5%		–	In early infancy: often heart failure, sometimes with cough (pulmonary oedema); may be asymptomatic Variable femoral arterial pulse	Systolic murmur, maximal, in the back	In infants, normal or RVH; later, normal or mild LVH	Cardiomegaly. Pulmonary oedema. Rarely seen after infancy	As in 2	Resection usually very early	Not operated: several months, rarely a few years. Operated: normal
9	Coarctation of the aorta, juxta or postductal or isolated			–	Femoral pulse week or impalpable	As in 6, but may also have diastolic murmur	As in 6	Normal or cardiomegaly; or signs of left ventricular enlargement. Double aortic indentation. After infancy rib notching possible	As in 2. Cerebral haemorrhage; aortic ruptures (late). Arteriosclerotic changes	Resection before school age	Not operated: many patients die before 40 years of age. Operated: normal but often persisting arterial hypertension
10	Aortic arch anomaly	Less than 1%		–	High-pitched cry; stridor, later dysphagia	–	Normal	Normal, except on barium swallow	Tracheomalacia; aspiration	As early as possible if severe symptoms	Not operated: high mortality (already in infancy), depending on type of anomaly Tracheomalacia: aspiration. Operated normal
11	Truncus arteriosus	1–2%		+/++	In early infancy, mild cyanosis and dyspnoea, gradually increasing. Clinical signs as in VSD or PDA, but early onset	Often as in VSD, with loud but single second sound. Systolic thrill. Diastolic component not uncommon	P-pulmonale; BVH	Cardiomegaly increased pulmonary vascularity, in type 1 left pulmonary artery high	Heart failure; frequent pulmonary infections	Early operation to prevent pulmonary hypertension: primary total correction or PA banding followed by total correction soon after	Not operated: very poor Early development of pulmonary hypertension. Operated: high operative mortality in infancy (to avoid pulmonary hypertension), after infancy survival chances significantly improved (long term results still uncertain)

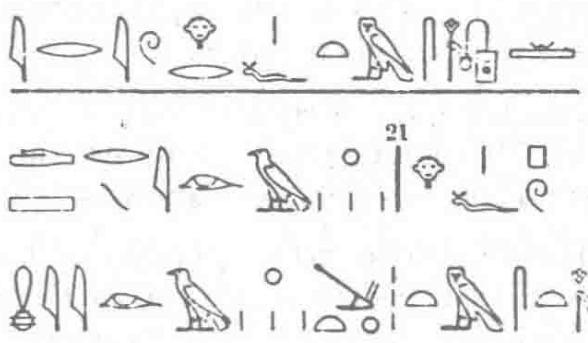
Part 1 General aspects

1

A backward glance

William J. Rashkind

Of the various manifestations of congenital heart disease, cyanosis is a common, and often striking, finding. The Dutch artist, Dirk Ket, left several self-portraits which clearly show his cyanosis and clubbing. He died at the age of 38 in AD 1940, and was proved to have tetralogy of Fallot. *Circa* 2940 BC the document known as the Smith papyrus was written, and contains this hieroglyph:



Breasted translated the above hieroglyphic phrase, 'his lips are ruddy'. Luckhardt, a collaborator of Breasted, added: 'I am inclined to the view that the colour meant is the one medical men have in mind when they say the person is cyanotic. It is a mixture of a red and a blue.' Human figures with blue coloured skin are portrayed in many ancient Egyptian frescoes. Heer Ket, and other twentieth-century long-lived cyanotic victims of congenital heart disease,* had no better specific treatment available to them than did their possible cosufferers five millennia earlier.

The first surgical attempts at relief of cyanosis due to congenital heart disease occurred three years after Ket's death, and have been used on a wide scale only in the latter half of the twentieth century. Between the earliest recording of cyanosis and the modern era, congenital heart disease was either ignored, or the subject of limited curiosity. In 1913, in his monumental tome *The Principles and Practice of Medicine*, Sir William Osler[60] adequately summarized the state of the art at that time regarding the treatment of children with congenital heart disease. His entire section on the subject reads:

> The child should be warmly clad and guarded from all circumstances liable to cause bronchitis. In the attacks of urgent dyspnoea with lividity blood should be let. Saline cathartics are also useful. Digitalis must be used with care; it is sometimes beneficial in the later stages. When the compensation fails, the indications for treatment are those of valvular disease in adults.

His total entry on congenital heart disease was a scant four and a half pages.

Within 25 years, Robert Gross[34] was to trigger a veritable explosion of interest in the subject. On August 26, 1938, he successfully ligated a persistently patent ductus arteriosus and propelled an entire new field into orbit. An analysis of the historical background of that event will be considered under the following divisions: (1) the fetal circulation, (2) anatomopathological descriptions leading to clinical recognition of specific lesions, (3) cardiac catheterization, and (4) cardiovascular surgery. Of course, such fields as embryology, bacteriology, haematology, radiology, electrophysiology, etc. played major roles in the process, but fall outside the compass of this chapter.

The fetal circulation

The earliest observations on the fetal circulation are generally attributed to Aristotle. William Harvey,[38] in his *Exercitationes*, quotes Aristotle:

> The pulsation is evident from the very outset in a developing heart, as can be noticed in the dissection of living animals and in the growth of the chick from the egg.

Ogle[59] thought Aristotle had described the ductus arteriosus, but Platt[62] has offered a serious challenge to this idea. He eschewed a knowledge of modern anatomy, but brought to the problem a profound

* White and Sprague[78] described a 60-year-old, and Marquis a 64-year-old patient with tetralogy of Fallot.

understanding of the ancient Greek language and of the mind and method of Aristotle. He pointed out that the phrase which misled Ogle had been mistranslated for centuries because of the substitution of *aortus* for *arterias* (aorta for trachea), so, rather than describing the pulmonary artery going to the bifurcation of the aorta, what was really described was the superior vena cava ascending towards the bifurcation of the trachea. Since Aristotle studied only adult animals, he could never have seen a ductus, although Platt admits, indeed offers evidence to suggest, that he probably saw the ligamentum arteriosum.

Galen[30] clearly understood the ductus and the foramen ovale. In his superb translation (into Latin, 1555) Sylvius[42] quotes Galen:

> 'Nature is neither lazy nor devoid of foresight. Having given the matter thought, she knew in advance that the lung of the fetus, a lung still contained in the uterus and in the process of formation and spared continual motion, does not require the same arrangements of a perfected lung endowed with motion. She has, therefore, anastomosed the pulmonary artery with the aorta, and the left and right atria. . . . There is a certain membrane in the right atrium connecting, in the fetus, the right atrium with the left atrium, whose appearance is rather like that of a little lid. It is easily deflected toward the pulmonary artery, . . . and thereby the blood of the right atrium is prevented from flowing into the lungs. This membranous protrusion is thickened and grows together, sometimes on the first day after birth, sometimes after several days, when at length its whole body hangs down in such a way into the cavity of the vessel that it completely occludes it and it cannot be split asunder. There is also a similar projection of membrane at the mouth of the azygous vein and often at those of several other large vessels such as the jugulars, brachials and crural veins and the trunk of the vena cava as it leaves the liver. The uses of these are the same as that of the membranes closing the mouths of the vessels of the heart.'

In addition to the ductus and the foramen ovale, Galen observed the valve of the inferior vena cava now named after Eustacchio. Eustacchio[22] had been credited by Haller[35] with having pictured the ductus venosus as well, but Franklin* has examined the illustrations quoted by Haller, and does not think that they support Haller's contention. Aranzi's name[1] has been attached to the ductus venosus, although Vesalius[75] clearly described it three years earlier. Although Aranzi's discovery was undoubtedly without foreknowledge of Vesalius' discovery, such are the perversities of eponymity. Even Fallopius,[23] who was usually credited with describing the ductus arteriosus first, merely added to Galen that it was of large calibre. The term duct of Botallo persists to this day. Is Botallo[8] to be blamed that, in investigating the fetal route from the right to the left side of the heart in calves, he used the term 'ductus' to describe the channel connecting the two atria formed by the valve of the foramen ovale? Botallo innocently scattered a seed in 1564; it was watered by Folius[26] who reprinted Botallo's short note; and in 1660 it reappeared, thoroughly fertilized, in van Horn's *Observatio anatomica. III.*[74] Van Horn annotated Botallo's text, and inserted a plate which pictured the foramen ovale as described by Botallo, but also added a drawing of his own of the ductus arteriosus. Final fruition was at the hands of the Anatomical Nomenclature Commission at Basle which harvested all under the term ductus arteriosus Botalli. Sylvius describes Galen's concern with nomenclature:

> 'How Galen had often wished it were possible to teach a thing without the use of names, for the names themselves are but the shadow of reality.'

William Harvey added little to Galen, although he did write about the fetal circulation in *De generatione*,[38] a late-in-life writing which has been said to be aptly titled, reflecting the last infirmity of a noble mind. The main criticism of the section on the fetal circulation is that the observations were entirely anatomical rather than physiological. This same criticism can be levelled at almost all subsequent writers until the modern era of physiological investigation was started in the twentieth century. A striking exception was the work of the remarkable Oxford group who, only 40 years after Harvey, in the single decade between 1660 and 1670, defined the contribution of the lung to gas exchange, and the function of the placenta as a 'uterine lung'. In 1660 Robert Boyle[9] showed that part of the air is essential to life, Hooke (1668)[39] postulated that blood changes from dark to red on passing through the lungs because of its mixture with air, and Lower (1669)[51] verified Hooke's hypothesis experimentally.

For two and a half centuries understanding of the fetal circulation was mixed in protracted arguments regarding the distribution of inferior vena cava and superior vena cava flow across the tricuspid valve or the foramen ovale, the contribution of the valve flap in the right atrium to this flow, and

* *Ductus venosus* (*Arantii*) *and ductus arteriosus* (*Botalli*) *Bulletin of the History of Medicine* **9**, 580–584, 1941.

whether or not there was significant pulmonary blood flow. Pohlman[63] initiated the experimental approach to the fetal circulation. He injected starch granules into veins at various sites, determined the differential distribution of the granules, and measured the pressure in both ventricles directly. Similar studies were performed by other investigators, but the methods remained crude until twentieth-century technology led to comprehensive studies by several teams; including Barclay *et al.*[4] in England; Lind and Wegelius[50] in Sweden, Rudolph[70] in the United States, and others.

Anatomopathological descriptions

In the library at Windsor Castle, the entire folio of Leonardo da Vinci's *Quadernia de Anatomia* (1513)[47] is stored. A brief sketch and description of an atrial septal defect by this incomparable Renaissance genius is the first description that I could find of a congenital cardiac defect in the human. Although many other earlier and contemporary writers described the foramen ovale in animals (see section on fetal circulation) da Vinci was the first to describe it in the human.

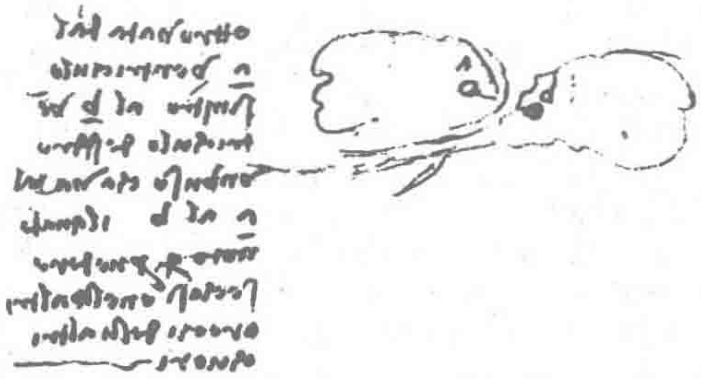


Figure 1.2 The inscription (since da Vinci was a mirror writer, it reads right to left) states: 'I have found from a, left auricle, to b, right auricle, a perforating channel from a to b, which I note here to see whether this occurs in other auricles of other hearts.'

I have been able to find six papers describing a variety of congenital heart defects which were published in the seventeenth century. They included simple septal defects, single ventricle, tetralogy of Fallot, and a remarkable report by Chemineau[14] in 1699. He reported a single ventricle with diminutive outflow chamber, a clear description of what is now commonly called 'corrected transposition'. Stensen* clearly described the anatomical features of tetralogy of Fallot in 1671. Of the 24 eighteenth-century papers on congenital heart disease that could be found, several deserve emphasis. LeCat's[46] presentation of 1747 is notable for the scholarly study of atrial septal defects in humans. Morgagni[55] described four patients with different congenital cardiac lesions, and, as he did for so many diseases, provided clear, clinical–pathological correlation. One of them had pulmonary stenosis with atrial septal defect, and he attributed the cyanosis to obstruction. William Hunter[40] described three patients with congenital heart disease: one had the features of tetralogy of Fallot; another had pulmonary atresia with intact ventricular septum. He believed that cyanosis was due to admixture of blood in the heart. Each of these two points of view, obstruction versus admixture, acquired devoted and renowned supporters and a 100 years' war was waged in the literature. The supporters of the obstruction theory, including Thomas Peacock, repeatedly cited the occurrence of septal defects without clinical cyanosis. On the other hand, the supporters of the admixture theory, including E. Gintrac, quoted cases of obstruction without cyanosis. The resolution of this argument had to wait for reliable measurement of intracardiac pressures.

In the first half of the nineteenth century, several remarkable compendia of congenital cardiac defects appeared. Prominent among them are: (1) *Pathological Researches. Essay I. on Malformations of the Human Heart* by J. R. Farre, London 1814; (2) *Observations and Researches on Cyanosis or Blue Disease* by E. Gintrac, Paris 1824; (3) J. F. Meckel's 'On Malformation of the Heart' (*Virchow's Archives of Physiology*, pp. 594–610, 1805 and pp. 221–284, 1815); and (4) Paget's series of articles in the *Edinburgh Medical and Surgical Journal* 1831. Subsequent works in the latter half of the nineteenth century which added immeasurably to our knowledge of congenital heart disease include Peacock's *Malformation of the Human Heart*, London 1858, Carl Rokitansky's *Defects of the Cardiac Septa*, Vienna 1875, and Arthur Keith's Hunterian Lectures Malformation of the Heart (*Lancet* 1909). One might well add Fallot's 'Contribution à en'anatomie pathologique de la maladie bleu (cyanose cardiaque) (*Marseille-Médicale* 1888), since it runs over 100 pages. The eponymity afforded to Fallot, and several of his late nineteenth-century contemporaries, may or may not be justified. Certainly Fallot,[24] Roger,[68] Eisenmenger,[21] etc. were not the first to describe the conditions that carry their names. In fact, I have been able to uncover nearly 200 reports of what Fallot called tetralogy which appeared prior to his 1888 publication. But Fallot was the first to emphasize adequately the clinical aspects of the lesion, and did make an accurate pre-mortem diagnosis in one of his patients. Finally, one must include the works by the two *grandes dames* of the twentieth cen-

* Stensen, N. in E. Warburg: *Nordisk Medicin* **16** : 3550–3551, 1942.

tury, Maude Abbott's *Atlas of Congenital Cardiac Disease*, and Helen Taussig's two-volume *Congenital Malformations of the Heart*.

Cardiac catheterization

Cardiac catheterization must have been an idea whose time had come. In a bare 50-year period covering the latter quarter of the nineteenth century and the first quarter of the twentieth century, both animal and human cardiac catheterizations were performed. Because of the inaccessibility of the journal, and the outmoded concepts in treatment used by him J. F. Dieffenbach's early studies (1832)[19] on both animals and humans have been overlooked. He states that experiments on animals taught him that the introduction of foreign bodies into the large vessels and the heart 'was tolerated in a wonderful way'. He added that it was known that the external surface of the heart possessed a certain degree of insensibility to mechanical stimuli 'but that this was also the case to a certain extent with its interior walls'. He should certainly receive credit both for his early animal studies in which he showed how well the introduction of foreign bodies into the heart could be tolerated, and for the following description of a human catheterization:

> 'In an almost dying patient (cholera) suffering from great anxiety and breathlessness I opened, with the agreement of Herr Medical Counsellor Casper, the brachial artery in its upper third. As not a drop of blood flowed, I introduced, as I had planned, an elastic catheter into the vessel approximately as far as the heart. Nevertheless no blood appeared through the catheter. The heartbeat became clearer and more rapid, and I now withdrew the catheter. . . . It is greatly to be regretted that this operation of interest for all physiology was performed on a man who was so near to death and who shortly afterwards was seized by convulsions and rendered his soul.'

At that time cholera was considered to be a disease in which there was centripetal movement of the blood towards the heart emptying the periphery and overloading the heart. Since the periphery was empty Dieffenbach was attempting to reach the heart to remove the 'extra blood' that was there. His pioneering in human cardiac catheterization should not be downgraded because his purposes were misguided.

Twelve years later the illustrious Claude Bernard,[5] while working as an assistant to Magendie, catheterized both ventricles of a horse with thermometers. These and subsequent studies measuring the differential temperatures of the two ventricles via catheter thermometers were not published until 1846. At that time he also published results of his studies commencing in 1847, on the transjugular measurement of right ventricular pressure with glass catheters, proving it to be significantly lower than the aortic pressure simultaneously measured. Although the manometry was crude, this was the first direct approximation of intracardiac pressure in the closed chest animal. An English contemporary of Bernard's, Frederick Pavy,[61] obtained blood from the right ventricle in the closed-chest animal by what he called 'cardiac catheterism', also by inserting a transjugular catheter into the right ventricle. These studies were reported in his Lettsomian lectures published in the 1857–60 *Proceedings of the Royal Society of Biology*. The definitive animal studies on cardiac catheterization had to wait for improved manometric techniques. There had been, until the work of Chauveau and Marey,[12, 13] little improvement on the brilliant, but cumbersome experiments of Steven Hales in 1727.* Chauveau had been working on cardiac movements, heart sounds, and cardiac physiological events. Marey had devised a sphygmograph for recording pressures in flowing blood, had measured arterial pulse transmission, and had explained the dicrotic notch seen in peripheral arterial pulse waves. His *Medical Physiology of the Blood Circulation* was published in Paris in 1859. The collaboration between these two outstanding scientists led to the development of the first reasonably reliable catheter manometric recording system. Although Adolph Fick[25] was critical of Chauveau and Marey, his own published pressure curves left a great deal to be desired, and his criticism was largely unjustifiable. However, he deserves credit for one of the most exquisite contributions to biological science. His concept of a method of measuring cardiac output is both brilliant and ingenious, and is founded on the tripod of simplicity, utility, and accuracy. To this was added the delightful adjunct of brevity. The concept was presented in its entirety on one page.

The subject of human cardiac catheterization is clouded with debate about priority. The quotation above of Dieffenbach, although indicating the first attempt, leaves in question the matter of whether the heart was actually reached. The same criticism applies to the studies of Bleichroeder, Unger, and Loeb, who published (*Klinische Wochenschrift* **49**, 1503, 1912) descriptions of experiments done seven years

* A facsimile reproduction of the remarkable studies of Hales has been published in New York by the Hafner Publishing Company 1964 entitled 'Experiment Three in Statical Essays: containing haemastaticks'.