

Heart Disease in Infants and Children

Edited by Gerald Graham

and Ettore Rossi

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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 com-

prehensive 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.

Contents

Part 1 General aspects	1	Placental transfusion	48
1 A backward glance		Electrocardiogram of the full-term infant	52
<i>William J. Rashkind</i>	3	The phonocardiogram of the newborn infant	52
The fetal circulation	3	Fetal and postnatal circulatory adjustment	
Anatomopathological descriptions	5	in congenital heart disease	54
Cardiac catheterization	6	General references	55
Cardiovascular surgery	7	Special references	55
Summary	9		
References	9	5. Haemodynamics: perinatal circulatory changes in various congenital cardiac anomalies	
2 Development of the human heart		<i>Gerald Graham</i>	59
<i>Georg Töndury</i>	13	Atrial septal defect (ASD)	59
First phase of cardiac development	13	Ventricular septal defect (VSD)	60
Second phase of the development of the heart: formation of the definitive cardiac form and septation	19	Persistent ductus arteriosus (PDA)	61
The significance of blood flow in the shaping and septation of the heart	23	Truncus arteriosus	61
Development of the heart valves	24	Total anomalous pulmonary venous drainage (TAPVD)	61
References	25	Pulmonary stenosis (PS)	61
3 Aetiology, incidence and genetics of congenital heart disease		Pulmonary atresia	61
<i>Wedikund Lenz</i>	27	Fallot's tetralogy (FT)	62
Genetic causes	29	Transposition of the great arteries (TGA)	62
Chromosomal aberrations	31	Tricuspid atresia (TA)	63
Incidence	33	Aortic stenosis (AS)	63
References	34	Coarctation of the aorta (CAo)	63
4 Fetal and perinatal circulation		Hypoplastic left heart syndrome (HLH)	64
<i>John Lind</i>	37	Further reading	64
Introduction	37	6 The lung in congenital heart disease	65
Special features of the fetal circulation	37	Respiratory problems in congenital heart disease	
Course of the fetal circulation	39	<i>Hans Peter Gurtner and Franco P. Stocker</i>	65
Autonomic nervous control of the circulation	40	Introduction	65
The fetal heart rate, cardiac output and blood pressure	40	References	67
Adaptation to low arterial oxygen tension <i>in utero</i> and immediately after birth	40	Mechanical changes in the lungs in congenital heart disease	
Changes in the circulation at birth	41	<i>David J. Hatch</i>	67
Heart size and cardiac output	48	Lung function studies in the pathophysiology of CHD	67
		Lung function studies in clinical management	68
		Methods of measurement	69
		References	72

The problem of pulmonary hypertension in congenital heart disease	Eric D. Silove	73	Cardiac arrhythmias in infants and children: a clinical approach	Kim M. Fox	127
Physiological considerations		73	Introduction		127
Neonatal pulmonary circulation		74	Tachyarrhythmias		127
Left-to-right shunts		74	Bradyarrhythmias		131
Pulmonary vasomotor mechanisms		75	Treatment		135
Evaluation of elevated pulmonary vascular resistance		76	References		135
References		76	Angiocardiography: investigative techniques and normal radiological anatomy	Walter A. Fuchs and Heinz Tschäppeler	136
Pulmonary hypertension: the relation between structure and function	Sheila G. Haworth	77	Investigative technique		136
Obliterative pulmonary vascular disease		77	Special considerations		137
Relation between structure and function in the immature lung with pulmonary hypertension		78	Normal radiological anatomy		138
Causes of a raised pulmonary vascular resistance		80	References and bibliography		142
The development of pulmonary vascular change in different types of congenital heart disease		82	Echocardiography	Bertrand G. Wells	143
Effect of high altitude in promoting pulmonary hypertension		84	The heart valves		144
Reversibility of pulmonary vascular disease		84	The ventricular cavities		144
References		84	The heart walls and septa		144
7 General diagnosis	Franco P. Stocker	87	Other heart conditions		145
Introduction		87	Contrast echocardiography		147
History and general examination		87	Practical value of M-mode scan		147
Specific cardiological examinations		88	References		149
References		104	9 The management of heart failure in paediatric practice	James F. N. Taylor	151
8 Special methods		105	General considerations		151
Cardiac catheterization	Gerald Graham	105	General management		151
Indications		105	Long-term management		158
Contraindications		105	Additional problems in management		158
Approach to cardiac catheterization: site and technique		105	Special problems of management		159
Risks		106	References		165
Management of the patient during cardiac catheterization/angiography		107	10 Surgical treatment of congenital heart disease: general aspects	Marc de Leval and Gerald Graham	167
Measurements in cardiac catheterization		107	Further reading		168
Calculation of flows and shunts		110	11 Growth in children with congenital heart disease	Leslie Shelton	171
Calculation of resistance		116	Aetiology of congenital heart disease as related to growth retardation		171
Electrocardiography	Gerald Graham	118	Possible factors relating to severity of growth retardation		172
Introduction		118	Growth in various lesions		175
Genesis of the electrocardiogram		118	Treatment		175
Why the e.c.g. changes after birth		119	References		176
Normal standards		122	12 Psychological and social aspects of cardiac disease in children	Arnon Bentovim	179
How to record the e.c.g. in children		122	Introduction		179
How to interpret the e.c.g.		123			
Diagnostic criteria		123			
Further reading		127			












The birth of a child with congenital heart disease	179	Management	227
Later development	180	Pregnancy and the contraceptive pill	229
The child of school age	181	Summary of indications for VSD closure	229
Hospitalization and its impact on child and family	182	Traumatic ventricular septal defect	229
Results of operation	183	References	230
Conclusions	184		
References	184		
Part 2 Congenital heart disease	187		
13 Nomenclature and classification of congenital heart disease		16 Atrial septal defects Kim M. Fox	233
Robert H. Anderson	189	Introduction	233
Plan of sequential chamber localization	189	Aetiology	233
Connections and relations of the chambers	190	Embryology	233
Connection of atria to ventricles	191	Fetal and postnatal circulation	234
Relationships between the ventricular chambers	193	Secundum atrial septal defect	234
Ventricular morphology	193	Ostium primum defect	238
The musculature of the outflow tracts	195	Common atrioventricular canal	240
Description of abnormalities	196	Single atrium	242
References	197	Treatment of atrial septal defects	243
		References	244
14 Persistent ductus arteriosus		Cor triatriatum Kim M. Fox	245
Franz J. P. Real	199	References	247
Anatomy	199		
Incidence	199	17 A glance forward: closure of cardiac defect without surgery	
Haemodynamics	199	William J. Rashkind	249
References	206	Closure of atrial septal defects	249
		Closure of persistent ductus arteriosus	250
15 Ventricular septal defect		References	250
Celia Oakley	209		
Incidence	209	18 Total anomalous pulmonary venous drainage Eric D. Silove	251
Anatomy (types of VSD)	209	Anatomical definition and embryology	251
Haemodynamics	210	Incidence and natural history	251
Clinical picture	211	Clinical features	251
Diagnosis of the large ventricular septal defect in infancy	214	Diagnosis	251
Investigation of ventricular septal defect	216	Differential diagnosis	255
Differential diagnosis of ventricular septal defect in infancy	218	Management	256
Differential diagnosis of small ventricular septal defect in older children	220	References	256
Large ventricular septal defect with left-to-right shunt	222		
Ventricular septal defect with severe pulmonary vascular obstruction and cyanosis (Eisenmenger complex)	222	19 Congenital aortic stenosis	
Complicated ventricular septal defect	222	Jann W. Weber	259
Complications of VSD	225	Anatomy	259
Natural history	226	Pathophysiology	260
		Natural course	260
		Clinical diagnosis	261
		Differential diagnosis	266
		Treatment	267
		References	267
		20 Coarctation of the aorta	
		Jann W. Weber	269
		Anatomy	269
		Natural history	270
		Clinical diagnosis	270
		Coarctation of the aorta with symptoms (infants)	270

Coarctation of the aorta in asymptomatic patients	272	Pulmonary atresia with ventricular septal defect	318
Echocardiography	274	References	323
Special forms of coarctation of the aorta	276		
References	276		
21 Anomalies of the aortic arch		25 Tricuspid atresia	
<i>Jann W. Weber</i>	277	<i>James F. N. Taylor</i>	325
Embryology	277	Anatomical definition, classification and physiology	325
Classification of the anomalies	279	Incidence	327
Double aortic arch (type A1)	279	Natural history	327
Aberrant right subclavian artery	281	Clinical features	327
Right aortic arch (types III A1 and III B1)	282	Special tests	328
References	282	Management	332
		References	333
22 Pulmonary stenosis	283	26 Transposition of the great arteries	
<i>Jann W. Weber</i>	283	<i>Michael Tynan</i>	335
Anatomy	283	Introduction	335
Additional anomalies	283	Definition and classification	335
Haemodynamics	284	Morphogenesis	336
Natural history	284	Natural history	337
Clinical diagnosis	284	Clinical features	338
Clinical findings in subvalvar and supra-valvar pulmonary stenosis	289	Haemodynamics	338
Differential diagnosis	289	Diagnosis	342
Treatment	290	Treatment	344
References	291	Specific treatment	344
		References	348
23 Tetralogy of Fallot	293	27 'Corrected' transposition of the great arteries	
<i>Celia Oakley</i>	293	<i>Hans Peter Gurtner</i>	351
Definition	293	Definition	351
Incidence	293	Anatomy	351
Anatomy	293	Embryology	351
Variants of the tetralogy of Fallot	294	Morbid anatomy	352
Haemodynamics	295	Incidence	352
The blood	296	Natural history	352
Clinical picture	297	Clinical diagnosis	352
Associated abnormalities	298	Special investigations	352
Electrocardiogram	299	Differential diagnosis	353
Radiology	300	Treatment	353
Cardiac catheterization and angiography	301	References	354
Differential diagnosis	302		
Natural history and prognosis	304	28 Ebstein's anomaly	357
Complications	305	<i>Jann W. Weber</i>	357
Treatment	306	Anatomy	357
Treatment of associated anomalies	308	Haemodynamics	357
Preparation of the patient and the parents for surgical treatment	309	Incidence	358
References	311	Natural history	358
		Clinical course	358
24 Truncus and 'pseudotruncus'		Radiology	358
<i>Fergus Macartney</i>	313	Electrocardiogram	358
Definitions	313	Catheterization	358
Persistent truncus arteriosus	314	Angiocardiography	359
		Intracardiac electrogram	359
		Differential diagnosis	359












Treatment	359	The Taussig-Bing malformation	383
References	361	References	384
29 Single ventricle: univentricular heart		32 Positional anomalies of the heart	
<i>Felix Wyler</i>	363	<i>Ralph Kuenzler</i>	387
Definition	363	Dextrocardia and laevocardia	387
Anatomy	363	Ectopia and diverticulum of the heart	391
Incidence	363	References	392
Embryology	363	33 Rare anomalies <i>Jann W. Weber</i>	395
Haemodynamics	363	Mitral stenosis	395
Clinical features	365	Mitral insufficiency	397
Radiography	365	The 'click' syndrome	399
Electrocardiography	366	Hypoplasia or aplasia of the pulmonary	
The phonocardiogram	366	valve	401
Cardiac catheterization	366	References	403
Angiocardiography	366		
Total surgical correction	366		
References	367	Part 3 Acquired heart disease	405
30 The hypoplastic left heart (HLH) syndrome <i>Ursula Sauer</i>	369	34 Rheumatic fever and rheumatic heart disease <i>Colin H. M. Walker</i>	407
Definition	369	Introduction	407
Genetics	369	Aetiology	407
Embryology	369	Clinical features of acute rheumatic	
Incidence	370	fever	411
Haemodynamics	370	Chronic rheumatic heart disease	420
Pulmonary circulation	371	Treatment	422
Sex ratio and age at death	371	Prognosis	425
Anatomical findings	371	Prevention of rheumatic fever	426
Clinical features	372	References	430
Diagnosis	373	35 Hypertension in children	
Differential diagnosis	373	<i>Rudolf König</i>	433
Angiocardiography	373	Introduction	433
Cardiac catheterization	374	Definition	433
Echocardiography	374	Possible pathophysiological mechanisms	434
Management	375	Aetiology	434
References	375	Cause	435
31 Origin of both great arteries from the right ventricle, including the Taussig-Bing malformation <i>Arthur Hollman</i>	379	Clinical signs	435
Introduction	379	Diagnostic investigations	435
Pathology	379	Treatment	435
Haemodynamics	380	Prevention	435
Clinical features	380	References	436
Electrocardiography	380	36 Tumours of the heart in childhood	
Radiology	381	<i>Michael Tynan</i>	437
Angiocardiography	381	Classification	437
Differential diagnosis	382	Benign tumours	437
Treatment	383	Secondary tumours	439
Origin of both great arteries from the 'left' ventricle	383	Clinical features and diagnosis	439
		Treatment	439
		References	440

37 Cardiomyopathies	Ettore Rossi	441	Congenital Heart Disease:	
Definition		441	Summary of differential diagnosis and other	
Differential diagnosis		441	features of the more common forms	1-11 Front
Classification		441	end papers, 12-22	Back end papers
Congestive cardiomyopathies		441	Abbreviations for end papers	
Hypertrophic cardiomyopathies		463	ASD = atrial septal defect	
Cardiomyopathies in other diseases		464	BVH = biventricular hypertrophy	
Endocardial fibroelastosis		467	ICS = intercostal space	
References and bibliography		474	LA = left atrium	
Index		485	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 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 asymptomatic	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 (Eisenmenger 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; pneumonia; 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 weak 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)

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) As in 9
13 Aortic stenosis, subvalvar			-	As in 9	As in 9, but normal A ₂	As in 9	As in 9, without aortic dilatation	As in 9	As in 9	
14 Aortic stenosis, supralvalvar			-	Sometimes characteristic facies. Possibly hypercalcaemia	As in 9, but much accentuated in A ₂	As in 9	Normal or high aortic dilatation	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 acyrotic)	Usually moderate cyanosis. Hypercyanotic spells, squatting; clubbed fingers and toes	Systolic murmur in 3-4 ICS; diminished P ₂ . Soft, short systolic 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 rhythm. 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

Part 1

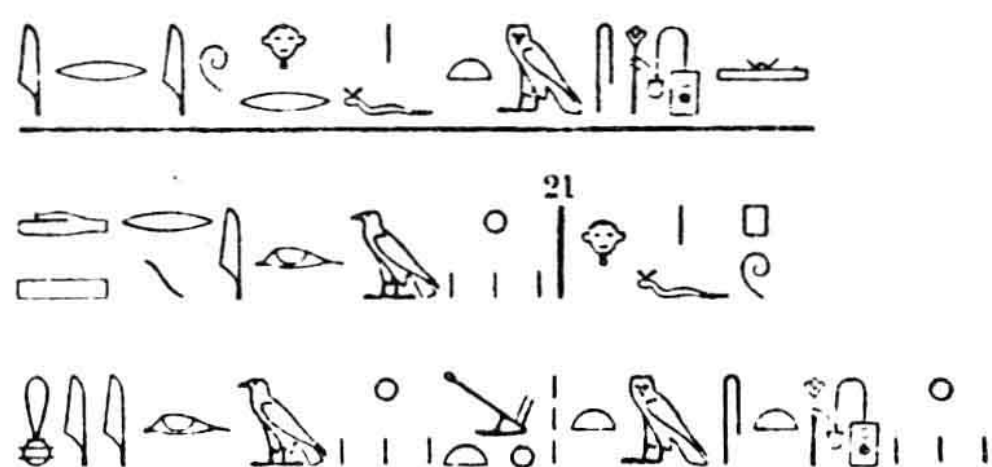
General aspects

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 Osler⁶⁰ adequately summarized the state of the art at that time regarding the

* White and Sprague⁷⁸ described a 60-year-old, and Marquis a 64-year-old patient with tetralogy of Fallot.

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 Gross³⁴ 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.

Ogle⁵⁹ thought Aristotle had described the ductus arteriosus, but Platt⁶² has offered a serious challenge to this idea. He eschewed a knowledge of modern anatomy, but brought to the problem a profound

4 A backward glance

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*.

Galen³⁰ clearly understood the ductus and the foramen ovale. In his superb translation (into Latin, 1555) Sylvius⁴² 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. Eustacchio²² had been credited by Haller³⁵ 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 name¹ has been attached to the ductus

venosus, although Vesalius⁷⁵ 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 Botallo⁸ 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 Folius²⁶ 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 Boyle⁹ 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. Pohlman⁶³ 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 Wegelius⁵⁰ in Sweden, Rudolph⁷⁰ 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.

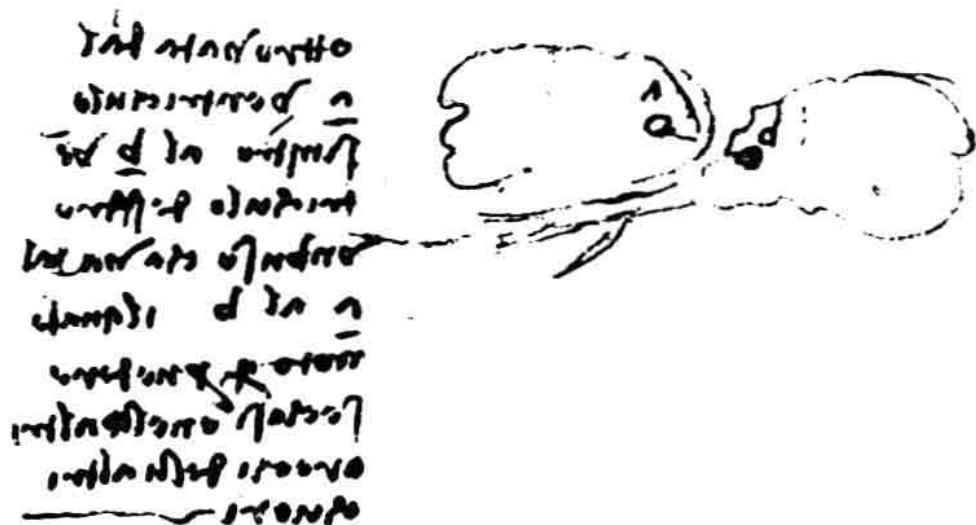


Figure 1.2 The inscription (since da Vinci was a mirror writer, it reads right to left) states: 'I have found from a, left auricle, to b, right auricle, a perforating channel from a to b, which I note here to see whether this occurs in other auricles of other hearts.'

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 Chemineau¹⁴ 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's⁴⁶ presentation of 1747 is notable for the scholarly

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

study of atrial septal defects in humans. Morgagni⁵⁵ 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 Hunter⁴⁰ 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 l'anatomie pathologique de la maladie bleue (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-

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 Fick²⁵ 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 haemastatics'.