3rd Edition

ANESTHESIA FOR CONGENITAL HEART DISEASE

Editor-in-Chief
Dean B Andropoulos

Editors
Stephen Stayer
Emad B Mossad
Wanda C Miller-Hance

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Anesthesia for Congenital Heart Disease

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EDITOR IN CHIEF

Dean B. Andropoulos MD, MHCM
Anesthesiologist-in-Chief Texas Children's Hospital;
Professor, Anesthesiology and Pediatrics;
Vice Chair, Department of Anesthesiology;
Baylor College of Medicine
Houston, TX, USA

EDITORS

Stephen Stayer MD
Associate Chief of Anesthesiology and Medical Director of Perioperative Services Texas Children's Hospital;
Professor, Anesthesiology and Pediatrics;
Baylor College of Medicine
Houston, TX, USA

Emad B. Mossad MD
Director, Arthur S. Keats Division of Pediatric Cardiovascular Anesthesiology
Texas Children's Hospital;
Professor, Anesthesiology and Pediatrics
Baylor College of Medicine
Houston, TX, USA

Wanda C. Miller-Hance MD, FACC, FAAP, FASE
Associate Director, Arthur S. Keats Division of Pediatric Cardiovascular Anesthesiology
Director of Intraoperative Echocardiography, Texas Children's Hospital
Professor, Anesthesiology (Pediatric Anesthesiology) and Pediatrics (Cardiology)
Baylor College of Medicine
Houston, TX, USA

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Cover design: From left to right: 1. (Left) Echocardiogram during fetal intervention for restrictive atrial septum in a fetus with hypoplastic left heart syndrome. Catheter with balloon can be visualized crossing atrial septum. Image courtesy of Shaine Morriss, M.D., Texas Children's Hospital. 2. (Top Center) Neonate with dextro transposition of the great arteries, after induction of anesthesia and placement of monitors and invasive catheters. Photo courtesy of Phillip Steffek, Texas Children's Hospital. 3. (Bottom Center) Surgical field during regional cerebral perfusion for aortic arch reconstruction for hypoplastic left heart syndrome. Aortic cannula is inserted into the distal end of a 3.5 mm polytetrafluoroethylene shunt anastomosed to the right innominate artery to provide cerebral blood flow. A bloodless surgical field is established by snaring brachiocephalic vessels and descending aorta. Photo courtesy Charles D. Fraser, MD, Texas Children's Hospital 4. (Right) Three-dimensional reconstruction of a computed tomographic angiogram of a 12 year old with untreated coarctation of the aorta. Severe coarctation of the aortic isthmus, presumably at the site of ductal insertion, located 2.1-cm distal to the takeoff of the left subclavian artery, with minimum caliber of 5.6 × 5.1 mm. Bilobed ductal aneurysm protruding ventrally at the site of the coarctation. Associated hypoplasia, tortuosity, and mild kinking of the distal transverse arch. Mild stenosis of the origin of the left subclavian artery with poststenotic dilation. Significant dilation of the mammary and intercostal arteries, which provide collateral blood flow to the body

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Contents

List of Contributors

Dean B. Andropoulos MD, MHCM

Anesthesiologist-in-Chief
Texas Children's Hospital
Professor, Anesthesiology and Pediatrics
Vice Chair, Department of Anesthesiology
Baylor College of Medicine
Houston, TX, USA

Philip Arnold BM, FRCA

Consultant Cardiac Anaesthetist
Alder Hey Hospital
Royal Liverpool Children's NHS Trust
Liverpool, United Kingdom

Catherine Ashes MBBS, FANZCA

Anaesthetist
Brian Dwyer Department of Anaesthetics
St Vincent's Hospital
Darlinghurst
New South Wales, Australia

Rahul Baijal MD

Staff Pediatric Anesthesiologist, Texas Children's Hospital; and Assistant Professor, Anesthesiology and Pediatrics, Baylor College of Medicine, Houston, TX, USA

Mirela Bojan MD, PhD

Consultant Pediatric Anesthesiologist, Department of Anesthesiology and Critical Care, Necker-Enfants Malades University Hospital, Paris, France

Ken Brady MD

Associate Professor of Pediatrics, Anesthesia, and Critical Care, Texas Children's Hospital, Baylor College of Medicine, Houston, TX, USA

Lisa Caplan MD

Staff Pediatric Cardiovascular Anesthesiologist, Texas Children's Hospital; and Assistant Professor, Departments of Anesthesiology and Pediatrics, Baylor College of Medicine, Houston, TX, USA

Rahul Dasgupta MD

Assistant Professor of Anesthesiology
Arkansas Children's Hospital/University of Arkansas for Medical Sciences
Little Rock, AR, USA

Suanne Daves MD

Associate Professor, Anesthesiology and Pediatrics, Vanderbilt University School of Medicine; Anesthesiologist in Chief, Monroe Carell Jr. Children's Hospital; and Medical Director, Perioperative Services, Pediatric Heart Institute, Nashville, TN, USA

Laura K. Diaz MD

The Children's Hospital of Philadelphia
Department of Anesthesiology and Critical Care Medicine
Assistant Professor of Clinical Anesthesiology and Critical Care
Perelman School of Medicine at the University of Pennsylvania
Philadelphia PA, USA

James A. DiNardo MD, FAAP

Chief, Division of Cardiac Anesthesia
Senior Associate in Cardiac Anesthesia
Boston Children's Hospital
Professor of Anaesthesia Harvard Medical School
Boston, MA, USA

Brian Donahue MD, PhD

Associate Professor of Anesthesiology, Division of Pediatric Cardiac Anesthesiology, Vanderbilt University School of Medicine, Nashville, TN, USA

R. Blaine Easley MD

Associate Professor, Anesthesiology and Pediatrics, Baylor College of Medicine; Fellowship Director, Pediatric Anesthesiology; and Director of Education, Department of Pediatric Anesthesiology, Texas Children's Hospital, Houston, TX, USA

Robert H. Friesen MD

Professor of Anesthesiology,
University of Colorado School of Medicine Vice Chair, Department of Anesthesiology,
Children's Hospital Colorado
Aurora, CO, USA

Ralph Gertler MD

Consultant Anesthesiologist
Institute of Anesthesiology and Intensive Care
German Heart Centre of the State of Bavaria
Technical University Munich
Munich, Germany

Erin A. Gottlieb MD

Staff Cardiovascular Anesthesiologist
Texas Children's Hospital
Associate Professor of Anesthesiology
Baylor College of Medicine
Houston, TX, USA

Nina A. Guzzetta MD

Associate Professor, Departments of Anesthesiology and Pediatrics, Emory University School of Medicine, Children's Healthcare of Atlanta, Atlanta, GA, USA

Gregory B. Hammer MD

Professor of Anesthesiology and Pediatrics
Stanford University School of Medicine Attending Pediatric Cardiac Anesthesiologist Associate Director, Pediatric Intensive Care Unit
Lucille Salter Packard Children's Hospital
Palo Alto CA, USA

Dolly D. Hansen MD

Emeritus Associate Professor, Department of Anesthesia, Boston Children's Hospital and Harvard Medical School, Boston, MA, USA

Jane Heggie MD, FRCP

Associate Professor, Department of Anesthesia and Pain Management, University of Toronto and Toronto General Hospital, Toronto, ON, Canada

Paul A. Hickey MD

Anesthesiologist-in-Chief and Professor of Anaesthesia, Boston Children's Hospital and Harvard Medical School, Boston, MA, USA

Stephen B. Horton PhD, CCP(Aus), CCP(USA), FACBS

Associate Professor /Director of Perfusion
Faculty of Medicine, Department of Paediatrics – The University of Melbourne
Honorary Research Fellow, Murdoch Children's Research Institute
Cardiac Surgery Royal Children's Hospital
Melbourne, Australia

Kenji Kayashima MD

Chief, Department of Anesthesiology, Japan Community Health Care Organization, Kyushu Hospital, Kitakyushu, Japan

Jeffrey J. Kim MD

Director, Electrophysiology and Pacing, Texas Children's Hospital; and Associate Professor, Department of Pediatrics, Section of Cardiology, Baylor College of Medicine, Houston, TX, USA

Raj Krishnamurthy MD

Section Chief, Radiology Research and Cardiac Imaging, Texas Children's Hospital; and Associate Professor, Radiology, Baylor College of Medicine, Houston, TX, USA

Barry D. Kussman FFA(SA), FAAP

Associate Professor of Anaesthesia, Harvard Medical School; and Senior Associate in Cardiac Anesthesia, Department of Anesthesiology, Perioperative and Pain Medicine, Boston Children's Hospital, Boston, MA, USA

Peter C. Laussen MBBS, FCIM

Chief, Department of Critical Care Medicine, Hospital for Sick Children; and Professor, Department of Anaesthesia, University of Toronto, Toronto, Canada

Richard J. Levy MD, FAAP

Vice Chair for Pediatric Laboratory Research, Department of Anesthesiology
Division of Pediatric Anesthesia Professor of Anesthesiology
Columbia University Medical Center
New York, NY, USA

Andreas W. Loepke MD, PhD

Staff Anesthesiologist, Division of Cardiac Anesthesia
Cincinnati Children's Hospital Medical Center
Professor of Clinical Anesthesia and Pediatrics
University of Cincinnati College of Medicine
Cincinnati, OH, USA

Mariepi Manolis MA MB BChir (Cantab) FRCA

Clinical Fellow in Anaesthesia, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK

Ian McKenzie MBBS, DipRACOG, FANZCA

Director, Department of Anaesthesia & Pain Management
The Royal Children's Hospital Melbourne
Melbourne, Australia

Angus McEwan FRCA

Consultant Paediatric Anaesthetist, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK

Bruce E. Miller MD

Associate Professor, Departments of Anesthesiology and Pediatrics, Emory University School of Medicine; and Director of Pediatric Cardiac Anesthesiology, Children's Healthcare of Atlanta, Atlanta, GA, USA

Wanda C. Miller-Hance MD, FACC, FASE

Professor of Anesthesiology and Pediatrics, Baylor College of Medicine;
Associate Director Division of Pediatric Cardiovascular, Anesthesiology and Director of Intraoperative, Echocardiography
Texas Children's Hospital
Houston, TX, USA

Alexander Mittnacht MD

Professor of Anesthesiology Icahn School of Medicine at Mount Sinai
Director Pediatric Cardiac Anesthesia
Department of Anesthesiology The Mount Sinai Medical Center
New York, NY, USA

Emad B. Mossad MD

Director, Arthur S. Keats Division of Pediatric Cardiovascular Anesthesiology
Texas Children's Hospital;
Professor, Anesthesiology and Pediatrics
Baylor College of Medicine
Houston, TX, USA

Pablo Motta MD

Staff Cardiovascular Anesthesiologist
Texas Children's Hospital Assistant Professor, Anesthesiology and Pediatrics
Baylor College of Medicine
Houston, TX USA

Viviane G. Nasr MD

Assistant in Anesthesia, Boston Children's Hospital
Department of Anesthesia, Instructor in Anesthesiology, Harvard Medical School
Boston, MA, USA

Lori Newman M.Ed

Principal Associate in Medical Education, Harvard Medical School
Director of the Office for Professional, Development, Center for Education
Co-Director of the Rabkin Fellowship in Medical, Education, and Co-Chair of the Academy of Medical Educators
Beth Israel Deaconess Medical Center
Boston, MA, USA

Susan C. Nicolson MD

Medical Director, Cardiac Center Operations, The Cardiac Center
The Children's Hospital of Philadelphia
Department of Anesthesiology and Critical Care Medicine
Professor of Anesthesia Perelman School of Medicine at the University of Pennsylvania
Philadelphia PA, USA

Kirsten C. Odegard MD

Senior Associate in Anesthesia, Boston Children's Hospital; and Associate Professor in Anaesthesia, Harvard Medical School, Boston, MA, USA

Philippe Pouard MD

Head of Intensive Care, Anaesthesia and Perfusion Unit, Reference Center for Complex Congenital Heart Disease, University Hospital Necker Enfants Malades, René Descartes University, Paris, France

Chandra Ramamoorthy MB BS, FFA (UK)

Professor of Anesthesiology, Stanford University School of Medicine; and Director, Pediatric Cardiac Anesthesia, Lucile Packard Children's Hospital, Stanford, CA, USA

Stephen J. Roth MD, MPH

Professor of Pediatrics (Cardiology) Chief, Division of Pediatric Cardiology
Stanford University School of Medicine
Director, Children's Heart Center
Lucile Packard Children's Hospital Stanford
Palo Alto, CA, USA

V. Ben Sivarajan MD MS FRCPC

Assistant Professor of Critical Care Medicine & Paediatrics
Departments of Critical Care Medicine & Paediatrics
Medical Director, Organ & Tissue Donation
The Hospital for Sick Children, Toronto
Faculty of Medicine, University of Toronto
Toronto, Ontario, Canada

Ehrenfried Schindler MD

Medical Director, German Pediatric Heart Center, Department of Pediatric Anesthesiology, Asklepios Klink Sankt Augustin, Sankt Augustin, Germany

Annette Y. Schure MD, DEAA

Senior Associate in Anesthesia, Boston Children's Hospital and Instructor in Anaesthesia, Harvard Medical School, Boston, MA, USA

Michael L. Schmitz MD

Professor, Departments of Anesthesiology and Pediatrics
Arkansas Children's Hospital
University of Arkansas for Medical Sciences
Little Rock, AR, USA

Aarti Shah MB ChB FCARCSI

Cardiac Anaesthetist
Alder Hey Hospital Royal Liverpool Children's NHS Trust
Liverpool, United Kingdom

Anshuman Sharma MD, MBA

Professor, Department of Anesthesiology
Washington University School of Medicine
St. Louis, MO, USA

Adam Skinner BSC, MBChB, MRCP, FRCA

Consultant Paediatric Anaesthetist
Department of Anaesthesia Royal Children's Hospital
Melbourne, Australia

James P. Spaeth MD

Director of Cardiac Anesthesia
Cincinnati Children's Hospital Medical Center
Associate Professor of Clinical Anesthesia and Pediatrics
University of Cincinnati College of Medicine
Cincinnati, OH, USA

Stephen A. Stayer MD

Professor, Anesthesiology and Pediatrics, Baylor College of Medicine; and Medical Director of Perioperative Services, Texas Children's Hospital, Houston, TX, USA

James M. Steven MD, SM

Chief, Division of Cardiac Anesthesia
The Cardiac Center
The Children's Hospital of Philadelphia
Department of Anesthesiology and Critical Care Medicine
Associate Professor of Anesthesia Perelman School of Medicine at the University of Pennsylvania
Philadelphia PA, USA

Sugantha Sundar MB, BS

Program Director, Adult Cardiothoracic Anesthesia Fellowship Program
Beth Israel Deaconess Medical Center
Assistant Professor of Anaesthesia
Harvard Medical School
Boston, MA, USA

Lorraine L. Thompson MD

Assistant Professor of Anesthesiology
Arkansas Children's Hospital/University of Arkansas for Medical Sciences
Little Rock, AR, USA

Mark D. Twite MB BChir

Associate Professor of Anesthesiology
University of Colorado School of Medicine Director, Cardiac Anesthesiology, Children's Hospital Colorado
Aurora, CO, USA

Shoichi Uezono MD

Professor and Chair, Department of Anesthesiology, Jikei University, Tokyo, Japan

Sana Ullah MB, ChB

Associate Professor of Anesthesiology University of Texas Southwestern Children's Medical Center of Dallas
Dallas, TX, USA

Santiago O. Valdes MD

Attending Physician, Electrophysiology and Pacing, Texas Children's Hospital; and Assistant Professor, Department of Pediatrics, Section of Cardiology, Baylor College of Medicine, Houston, TX, USA

Annette Vegas MD, FRCPC, FASE

Staff Anesthesiologist and Director of Perioperative TEE, Department of Anesthesia and Pain Management, Toronto General Hospital and Associate Professor of Anesthesiology, University of Toronto, Toronto, USA

David F. Vener MD

Staff Pediatric Cardiovascular Anesthesiologist, Texas Children's Hospital; and Associate Professor, Departments of Anesthesiology and Pediatrics, Baylor College of Medicine
Houston, TX, USA

Scott G. Walker MD

Associate Professor of Clinical Anesthesia
Gopal Krishna Scholar in Pediatric Anesthesiology, Indiana University School of Medicine
Director, Division of Pediatric Anesthesiology, Chief of Pediatric Anesthesia
Riley Hospital for Children at IU Health
Indianapolis, IN, USA

Gina Whitney MD

Associate Professor of Anesthesiology and Pediatrics
University of Colorado School of Medicine
Podiatric Cardiovascular Anesthesiologist
Children's Hospital, Colorado
Aurora CO, USA

Glyn D. Williams MBChB, FFA

Professor, Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine and Lucile Packard Children's Hospital, Stanford, CA, USA

Lisa Wise-Faberowski MD

Assistant Professor of Anesthesiology, Perioperative and Pain Medicine, Stanford University Medical Center, Stanford, CA, USA

Justin C. Yeh MD

Clinical Assistant Professor of Pediatrics (Cardiology)
Stanford University School of Medicine
Director, Cardiac ECMO Program
Lucile Packard Children's Hospital Stanford
Palo Alto, CA, USA

Maria Markakis Zestos MD

Chief of Anesthesiology
Children's Hospital of Michigan
Associate Professor Wayne State University
Detroit, MI, USA

Preface

The third edition of *Anesthesia for Congenital Heart Disease* is a major update and expansion of the textbook that reflects the ongoing development of the practice of pediatric and congenital cardiac anesthesia, and the burgeoning knowledge base in this exciting field. All chapters have been thoroughly revised and updated with new sections and numerous recent references. Additional chapters have been included in two important areas of critical knowledge and practice, addressing anesthetic and sedative neurotoxicity in the patient with congenital heart disease (Chapter 9) and anesthesia in the patient with pulmonary hypertension (Chapter 28). Both of these chapters are written by true experts in these fields and are worthy of their own separate treatment. Also, for the first time, this edition of the textbook is in color, and numerous new illustrations and figures have been added to present a vibrant representation of cardiovascular anatomy and surgical approaches that are essential to the knowledge base for the congenital cardiac anesthesiologist. In addition, after each major section in every chapter, key learning points are presented to highlight important concepts and enhance knowledge retention. Each chapter is accompanied by five multiple-choice questions covering the most crucial learning points in each chapter, to optimize the learning experience for readers at all levels of training and clinical experience. These questions can be found in the on-line book supplement at http://www.wiley.com/go/andropoulos/congenitalheart.

We are pleased to welcome our Texas Children's Hospital colleague, Wanda C. Miller-Hance, MD, as Co-Editor of this text. Dr. Miller-Hance is a fully trained pediatric and congenital cardiac anesthesiologist, pediatric cardiologist, and recognized authority in intraoperative echocardiography for congenital heart surgery. Reflecting the international scope of anesthesia for congenital heart disease and the many outstanding practitioners all over the world, a number of new international authors have been added from Germany, the United Kingdom, Australia, France, Japan, and Canada.

Finally, caring for patients with congenital heart disease requires a team of dedicated professionals that include congenital cardiac anesthesiologists, congenital heart surgeons, pediatric and adult congenital cardiologists, cardiac intensivists, cardiac interventionalists and imaging specialists, nurses, perfusionists, respiratory therapists, technicians, child life and social workers, and interpreters, among many others. We greatly appreciate the passion and commitment of the people in these disciplines, without whom we could not do our work. Finally, the patient and family are the focus of the team, and their courage and goodwill in the face of serious and complex illness always amaze and inspire us. It is to our patients and their families that *Anesthesia for Congenital Heart Disease*, third edition, is dedicated, in the hope that the knowledge contained in these pages will contribute to better outcomes for them.

It is the purpose of this, our third edition of *Anesthesia for Congenital Heart Disease*, to contribute to the fund of knowledge in our field and to enhance the care of children with heart disease by individuals from various disciplines worldwide.

Dean B. Andropoulos, MD, MHCM (Editor-in-Chief)
Stephen A. Stayer, MD
Emad B. Mossad, MD
Wanda C. Miller-Hance, MD

List of Abbreviations

α_2M	α_2-macroglobulin
AA	aortic atresia
ABC	Aristotle Basic Complexity
ABO-C	ABO-compatible
ABO-I	ABO-incompatible
ACE	angiotensin-converting enzyme
ACGME	Accreditation Council for Graduate Medical Education
ACHD	adult congenital heart disease
ACT	activated clotting time
ACTH	adrenocorticotropic hormone
AEG	atrial electrogram
AI	aortic insufficiency
AICD	automatic internal cardiac defibrillator
AIDS	acquired immunodeficiency syndrome
AKI	acute kidney injury
Akt	protein kinase B
ALCAPA	anomalous left coronary artery arising from the pulmonary artery
ALI	acute lung injury
ANF	atrial natriuretic factor
ANH	Acute normovolemic hemodilution
APAF-1	apoptotic protease activating factor 1
APERP	accessory pathway effective refractory period
APOE	apolipoprotein E
APRV	airway pressure release ventilation
aPTT	activated partial thromboplastin time
APW	aortopulmonary window
AR	adrenergic receptor
ARCAPA	anomalous right coronary artery from the pulmonary artery
ARDS	acute respiratory distress syndrome
ARF	acute renal failure
ASD	atrial septal defect
ASE	American Society of Echocardiography
ASO	arterial switch operation
AT	atrial tachycardia
ATIII	antithrombin III
ATP	adenosine triphosphate
AUC	area under the curve
AV	atrioventricular
AVC	atrioventricular canal
AVNRT	atrioventricular nodal re-entry tachycardia
AVSD	atrioventricular septal defect
BAV	bicuspid aortic valve
Bax	B-cell lymphoma-2-associated X protein
BCAS	The Boston Circulatory Arrest Study
BCL-2	B-cell lymphoma-2
BCL-xL	B-cell lymphoma-extra large
BCPC	bi-directional cavopulmonary connection
BDNF	Brain-derived neurotrophic factor
BiVAD	biventricular ventricular assist device
BNP	brain natriuretic peptide
BOS	bronchiolitis obliterans syndrome
BPA	branch pulmonary artery
BPD	bronchopulmonary dysplasia
BSA	body surface area
BSID	Bayley Scales of Infant Development
BUN	blood urea nitrogen
C3PO	Congenital Cardiac Catheterization Project on Outcomes
CABG	coronary artery bypass grafting
CALM	congenital atresia of the left main coronary artery
cAMP	cyclic adenosine monophosphate
CAV	coronary artery vasculopathy
CAVC	complete atrioventricular canal
CAVF	coronary arteriovenous fistula
CBF	cerebral blood flow
CBG	corticosteroid-binding globulin
CCA	common carotid artery
CCAN	Congenital Cardiac Anesthesia Network
CCAS	Congenital Cardiac Anesthesia Society
CCB	calcium channel blocker
CCTGA	congenitally corrected transposition of the great arteries
CF	cystic fibrosis
cGMP	cyclic guanosine monophosphate
CHARM	Catheterization for Congenital Heart Disease Adjustment for Risk Method
CHD	congenital heart disease
CHF	congestive heart failure
CICU	cardiac intensive care unit
CIED	cardiovascular implantable electronic device

CIRCI	critical illness-related corticosteroid insufficiency
CL	cardiolipin
CLAD	chronic lung allograft dysfunction
CMR	cardiac magnetic resonance
$CMRO_2$	cerebral metabolic rate for oxygen consumption
CMV	cytomegalovirus
CO	carbon monoxide
CO	cardiac output
CoA	coarctation of the aorta
COP	colloid osmotic pressure
COx	cerebral oximetry index
CPAP	continuous positive airway pressure
CPB	cardiopulmonary bypass
CPVT	catecholaminergic polymorphic ventricular tachycardia
CRBSIs	catheter-related bloodstream infections
CRMDs	cardiac rhythm management devices
CSA	cross-sectional area
CSOR	cerebral–splanchnic oxygen ratio
CT	computed tomography
CUF	conventional ultrafiltration
CVC	central venous catheter
CVVH	continuous veno-venous hemofiltration
CVVH/D	continuous veno-venous hemofiltration and dialysis
dATP	deoxyadenosine triphosphate
DBD	donation after brain death
DCD	donation after cardiac death
DCM	dilated cardiomyopathy
DCRV	double-chambered right ventricle
DHCA	deep hypothermic circulatory arrest
DIC	diffuse intravascular coagulation
DIVA	difficult intravenous access
DLCO	diffusing capacity for carbon monoxide
DLT	double-lumen tube
DNA	deoxyribonucleic acid
DO_2	oxygen delivery
DORV	double outlet right ventricle
D-TGA	dextro-transposition of the great arteries
DVT	deep vein thrombosis
EA	Ebstein's anomaly
EACA	ε-aminocaproic acid
EACTS	European Association for Cardio-Thoracic Surgery
EAT	ectopic atrial tachycardia
EBV	estimated blood volume
ECG	electrocardiogram
ECMO	extracorporeal membrane oxygenation
ECPR	extracorporeal cardiopulmonary resuscitation
ECPR	extracorporeal membrane oxygenation as part of cardiopulmonary resuscitation
EDA	end-diastolic area
EDV	end-diastolic volume
EEG	electroencephalogram
EF	ejection fraction
EFE	endocardial fibroelastosis
EJV	external jugular vein
ELSO	Extracorporeal Life Support Organization
EMA	European Medicines Agency
EMI	electromagnetic interference
EP	electrophysiological
EPDCs	epicardially derived cells
EPO	recombinant human erythropoietin alpha
ERA	endothelin receptor antagonist
ERK	extracellular signal-regulated protein kinase
ESA	end-systolic area
ESV	end-systolic volume
ET-1	endothelin-1
$EtCO_2$	end-tidal CO_2
ETT	endotracheal tube
FAC	fractional area change
FDA	Food and Drug Administration
FEV_1	forced expiratory volume in 1 second
FFP	fresh frozen plasma
FHF	first heart field
FiO_2	fraction of inspired oxygen
FOB	fiberoptic bronchoscope
FRC	functional residual capacity
FTR	failure to resuscitate
FV	femoral vein
FVC	forced vital capacity
FVL	FV Leiden
GABA	γ-aminobutyric acid
GDP	guanosine diphosphate
GFR	glomerular filtration rate
GI	gastrointestinal
GLUTs	glucose transporters
Gp	glycoprotein
GSK-3β	glycogen synthase kinase-3β
GTP	guanosine triphosphate
HAT	heparin-associated thrombocytopenia
HCII	heparin cofactor II
Hct	hematocrit
HEAL	Health Education Assets Library
HFOV	high-frequency oscillatory ventilation
HIT	heparin-induced thrombocytopenia
HIV	human immunodeficiency virus
HLA	human leukocyte antigens
HLHS	hypoplastic left heart syndrome
HPA	hypothalamic–pituitary–adrenal axis
HPAH	heritable pulmonary artery hypertension
HPV	hypoxic pulmonary vasoconstriction
HR	heart rate
HTK	histidine-tryptophan-ketoglutarate
HUS	head ultrasound
IAA	interrupted aortic arch
IABP	intra-arterial blood pressure
IAS	interatrial septum
ICE	Intracardiac echocardiography
ICH	intracranial hemorrhage
ICU	intensive care unit
IE	infective endocarditis

IgG	immunoglobulin G
IJV	internal jugular vein
IM	intramuscular
iNO	inhaled nitric oxide
INR	international normalized ratio
IO	inflow occlusion
IPAH	idiopathic pulmonary artery hypertension
IPCCC	International Pediatric and Congenital Cardiac Code
ISHLT	Scientific Registry of the International Society for Heart and Lung Transplantation
IU	international unit
IV	intravenous
IVC	inferior vena cava
IVH	intraventricular hemorrhage
JCAHO	Joint Commission for the Accreditation of Hospital Organizations
JET	junctional ectopic tachycardia
KIM-1	kidney injury molecule-1
LA	left atrium
LAA	left aortic arch
LAA	left atrial appendage
LAP	left atrial pressure
LAS	lung allocation score
LBBB	left bundle branch block
LBW	low birth weight
LBWN	low-birth-weight neonate
LCOS	low cardiac output syndrome
LDLLT	living donor lobar lung transplant
LE	lower esophageal
L-FABP	liver fatty acid-binding protein
LiDCO	lithium dilution CO
LMA	laryngeal mask airway
LMWH	low-molecular-weight heparin
LPA	left pulmonary artery
LQTS	long QT syndrome
LSVC	persistent left superior vena cava
L-TGA	levo-transposition of the great arteries
LV	left ventricle, left ventricular
LVEDP	left ventricular end-diastolic pressure
LVEDV	left ventricular end-diastolic volume
LVNC	left ventricular non-compaction
LVOT	left ventricular outflow tract
MAC	minimum alveolar concentration
MAP	mean arterial pressure
MAS	meconium aspiration syndrome
MAT	multifocal atrial tachycardia
mBTS	modified Blalock–Taussig shunt
MCS	mechanical circulatory support
MDI	Mental Development Index
MMF	mycophenolate mofetil
MOD	method of discs
MPA	main pulmonary artery
mPAP	mean pulmonary artery pressure
MPTP	mitochondrial permeability transition pore
MR	mitral regurgitation
MRI	magnetic resonance imaging
MRSA	methicillin-resistant *Staphylococcus aureus*
MSOF	multisystem organ failure
mTOR	mammalian target of rapamycin
MUF	modified ultrafiltration
MV	mechanical ventilation
NAC	N-acetylcysteine
NEC	necrotizing enterocolitis
NGAL	neutrophil gelatinase-associated lipocalin
NICU	neonatal intensive care unit
NIRS	near-infrared spectroscopy
NMDA	*N*-methyl-D-aspartate
NOS	nitric oxide synthase
OB	obliterative bronchitis
OEF	oxygen excess factor
OER	oxygen extraction rate
OHT	orthotopic heart transplantation
OPTN	Organ Procurement and Transplant Network
OR	operating room
$p75^{NTR}$	p75 neurotrophic receptor
PA	pulmonary artery
PA	pulmonary atresia
PA/IVS	pulmonary atresia with intact ventricular septum
PAA	pharyngeal arch arteries
PAC	premature atrial contraction
$PaCO_2$	partial pressure of carbon dioxide in arterial blood
PAD	preoperative autologous donation
PAH	pulmonary artery hypertension
PAH-CHD	pulmonary artery hypertension associated with congenital heart disease
PAI	plasminogen activator inhibitor
PAO_2	alveolar oxygen tension
PaO_2	partial pressure of oxygen in arterial blood
PAPVC	partial anomalous pulmonary venous connection
PAPVD	partial anomalous pulmonary venous drainage
PAPVR	partial anomalous pulmonary venous return
PASP	pulmonary artery systolic pressure
PBF	pulmonary blood flow
PC	protein C
pCAS	pediatric cardiopulmonary assist system
PCC	prothrombin complex concentrate
PCWP	pulmonary capillary wedge pressure
PD	peritoneal dialysis
PDA	patent ductus arteriosus
PDC	peritoneal drainage catheter
PDE	phosphodiesterase
PDE-5	phosphodiesterase-5
PDEIs	phosphodiesterase inhibitors
PEEP	positive end-expiratory pressure
PEO	proepicardial organ
PF4	platelet factor 4
PFO	patent foramen ovale
PG	pressure gradient
PGE_1	prostaglandin E_1

PH	pulmonary hypertension
PHT	pulmonary hypertension
PI	pulmonary insufficiency
PICC	peripherally inserted central catheter
PIP	peak inspiratory measurement
PI-PLC	phosphatidylinositol-specific phospolipase C
PKA	protein kinase A
PKC	protein kinase C
PLC	phospolipase C
PMP	poly-(4-methyl-1-pentene)
POCA	Pediatric Perioperative Cardiac Arrest Registry
PPL	polypropylene
PPS	postpericardiotomy syndrome
PPV	positive pressure ventilation
PRA	panel reactive antibody
pRIFLE	pediatric modification of the RIFLE score
PRISM	Pediatric Risk of Mortality
PS	protein S
PS	pulmonary stenosis
PS/IVS	pulmonary stenosis with intact ventricular septum
PT	prothrombin time
PTLD	post-transplant lymphoproliferative disorder
PTT	partial thromboplastin time
PV	pulmonary valve
PVCs	premature ventricular contractions
PVD	pulmonary vascular disease
PVP	pulmonary valve perforation
PVR	pulmonary vascular resistance
PVRI	pulmonary vascular resistance index
Qp	pulmonary blood flow
Qs	systemic blood flow
RA	right atrium
RAA	right aortic arch
RACHS-1	Risk Adjustment for Congenital Heart Surgery
RAP	right atrial pressure
RBBB	right bundle branch block
RBC	red blood cell
RCP	regional cerebral perfusion
RDS	respiratory distress syndrome
rFVIIa	recombinant activated factor VIIa
RIFLE	risk, injury, failure, loss and end-stage renal disease
RIPC	remote ischemic preconditioning
ROS	reactive oxygen species
RPA	right pulmonary artery
RV	right ventricle, right ventricular
RVDCC	right ventricle-dependent coronary circulation
RVOT	right ventricular outflow tract
RVOTO	right ventricular outflow tract obstruction
RVSP	right ventricular systolic pressure
SAN	sinoatrial node
SaO_2	arterial oxygen saturation
SCA	Society of Cardiovascular Anesthesiologists
SCPA	superior cavopulmonary anastomosis
SCV	subclavian vein
$ScvO_2$	central venous oxygen saturation
SERCA	sarcoplasmic reticulum Ca^{2+}-ATPase
SF	shortening fraction
SGOT	serum glutamic oxaloacetic transaminase
SHF	second heart field
SIRS	systemic inflammatory response syndrome
$SjvO_2$	jugular bulb venous oximetry
SLV	single-lung ventilation
SPA	Society for Pediatric Anesthesia
SpO_2	pulse oximeter saturation
SR	sarcoplasmic reticulum
SSI	surgical site infection
STAT	Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery Congenital Heart Surgery mortality score
STS	Society of Thoracic Surgeons
STS-CHSD	Society of Thoracic Surgeons Congenital Heart Surgery Database
subAS	subvalvular aortic stenosis
SV	stroke volume
SVAS	congenital supravalvular aortic stenosis
SVC	superior vena cava
SvO_2	percentage of oxygen saturation of mixed venous blood
SVR	systemic vascular resistance
SVRI	systemic vascular resistance index
SVT	supraventricular tachycardia
T3	triiodothyronine
T4	thyroxine
TA	tranexamic acid
TA	tricuspid atresia
TAFI	thrombin-activatable fibrinolysis inhibitor
TAPVC	total anomalous pulmonary venous connection
TAPVR	total anomalous pulmonary venous return
TCAD	transplant coronary artery disease
TDI	tissue Doppler imaging
TEE	transesophageal echocardiography
TEG	thromboelastography
TF	tissue factor
TFPI	tissue factor pathway inhibitor
TGA	transposition of the great arteries
TGC	tight glycemic control
TI	tricuspid valve (TV) insufficiency
TLC	total lung capacity
TNF-alpha	tumor necrosis factor-alpha
TOF	tetralogy of Fallot
TOR	target of rapamycin protein
tPA	tissue plasminogen activator
TPTD	transpulmonary thermodilution
TR	tricuspid regurgitation
TRALI	transfusion-related acute lung injury
TTE	transthoracic echocardiography

TV	tricuspid valve
UFH	unfractionated heparin
UNOS	United Network for Organ Sharing
URI	upper respiratory tract infection
V/Q	ventilation/perfusion
VA	ventriculoarterial
VAA	volatile anesthetic agent
VAC	video-assisted cardioscopy
VAD	ventricular assist device
VATS	video-assisted thoracoscopic surgery
VF	ventricular fibrillation
VMI	visual-motor integration
VO_2	oxygen consumption
vPEO	venous proepicardial organ
VSD	ventricular septal defect
VT	ventricular tachycardia
VTI	velocity time integral
vWF	von Willebrand factor
WHO	World Health Organization
WMI	white matter injury
WS	Williams syndrome
WUS	Wake Up Safe Database

About the Companion Website

Anesthesia for Congenital Heart Disease: Companion Website

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MCQ questions to accompany each chapter

Full reference lists

CHAPTER 1

History of Anesthesia for Congenital Heart Disease

Viviane G. Nasr, Paul A. Hickey and Dolly D. Hansen

Department of Anesthesia, Boston Children's Hospital and Harvard Medical School, Boston, MA, USA

Introduction

Over the last 70 years, pediatric cardiac anesthesia has developed as a subspecialty of pediatric anesthesia, or a subspecialty of cardiac anesthesia, depending on one's perspective. It is impossible to describe the evolution of pediatric cardiac anesthesia without constantly referring to developments in the surgical treatment of congenital heart disease (CHD) because of the great interdependency of the two fields. As pediatric anesthesia developed, surgical treatments of children with CHD began to be invented, starting with the simple surgical ligation of a patent ductus arteriosus (PDA), moving on to sophisticated, staged repair of complex intracardiac lesions in low-birth-weight neonates requiring cardiopulmonary bypass (CPB) and circulatory arrest and then on to the most recent complex biventricular repair. Practically every advance in the surgical treatment of CHD had to be accompanied by changes in anesthetic management to overcome the challenges that impeded successful surgical treatment or mitigated morbidity associated with surgical treatment.

This history will mostly be organized around the theme of how anesthesiologists met these new challenges using the anesthetic armamentarium that was available to them at the time. The second theme running through this story is the gradual change of interest and focus from events in the operating room (OR) to perioperative care in its broadest sense, including perioperative morbidity. The last theme is the progressive expansion in the age range of patients routinely presenting for anesthesia and surgery, from the 9-year-old undergoing the first PDA ligation in 1938 [1] to the first fetus to have an intervention for critical aortic stenosis *in utero*, as reported in *The New York Times* in 2002 [2], and, more recently, to the adult with CHD.

This story will be told working through the different time frames – the first years (1938–1954); CPB and early repair (1954–1970); deep hypothermic circulatory arrest (DHCA) and introduction of prostaglandin E_1 (PGE_1) for PDA (1970–1980); hypoplastic left heart syndrome (HLHS) (1980–1990); refinement and improvement in mortality/morbidity (1990–2000); introduction of extracorporeal membrane oxygenation (ECMO) and increased emphasis on interventional cardiology and imaging modalities (2000–2010); expansion to the fetus and adult with CHD (2011); and on to the present time.

The first years: 1938–1954

This period began with the ligation of the PDA and continued with palliative operations. The first successful operation for CHD occurred in August 1938 when Robert E. Gross ligated the PDA of a 9-year-old girl. The operation and the postoperative course were smooth, but because of the interest in the case, the child was kept in the hospital until the 13th day. In the report of the case, Gross mentions

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that the operation was done under cyclopropane anesthesia, and continues: "The chest was closed, the lung being re-expanded with positive pressure anesthesia just prior to placing the last stitch in the intercostal muscles."

A nurse using a "tight-fitting" mask gave the anesthetic. There was no intubation and, of course, no postoperative ventilation. The paper does not mention any particular pulmonary complications, so it cannot have been much different from the ordinary postoperative course of the day [1].

In 1952, Dr. Gross published a review of 525 PDA ligations where many, if not all, of the anesthetics were administered by the same nurse anesthetist, under surgical direction [3]. Here he states: "Formerly we employed cyclopropane anesthesia for these cases, but since about half of the fatalities seemed to have been attributable to cardiac arrest or irregularities under this anesthetic, we have now completely abandoned cyclopropane and employ ether and oxygen as a routine." It is probably correct that cyclopropane under these circumstances with insufficient airway control was more likely to cause cardiac arrhythmias than ether. An intralaryngeal airway was used, which also served "to facilitate suction removal of any secretions from the lower airway" (and, we may add, the stomach). Dr. Gross claims that the use of this airway reduced the incidence of postoperative pulmonary complications. Without having a modern, rigorous review of this series, it is hard to know what particular anesthetic challenges other than these were confronted by the anesthetist, but we may assume that intraoperative desaturation from the collapsed left lung, postoperative pulmonary complications, and occasional major blood loss from an uncontrolled, ruptured ductus arteriosus were high on the list.

The next operation to be introduced was billed as "corrective" for the child with cyanotic CHD and was the systemic to pulmonary artery (PA) shunt. The procedure was proposed by Helen Taussig as an "artificial ductus arteriosus" and was first performed by Albert Blalock at Johns Hopkins Hospital in 1944. In a very detailed paper, Drs. Blalock and Taussig described the first three patients to undergo the Blalock–Taussig shunt operation. Dr. Harmel anesthetized the first and third patients, using ether and oxygen in an open drop method for the first patient and cyclopropane through an endotracheal tube for the third patient. The second patient was given cyclopropane through an endotracheal tube by Dr. Lamont. Whether the first patient was intubated is unclear, but it is noted that in all three cases, positive pressure ventilation was used to reinflate the lung [4]. Interestingly, in this early kinder and gentler time, the surgical and pediatric authors reporting the Blalock–Taussig operation acknowledged by name the pediatricians and house officers who took such good care of the children postoperatively, but still did not acknowledge in their paper the contribution of the anesthesiologists Lamont and Harmel. Although intubation of infants was described by Gillespie as early as 1939, it is difficult to say when precisely intubations became routine [5].

Drs. Harmel and Lamont reported in 1946 on their anesthetic experience of 100 operations for congenital malformations of the heart "in which there is pulmonary artery stenosis or atresia." They reported 10 anesthetic-related deaths in the series, so it is certain that they encountered formidable anesthetic problems in these surgical procedures [6]. This is the first paper we know of published in the field of pediatric cardiac anesthesia.

In 1952, Damman and Muller reported a successful operation in which the main PA was reduced in size and a band was placed around the artery in a 6-month-old infant with a single ventricle (SV). They state that morphine and atropine were given preoperatively, but no further anesthetic agents are mentioned. At that time infants were assumed to be oblivious to pain, so we can only speculate on what was used beyond oxygen and restraint [7].

Over the next 20 years, many palliative operations for CHD were added and a number of papers appeared describing the procedures and the anesthetic management. In 1948 McQuiston described the anesthetic technique used at the Children's Memorial Hospital in Chicago [8]. This is an excellent paper for its time, but a number of the author's conclusions are erroneous, although they were the results of astute clinical observations and the knowledge at the time. The anesthetic technique for shunt operations (mostly Potts' anastomosis) is discussed in some detail, but is mostly of historical interest today. McQuiston explained that he had no experience of anesthetic management used in other centers, such as the pentothal–N_2O–curare used at Minnesota or the ether technique used at the Mayo Clinic. McQuiston used heavy premedication with morphine, pentobarbital and atropine, and/or scopolamine; this is emphasized because it was important "to render the child sleepy and not anxious." The effect of sedation with regard to a decrease in cyanosis (resulting in making the child look pinker) is noted by the authors. They also noted that children with severe pulmonic stenosis or atresia do not decrease their cyanosis "because of very little blood flow," and these children have the highest mortality.

McQuiston pointed out that body temperature control was an important factor in predicting mortality and advocated the use of moderate hypothermia (i.e., "refrigeration" with ice bags), because of a frequently seen syndrome of hyperthermia. McQuiston worked from the assumption that hyperthermia is a disease in itself, but did not explore the idea that the rise in central temperature might be a symptom of low cardiac output with peripheral vasoconstriction. Given what we now know about shunt physiology, it is interesting to speculate that this "disease" was caused by pulmonary hyperperfusion after the opening of what would now be considered as an excessively large shunt, stealing a large portion of systemic blood flow.

In 1950 Harris described the anesthetic technique used at Mount Zion Hospital in San Francisco. He emphasized the use of quite heavy premedication with morphine, atropine, and scopolamine. The "basal anesthetic agent" was Avertin (tribromoethanol). It was given rectally and supplemented with N_2O/O_2 and very low doses of curare.

Intubation was facilitated by cyclopropane. The FiO_2 was changed according to cyanosis; and bucking or attempts at respiration were thought to be due to stimulation of the hilus of the lung. This was treated with "cocainization" of the hilus [9].

In 1952 Dr. Robert M. Smith discussed the circulatory factors involved in the anesthetic management of patients with CHD. He pointed out the necessity of understanding the pathophysiology of the lesion and also "the expected effect of the operation upon this unnatural physiology." That is, he recognized that the operations are not curative. The anesthetic agents recommended were mostly ether following premedication.

While most of these previous papers had been about tetralogy of Fallot (TOF), Dr. Smith also described the anesthetic challenges of surgery for coarctation of the aorta, that was introduced by Dr. Gross in the U.S. and Dr. Craaford in Sweden simultaneously in the year 1945. He emphasized the hypertension following clamping of the aorta and warned against excessive bleeding in children operated on at older ages using ganglionic blocking agents. This bleeding was far beyond what anesthesiologists now see in patients operated on at younger ages, before development of substantial collateral arterial vessels [10].

The heart–lung machine: 1954–1970

From 1954 to 1970 the development of what was then called the "heart–lung machine" opened the heart to surgical repair of complex intracardiac congenital heart defects. At the time, the initial high morbidity of early CPB technology seen in adults was even worse in children, particularly smaller children weighing less than 10 kg. Anesthetic challenges multiplied rapidly in association with CPB, coupled with early attempts at complete intracardiac repair. The lung as well as the heart received a large share of the bypass-related injuries, leading to increased postoperative pulmonary complications. Brain injury began to be seen and was occasionally reported, in conjunction with CPB operations, particularly when extreme levels of hypothermia were used in an attempt to mitigate the morbidity seen in various organ systems after CPB.

In Kirklin's initial groundbreaking report of intracardiac surgery with the aid of a mechanical pump–oxygenator system at the Mayo Clinic, the only reference to anesthetic management was a brief remark that ether and oxygen were given [11]. In Lillehei's description of direct vision intracardiac surgery in humans using a simple, disposable artificial oxygenator, there was no mention of anesthetic management [12]. What strikes a "modern" cardiac anesthesiologist in these two reports is the high mortality: 50% in Kirklin's series and 14% in Lillehei's series. All of these patients were children with CHD ranging in age from 1 month to 11 years. Clearly, such mortality and the associated patient care expense would not be tolerated today.

At that time, pediatric anesthesia was performed with open drop ether administration and later with ether using different non-rebreathing systems. Most anesthetics were given by nurses under the supervision of the surgeon. The first physician anesthetist to be employed by a children's hospital was Robert M. Smith in Boston in 1946.

The anesthetic agent that came into widespread use after ether was cyclopropane; in most of the early textbooks, it was the recommended drug for pediatric anesthesia. Quite apart from being explosive, cyclopropane was difficult to use. It was obvious that CO_2 absorption was necessary with cyclopropane to avoid hypercarbia and acidosis, which might precipitate ventricular arrhythmias. However, administration with a Waters' absorber could be technically difficult, especially as tracheal intubation was considered dangerous to the child's "small, delicate airway."

In all the early reports, it is noted or implied that the patients were awake (more or less) and extubated at the end of the operation. In the description of the postoperative course, respiratory complications were frequent, in the form of either pulmonary respiratory insufficiency or airway obstruction. This latter problem was probably because "the largest tube which would fit through the larynx" was used. Another reason may have been that the red rubber tube was not tissue-tested. The former problem was probably often related to the morbidity of early bypass technology on the lung.

Arthur S. Keats, working at the Texas Heart Institute and Texas Children's Hospital with Denton A. Cooley, had much experience with congenital heart surgery and anesthesia from 1955 to 1960, and provided the most extensive description of the anesthetic techniques used in this era [13,14]. He described anesthesia for congenital heart surgery without bypass in 150 patients, the most common operations being PDA ligation, Potts' operation, atrial septectomy (Blalock–Hanlon operation), and pulmonary valvotomy. Premedication was with oral or rectal pentobarbital, chloral hydrate per rectum, intramuscular meperidine, and intramuscular scopolamine or atropine. Endotracheal intubation was utilized, and ventilation was assisted using an Ayres T-piece, to-and-fro absorption system, or a circle system. Cyclopropane was used for induction, and a venous cutdown provided vascular access. Succinylcholine bolus and infusion were used to maintain muscle relaxation. Light ether anesthesia was used for maintenance until the start of chest closure, and then 50% N_2O was used as needed during chest closure. Of note is the fact that the electrocardiogram (ECG), ear oximeter, and intra-arterial blood pressure (IABP) recordings were used for monitoring during this period, as well as arterial blood gases and measurements of electrolytes and hemoglobin. The following year he published his experiences with 200 patients undergoing surgery for CHD with CPB, almost all of whom were children. Ventricular septal defect (VSD), atrial septal defect (ASD), TOF, and aortic stenosis were the most common indications for surgery. The anesthetic techniques were

the same as described earlier, except that d-tubocurare was given to maintain apnea during the bypass. In 1957, in addition to ECG, IABP, and oximeter, Dr. Digby Leigh noted the importance of capnography in cardiac surgery. He described the effect of pulmonary blood flow on end-tidal CO_2 ($EtCO_2$) and the decrease in $EtCO_2$ after partial clamping of the PA during the Blalock–Taussig shunt procedure. However, it was not until 1995 that Smolinsky et al. reported the importance of $EtCO_2$ during PA banding [15–17].

Perfusion rates of 40–50 mL/kg/min were used in infants and children, and lactic acidemia after bypass (average 4 mmol/L) was described. No anesthetic agent was added during the bypass procedure, and "patients tended to awaken during the period of bypass," but apparently without recall or awareness. Arrhythmias noted ranged from frequent bradycardia with cyclopropane and succinylcholine to junctional or ventricular tachycardia, ventricular fibrillation (VF), heart block, and rapid atrial arrhythmias. Treatments included defibrillation, procainamide, digitalis, phenylephrine, ephedrine, isoproterenol, and atropine. Eleven out of 102 patients with VSD experienced atrioventricular block. Epicardial pacing was attempted in some of these patients but was never successful. Fresh citrated whole blood was used for small children throughout the case, and the transfusion of large amounts of blood was frequently necessary in small infants. The mortality rate was 13% in the first series (36% in the 42 patients less than 1 year old) and 22.5% in the second series (47.5% in the 40 patients less than 1 year old). Causes of death included low cardiac output after ventriculotomy, irreversible VF, coronary air emboli, postoperative atrioventricular block, hemorrhage, pulmonary hypertension, diffuse atelectasis, and aspiration of vomitus. No death was attributed to the anesthetic alone. Reading these reports provides an appreciation of the daunting task of giving anesthesia during these pioneering times.

Tracheostomy after cardiac operations was not unusual and in some centers was done "prophylactically" a week before the scheduled operation. These practices were certainly related to primitive (relative to the present) techniques and equipment used for both endotracheal intubation and CPB. Postoperative ventilatory support did not become routine until later when neonatologists and other intensive care specialists had proved it could be done successfully. Successful management of prolonged respiratory support was first demonstrated in the great poliomyelitis epidemics in Europe and the USA in 1952–1954 [18].

Halothane was introduced in clinical practice in the mid-1950s and it rapidly became the most popular agent in pediatric anesthesia, mostly because of the smooth induction compared with the older agents. Halothane was also widely used for pediatric cardiac anesthesia in spite of its depressive effect on the myocardium and the significant risk of arrhythmias. Halothane is no longer available, and the newer inhalational agents, isoflurane and sevoflurane, are now the mainstays of pediatric cardiac cases in US academic centers.

During this period, adult cardiac anesthesiologists, following the practice reported by Edward Lowenstein in 1970 [19], began to use intravenous anesthesia based on opiates. Initially, morphine in doses up to 1 mg/kg was given with 100% oxygen and this technique became the anesthetic of choice for adult cardiac patients, but vasodilation and hypotension associated with its use slowed the incorporation of this technique into pediatric cardiac anesthesia until the synthetic opiates became available.

Before CPB was developed, or when it still carried high morbidity and mortality, a number of modalities were used to improve the outcome for infants. One was inflow occlusion (IO) and another was the hyperbaric chamber. IO was useful and, if well managed, an elegant technique. The secret was the organization of the efforts of the entire operative team, and the technique required the closest cooperation between surgeons and anesthesiologists. The technique was as follows.

The chest was opened in the midline. After pericardiotomy, a side clamp was placed on the right atrial (RA) free wall and an incision made in the RA, or proximal on the PA, prior to placing the vascular clamps used to occlude caval return. Before application of the clamps, patients were hyperventilated with 100% O_2. During IO, the superior vena cava (SVC) and inferior vena cava (IVC) inflow were occluded, ventilation held, and the RA or PA clamp released; the heart was allowed to empty and the septum primum was excised or the pulmonic valve dilated. After excision of the septum or valvotomy, one caval clamp was released initially to de-air the atrium. The RA side clamp or the PA clamp was then reapplied and the other caval clamp released. The heart was resuscitated with bolus calcium gluconate (range 30–150 mg/kg) and bicarbonate (range 0.3–3 mEq/kg). Occasionally, inotropes were administered, most often dopamine. It was important to titrate the inotropes so as not to aggravate rebound hypertension caused by endogenous catecholamines. The duration of the IO was between 1 and 3 minutes – terrifying minutes for the anesthesiologist, but quickly over.

Another modality used to improve the survival after shunt operations, PA banding, and atrial septectomy was to operate in the hyperbaric chamber, thereby benefiting from the increased amount of physically dissolved oxygen. It was a cumbersome affair operating in crowded and closed quarters. There was room for only two surgeons, two nurses, one anesthesiologist, and one baby, as the number of emergency oxygen units limited access. Retired navy divers ran the chamber and kept track of how many minutes the personnel had been in the hyperbaric chamber in the previous week. Help was not readily available because the chamber was buried in a sub-basement and people had to be sluiced in through a side arm that could be pressurized. The chamber was pressurized to 2–3 atmospheres so it was unpleasantly hot while increasing the O_2 pressure and cold while decreasing the pressure;

people with glasses were at a disadvantage. It did not seem to add to survival and was abandoned around 1974.

Anesthesia was a challenge in the hyperbaric chamber. The infants were anesthetized with ketamine and nitrous oxide. As the pressure in the chamber increased, the concentrations of N_2O had to be decreased to avoid the hypotension and bradycardia that occurred rapidly.

Also in this era, the first infant cardiac transplant was performed by Kantrowitz in 1967 [20]. The recipient was an 18-day-old, 2.6 kg patient with severe Ebstein's anomaly, who had undergone a Potts' shunt on day 3 of life. The donor was an anencephalic newborn. The anesthetic technique is not described, and the infant died of pulmonary dysfunction 7 hours postoperatively.

The era of deep hypothermic circulatory arrest and the introduction of PGE_1: 1970–1980

Sometime around 1970 physiological repair of CHD, or "correction," had begun to come of age. In the adult world, coronary bypass operations and valve replacement spurred interest in cardiac anesthesia, which centered increasingly on use of high-dose narcotics and other pharmacological interventions. As synthetic opiates with fewer hypotensive side-effects became available, their use spread into pediatric cardiac anesthesia in the late 1970s and 1980s.

Children were still treated as "small adults" because major physiological differences were not yet well appreciated, particularly as they related to CPB morbidity. CPB was rarely employed during surgery on children weighing less than 9 kg because of the very high mortality and morbidity that had been experienced in the early years. The notion of repairing complex CHD in infancy was getting attention but was hindered by technical limitations of surgical techniques, CPB techniques, and anesthetic challenges in infants. Theoretically, physiological repair early in life provides a more normal development of the cardiovascular and pulmonary systems and might avoid palliation altogether. The advantage of this was that the sequelae after palliation, for instance distorted pulmonary arteries after shunts and PA banding, might be avoided. Pulmonary artery hypertension following Waterston and Potts' shunts occurred as a result of increased pulmonary blood flow and resulted in pulmonary vascular obstructive disease. This would not develop if the defect were physiologically repaired at an early age. Furthermore, parents could be spared the anxiety of repeated operations and the difficulties of trying to raise a child with a heart that continued to be impaired.

The perceived need for early repair, together with the high mortality of bypass procedures, in infants and small children led to the introduction of DHCA. It was first practiced in Kyoto, Japan, but spread rapidly to Russia, the west coast of the US at Seattle, Washington, and from there to Midwestern and other US pediatric centers. One example of the difficulties this presented to anesthesiologists was the introduction of DHCA in practice at Boston Children's Hospital. The newly appointed chief of cardiovascular surgery at the Boston Children's Hospital was Aldo R. Castaneda, MD, PhD, one of the first supporters of early total correction of CHD, who quickly embraced DHCA as a tool to accomplish his goals for repair in infants. In 1972, he immediately introduced DHCA into practice at Boston Children's Hospital and the rather shocked anesthesia department had to devise an anesthetic technique to meet this challenge, aided only by a couple of surgical papers in Japanese that Dr. Castaneda kindly supplied. Of course, these papers made little reference to anesthesia.

The first description of the techniques of DHCA from Japan in the English literature was by Horiuchi in 1963 [21]. This involved a simple technique with surface cooling and rewarming during resuscitation, using ether as the anesthetic agent, without intubation. In 1972 Mori et al. reported details of a technique for cardiac surgery in neonates and infants using deep hypothermia, again in a surgical publication [22]. Their anesthetic technique was halothane/N_2O combined with muscle relaxant; CO_2 was added to the anesthetic gas during cooling and rewarming (pH-stat) to improve brain blood flow. The infants were surface-cooled with ice bags and rewarmed on CPB.

Surprisingly, given the enormity of the physiological disturbances and challenges presented by DHCA, very few articles describing an anesthetic technique for DHCA were published, perhaps because DHCA and early correction were not widely accepted. A paper from Toronto described an anesthetic regime with atropine premedication occasionally combined with morphine [23]. Halothane and 50% N_2O were used, combined with d-tubocurare or pancuronium. CO_2 was added to "improve tissue oxygenation by maintaining peripheral and cerebral perfusion." The infants were cooled with surface cooling (plastic bags with melting ice) and rewarmed on CPB. It was noted that six of the 25 infants had VF when cooled to below 30 °C.

Given the lack of any scientific data or studies to guide anesthetic management of such cases, a very simple technique with ketamine–O_2–N_2O and curare supplemented by small amounts of morphine (0.1–0.3 mg/kg) was used at Boston Children's Hospital. This was the way in which infants were anesthetized for palliative cardiac surgical procedures in the hyperbaric chamber at Boston Children's Hospital. The infants were surface-cooled in a bathtub filled with ice water to a core temperature of approximately 30 °C. The bathtub consisted of a green plastic bucket (for dishwashing) bought at a Sears-Roebuck surplus store, keeping things as simple as possible (Figure 1.1). This method was used in hundreds of infants over the next couple of years and only one infant developed VF in the ice water bathtub. This was an infant with TOF who suffered a coronary air embolus either from a peripheral IV or during an attempted placement of a central venous line. In retrospect, it is amazing that so few

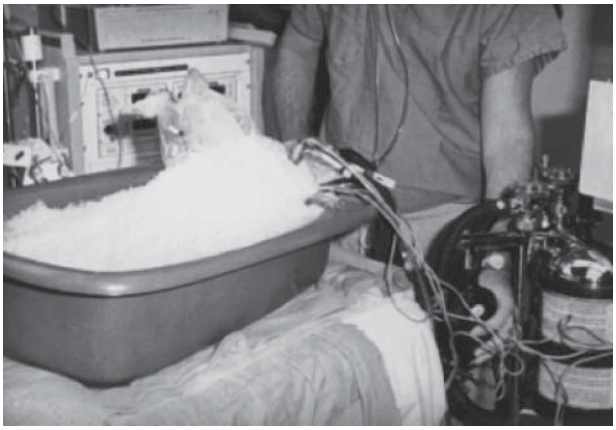

Figure 1.1 Infant submerged in ice water.

papers were published about the anesthetic management of this procedure, which was rapidly seen to be life-saving. The material that was published about these techniques was restricted to surgical journals and did not describe or make any attempt to study the anesthetic techniques used for DHCA. The published surgical articles were largely unknown to cardiac and pediatric anesthesiologists.

It was during this decade that the "team concept" developed, with cardiologists, cardiac surgeons, and anesthesiologists working together in the OR and the intensive care unit (ICU) in the larger centers. These teams were facilitated by the anesthesiologists' "invasion" of weekly cardiology–cardiac surgeons' conferences where the scheduled operations for the week were discussed. Dr. Castaneda, chief surgeon at Boston's Children's Hospital, was a leader in the creation of the cardiac team concept for pediatric cardiac surgery.

During the first year of using DHCA in Boston, it was noticed that a number of the infants had "funny, jerky" movements of the face and tongue. A few also had transient seizures during the postoperative period, but as they had normal electroencephalograms (EEGs) at 1-year follow-up, it was felt that significant cerebral complications were not a problem. In view of the knowledge developed subsequently, these clues to neurological damage occurring during and after pediatric cardiac surgery involving DHCA were overlooked. In hindsight, it is perhaps more accurate to say these clues were ignored, and as a result a great opportunity to study this problem was delayed for almost two decades. The issue of neurological damage with DHCA was raised repeatedly by surgeons such as John Kirklin, but was not really studied until the group at Boston Children's Hospital led by Jane Newburger and Richard Jonas systematically followed a cohort of infants who had the arterial switch operation in the late 1980s using DHCA techniques [24]. In the late 1980s and early 1990s, Greeley and co-workers at Duke performed a series of human studies delineating the neurophysiological response to deep hypothermia and circulatory arrest [25]. These studies provided the crucial data in patients from which strategies for cooling and rewarming, length of safe DHCA, blood gas management, and perfusion were devised to maximize cerebral protection.

Those ongoing studies were followed by a number of other studies comparing DHCA with hypothermic low-flow perfusion, with different hematocrit in the perfusate and with different pH strategies during hypothermic CPB, pH-stat versus alpha-stat.

During those years, the ketamine-morphine anesthetic technique had been supplanted by fentanyl-based high-dose narcotic techniques. For the neurological outcome studies, the anesthetic technique was very tightly controlled, using fentanyl doses of 25 μg/kg at induction, incision, onset of bypass and on rewarming, in addition to pancuronium. From the beginning of this period, surgical results as measured by mortality alone were excellent, with steady increases in raw survival statistics. Because anesthetic techniques were evolving over this period of time, it was difficult to definitely ascribe any outcome differences to different anesthetic agents. A 1984 study of 500 consecutive cases of cardiac surgery in infants and children looked at anesthetic mortality and morbidity. Both were very low – so low in fact that they were probably not universally believed [26].

As the new synthetic opioids such as fentanyl and sufentanil were developed, they replaced morphine to provide more hemodynamic stability in opiate-based anesthetic techniques for cardiac patients. In 1981 Gregory and his associates first described the use of "high-dose" fentanyl 30–50 μg/kg combined with pancuronium in 10 infants undergoing PDA ligation. It is noteworthy that transcutaneous oxygen tension was measured as part of this study. This paper was, in fact, the introduction of high-dose narcotics in pediatric cardiac anesthesia [27]. The technique was a great success; one potential reason for this was demonstrated 10 years later in Anand's paper showing attenuation of stress responses in infants undergoing PDA ligation who were given lesser doses of fentanyl in a randomized, controlled study [28].

During this same period, synthetic opioids were replacing morphine in adult cardiac surgery. This technique slowly and somewhat reluctantly made its way into pediatric anesthesia [29], replacing halothane and morphine, which had previously been the predominant choice of pediatric anesthesiologists dealing with patients with CHD. In the years from 1983 to 1995, a number of papers were published showing the effect of different anesthetic agents on the cardiovascular system in children with CHD. Ketamine, nitrous oxide, fentanyl, and sufentanil were systematically studied. Some misconceptions stemming from studies of adult patients were corrected, such as the notion that N_2O combined with ketamine raises PA pressure and pulmonary vascular resistance (PVR) [30]. On the other hand, the role of increased $PaCO_2$ or lower pH in causing higher PVR was also demonstrated and that subsequently became important in another connection [31]. A number of studies done at this time demonstrated in a controlled fashion the earlier clinical observation (Harmel and McQuiston in the late 1940s) [6,32] that in

cyanotic patients the O_2 saturation would rise during induction of anesthesia, almost irrespective of the agent used [33]. These events only serve to reinforce the value of acute clinical observation and provide an example of how the interpretation of such observations may well change as new knowledge is discovered.

PDA and the introduction of PGE_1

In the mid-1970s, several discoveries were made and introduced into clinical practice that turned out to be of great importance to the pediatric cardiac anesthesiologist and the rest of the cardiac team, the most important being the discovery that PGE_1 infused intravenously prevented the normal ductal closure [34]. These developments revolved around the role of the PDA in the pathophysiology of both cyanotic and acyanotic CHD. The critical role of PDA closing and opening in allowing early neonatal survival of infants with critical CHD began to be appreciated and clinicians sought methods of either keeping the PDA open or closing it, depending on what type of critical CHD the neonate was born with and the role of patency of the ductus arteriosus in the CHD pathophysiology. In some cases, particularly in very small neonates, the importance of closing the PDA was increasingly appreciated and, in other cases, the critical importance of maintaining the patency of a PDA was appreciated.

As the survival of very small premature infants ("preemies") began to improve, mostly because of technical improvements with the use of a warmed isolette and improved mechanical ventilation, it became apparent that in many of these infants the PDA would not undergo the normal closure over time. As the understanding of these infants' physiological problems improved and more infants survived, the role of continued patency of the PDA in neonates needing mechanical ventilation was appreciated. This led to medical therapy directed at promoting ductal closure using aspirin and indomethacin.

When such attempts failed, it was increasingly understood that necrotizing enterocolitis in the preemie was associated with decreased mesenteric blood flow secondary to the "steal" of systemic blood flow into the pulmonary circulation through a PDA. Thus, in cases when the PDA failed to close in premature infants, the need for operative treatment of the PDA in preemies arose as prophylaxis for necrotizing enterocolitis.

Pediatric and cardiac anesthesiologists were now faced with the task of anesthetizing these tiny preemies safely. This involved maintaining body temperature in infants of 1 kg or less with very large surface area/volume ratios. Intraoperative fluid restriction was important and low levels of FiO_2 were used to decrease the risk of retinopathy of prematurity. As the decade progressed, these issues emerged and were addressed. In 1980, Neuman [35] described the anesthetic management of 70 such infants using an O_2/N_2O muscle relaxant anesthesia technique with no mortality. Low FiO_2 was used to reduce the risk of retrolental fibroplasia and precautions were taken to prevent heat loss. In those days before human immunodeficiency virus (HIV) became a wide concern, 40% of the infants received blood transfusion. Interestingly, the question of whether to operate in the neonatal intensive care unit (NICU) or the OR for closure of the PDA in the preemie was debated at that time and remains unsettled today.

The PDA lesion presents an interesting story. In 1938 it was the first of the CHD lesions to be successfully treated surgically [1]. In the mid-1970s it was closed with medical therapy, first with aspirin and later with indomethacin. It was the first CHD lesion to be treated in the catheterization laboratory using different umbrella devices or coils [36]. Presently, if surgical closure is necessary, it is often done using a minimally invasive, thoracoscopic video-assisted technique [37]. Thoracoscopy has the benefit of using four tiny incisions to insert the instruments, avoiding an open thoracotomy and limiting dissection and trauma to the left lung. At the same time, this latest development of surgical technique required the anesthesiologist once again to change the anesthetic approach to these patients. Unlike adult anesthesiologists, who can use double-lumen endotracheal tubes for thoracoscopic procedures, pediatric anesthesiologists caring for 1–3 kg infants undergoing PDA ligation do not have the luxury of managing the left lung [37]. Another problem posed by thoracoscopic PDA ligation in the infant is the emerging need for neurophysiological monitoring of the recurrent laryngeal nerve's innervation of the muscles of the larynx to avoid injury, a known complication of PDA surgery [38]. The last issue is tailoring the anesthetic so that the children are awake at the end of the operation, extubated, and spend an hour or so in the post-anesthesia care unit, bypassing the cardiac ICU. In fact, in 2001, a group led by Hammer at Stanford published the first description of true outpatient PDA ligation in two infants aged 17 days and 8 months [39]. These patients were managed with epidural analgesia, extubated in the OR, and discharged home 10 hours postoperatively. This report brings PDA closure full circle from a 13-day hospital stay following an ether mask anesthetic for an open thoracotomy to a day surgery procedure in an infant undergoing an endotracheal anesthetic for a thoracoscopic PDA ligation.

Maintaining patency of the PDA using PGE_1 is probably now of considerably greater importance than its closure both numerically and in terms of being life-sustaining in neonates with critical CHD. The introduction of PGE_1 suddenly improved the survival rate of a large number of neonates, with CHD having ductal-dependent lesions to improve pulmonary blood flow, or to improve systemic blood flow distal to a critical coarctation of the aorta. The introduction of PGE_1 into clinical practice for therapy of neonatal CHD substantially changed the lives of pediatric cardiac surgeons and anesthesiologists, as frequent middle-of-the-night shunt operations with extremely cyanotic infants almost immediately became a thing of the past. These operations were particularly daunting when one realizes that these procedures were most common before the availability of pulse oximetry; the only warning

signs of impending cardiovascular collapse were the very dark color of the blood and preterminal bradycardia. To get an arterial blood gas with a PaO_2 in the low teens was not uncommon and PaO_2 measurements in single digits in arterial blood samples from live neonates during such surgical procedures were recorded. Even more dramatic was the disappearance of the child with critical post-ductal coarctation. These infants were extremely acidotic, with a pH of 7.0 or less at the start of the procedure (if it was possible to obtain an arterial puncture); they looked mottled and almost dead below the nipples. With the advent of PGE_1 therapy, they were resuscitated medically in the ICU and could be operated on the following day in substantially better condition than was previously the case.

But the introduction of PGE_1 had an effect that was not clearly foreseen except possibly by some astute cardiologists. Survival of a number of these neonates presented pediatric cardiologists and cardiac surgeons (and then anesthesiologists) with rare and severe forms of CHD that had hitherto been considered a "rare" pathological diagnosis. Foremost among these were the infants with HLHS and some forms of interrupted aortic arch. As further experience was gained, it became obvious that these forms of disease were not so rare, but infants who had survived with those forms of CHD were very rare.

The story of HLHS: 1980–1990

As mentioned in the previous section, the introduction of PGE_1 brought major changes to pediatric cardiac anesthesia, solving some problems and at the same time bringing new challenges for the cardiac team. New diagnoses of CHD presented for treatment and were recognized; some had been known previously but had until then presented insurmountable obstacles to any effective therapy.

One of these was HLHS. It had been accurately described in 1958 by Noonan and Nadas but only as a pathological diagnosis [40]. The syndrome is a ductus lesion, with 100% mortality within a few days to weeks when the ductus underwent physiological closure. HLHS was therefore of no practical interest from a therapeutic standpoint until ductal patency could be maintained. When it became possible to keep the ductus arteriosus patent with PGE_1, these neonates rapidly became a problem that could not easily be ignored. In the beginning, most of the infants were misdiagnosed as having sepsis and being in septic shock, and few babies reached the tertiary center without a telltale Band-Aid, indicating a lumbar puncture to rule out sepsis.

But even with the ability to diagnose the defect in a live neonate temporarily kept alive with a PGE_1 infusion, the outlook was not much better. There was no operation devised, and in some centers such neonates were kept viable on a PGE_1 infusion for weeks and even months in the (usually) vain attempt to get them to grow large enough for some surgical procedure to be attempted. In subsequent years, several centers tried different approaches with ingenious conduits, attempting to create an outlet from the right ventricle to the aorta and the systemic circulation.

Those were also the years during which President Ronald Reagan's Baby Doe regulations were in effect. Anyone who thought an infant was being mistreated (i.e., not operated upon) could call a "hotline number" which was posted in all neonatal ICUs to report the physicians' "mistreatment" of the infant. Fortunately, these regulations died a quiet death after a few chaotic years [41].

In the meantime, the search for a palliative operation went on, also spurred by the increasing success of the Fontan operation, which had been introduced in 1970 [42]. This meant that there now was a theoretical endpoint for HLHS as well as for other forms of SV physiology. It was William Norwood at Boston Children's Hospital who was the first person to devise a viable palliation and also to complete the repair with a Fontan operation the following year [43]. The publication of this landmark paper spurred considerable discussion. Many cardiologists and surgeons took the position that this operative procedure represented experimental and unethical surgery and that these infants "were better off dead."

The current approach to these infants varies from multistage physiological repair with palliation followed by Fontan operation. Another alternative is neonatal transplantation as proposed by the group at Loma Linda in California [44]. Some cardiologists are still advocates of conservative "comfort care" for neonates with HLHS. With eventual survival of about 70% being achieved in many centers, these infants can no longer be written off as untreatable. Now the question is more about quality of survival, especially intellectual development. It is also recognized that many have both chromosomal and non-chromosomal anomalies that affect the cerebral and gastrointestinal systems [45].

As was the case from the beginnings of pediatric cardiac surgery, this new patient population presented a management dilemma for the anesthesiologists; they posed a new set of problems that required a solution before acceptable operative results could be achieved. It was obvious that patients with HLHS were hemodynamically unstable before CPB because of the large volume load on the heart coupled with coronary artery supply insufficiency. The coronary arteries in HLHS are supplied from the PDA retrograde through a hypoplastic ascending and transverse aorta that terminates as a single "main" coronary artery. A common event at sternotomy and exposure of the heart was VF secondary to mechanical stimulation. This fibrillation was sometimes intractable, necessitating emergent CPB during internal cardiac massage. This was not an auspicious beginning to a major experimental open heart procedure.

It was during these years that there was a transition from morphine–halothane–N_2O to a high-dose narcotic technique with fentanyl or sufentanil combined with 100%

oxygen. This technique seemed to provide some protection against the sudden VF events compared with historical controls [46]. Despite this modest progress in getting patients successfully onto CPB, it soon became painfully clear that not much progress was made in treating this lesion when trying to wean the patients from bypass. The infants were still unstable coming off bypass and severely hypoxemic, and it took some time before we discovered a way to deal with the problem.

A chance observation led to a solution. Infants who came off bypass with low PaO_2 (around 30 mmHg) after the HLHS repair often did well, while the ones with immediate "excellent gases" ($PaO_2 \geq 40–50$ mmHg) became progressively unstable in the ICU a couple of hours later, developing severe metabolic acidosis and dying during the first 24 hours. This observation, combined with discussions with the cardiologists about PVR and systemic vascular resistance (SVR), led to attempts to influence these resistances to assure adequate systemic flow. In retrospect, infants with low PaO_2 after bypass had smaller aortopulmonary shunts and adequate systemic blood flow, while those with larger shunts and higher initial PaO_2 levels after weaning from bypass tended to "steal" systemic blood flow through the shunt. This would occur in the postoperative period, as the PVR remained elevated as a result of CPB before returning to more normal levels. These observations led to the technique of lowering the FiO_2 (sometimes as low as 0.21) and allowing hypoventilation to increase PVR in patients who had larger shunts placed to supply adequate systemic blood flow as part of what became known as the Norwood operation [46]. A different technique used at other institutions to deal with this problem was to add CO_2 to the anesthetic gas flow, increasing PVR and continuing to use "normal ventilation" in children who had larger shunts placed and excessive pulmonary blood flow [47]. Both techniques represented different approaches to the same problem: finding ways to deal with the need to carefully balance PVR and SVR after bypass in a fragile parallel circulation in the post-bypass period where dynamic changes were taking place in ventricular function.

These observations, and the subsequent modifications in anesthetic and postoperative management, improved the survival for the stage I palliation (Norwood procedure). It should be noted that the pediatric cardiac anesthesiologist was a full, contributing partner in the progressive improvement in outcome of this very complex and challenging lesion. More importantly, the techniques developed and the knowledge gained in this process also simplified the management of other patients with parallel circulation and SV physiology. The obvious example is truncus arteriosus, where the "usual" ST segment depression and frequent VF that occurred intraoperatively can almost always be avoided. Any decrease in PVR during anesthesia in a child with unrepaired truncus arteriosus can lead to pulmonary "steal" of systemic blood flow and decreased diastolic pressure through the common trunk to the aorta and PA, resulting in hypotension and insufficient systemic blood flow expressed initially as coronary insufficiency and ST depression (or elevation).

During the same decade, the surgical treatment of transposition of the great arteries (TGA) underwent several changes. The Mustard operations (as one type of atrial switch procedure) were feared because of the risk of SVC obstruction as a complication of this surgical procedure. At the end of a Mustard procedure, it was not uncommon to see a child with a grotesquely swollen head having to be taken back to the OR for immediate reoperation. Many of those children suffered brain damage, especially when reoperation was delayed. This resulted from low cerebral perfusion pressure during bypass because of venous hypertension in the internal jugular veins and SVC. The extent and prevalence of such damage were never systematically studied. The arterial pressure during bypass and in the immediate post-bypass period in the OR tended to be low and the pressure in the SVC high. An article from Great Ormond Street in London demonstrated arrested hydrocephalus in Mustard patients [48]. The Senning operation (another variant of the atrial switch approach to TGA) was better, but those children could develop pulmonary venous obstruction acutely in the OR, after the procedure or progressively after hospital discharge. When the diagnosis was not promptly made and acted upon, these infants were often quite sick by the time they came to reoperation.

The successful application of the arterial switch procedure described by Jatene then began to revolutionize operations for TGA [49]. It eliminated the risk of obstruction of the pulmonary and systemic venous return seen after the Mustard and Senning procedures. It also diminished the incidence of the subsequent sick sinus syndrome, a complication that might develop in the first 10 years postoperatively as a result of the extensive atrial suture lines and reconstructions required by these "atrial" switch procedures. The introduction of the arterial switch operation again involved anesthesiologists. The initial attempts at arterial switch operations in many institutions resulted in substantial numbers of infants who had severe myocardial ischemia and even frank infarcts. This was due to a variety of problems with the coronary artery transfer and reimplantation into the "switched" aorta that had been moved to the left ventricle outflow tract. Pediatric cardiac anesthesiologists gained extensive experience with intraoperative pressor and inotropic support and nitroglycerine infusions. They were expected by surgeons to provide support to get infants through what later turned out to be iatrogenically caused myocardial ischemia. As surgeons learned to handle coronary artery transfers and reanastomoses well, these problems largely disappeared, along with the need for major pressor and inotropic support and for nitroglycerine infusion inappropriately directed at major mechanical obstructions in the coronary arterial supply. The arterial switch operation has now been refined at most centers to the point where it is largely a "routine" procedure and it presents, for the most part, no unique anesthetic challenges.

It was during the same time period that a randomized strictly controlled study of stress response in infants undergoing cardiac surgery while anesthetized with high-dose sufentanil was performed. It showed that a high-dose narcotic technique would suppress but not abolish stress responses. It also seemed to show a reduction in morbidity and possibly mortality [50]. However, when the study was refined 10 years later using only high-dose narcotic anesthesia in various techniques, no mortality differences were seen between the various high-dose narcotic techniques. It must be pointed out that the patient population was older and the bypass technique had undergone some refinement [51].

Fontan and the catheterization laboratory: 1990–2000

After the anesthetic technique and preoperative management of the stage I palliation for HLHS had been refined and we had been encouraged by the initial successes of stage II, problems arose. The Fontan operation became problematic as it was applied to younger patients with a great variety of SV types of CHD. Many of the patients had seemingly perfect Fontan operations, but in the cardiac ICU they developed low cardiac output and massive pleural and pericardial effusions postoperatively. Many died in the postoperative period despite a variety of different support therapies; their course over the first 24–48 hours was relentlessly downward and could only be reversed by taking them back to the OR, reversing the Fontan operation and reconstructing a systemic to PA shunt. It was hard for the caretakers of these infants to accept such losses of children they had known from birth. They were our little friends and we knew the families too. All kinds of maneuvers were tried to avoid this sequence of events, from early extubation to the use of a G-suit to improve venous return to the heart. In some centers, a large balloon was placed tightly around the child's lower body and intermittently inflated by a Bird respirator asynchronous with ventilation.

After a couple of years, two innovations changed the outlook. Both were linked to the understanding that a major limitation of the Fontan operation was the need for a normal or near normal PVR to allow survival through the postoperative period when CPB had caused, through release of a variety of inflammatory mediators and cytokines, a marked elevation of PVR in the early postoperative period. When this bypass-related increase in PVR was associated with younger age (<2 years old) at the time a Fontan was attempted, the higher baseline PVR of the infant made the bypass-related PVR worse and resulted in inadequate pulmonary blood flow and (single) ventricular filling in the early postoperative period, leading to a cycle of low cardiac output, pulmonary and systemic edema, further increases in PVR, acidosis, and death.

One solution was to interpose a bidirectional (Glenn) cavopulmonary anastomosis (BDG) 6–12 months before completion of the Fontan operation. This procedure, and the related operation known as a "hemi-Fontan," directed only half of the systemic venous return through the lungs at a time when the infant's PVR had not fallen to normal levels and by preserving an alternative pathway for (single) ventricular filling through systemic venous return not routed through the lungs. This enabled the patients to maintain reasonable cardiac output, although they were a bit "blue" during the early postoperative period, when the PVR had been elevated by CPB. However, this made a third operation, the completion of the Fontan, necessary.

The other innovation was the "fenestrated" Fontan where a small fenestration in the atrial baffle allowed systemic venous return to bypass the lungs as a right-to-left shunt, thereby maintaining ventricular filling and systemic cardiac output during the early postoperative period of high PVR. Over time, the fenestration closed as PVR fell and shunting decreased. Alternatively, a device delivered during an interventional cardiac catheterization could close the fenestrations [52].

This whole process of testing the applicability of the Fontan principle and various modifications of the Fontan operation to a wide variety of types of severe cyanotic CHD involved another set of challenges for the pediatric cardiac anesthesiologist and for collaboration between anesthesiology, cardiology, and surgery. The net result of a great deal of work and collaboration among these groups was that the outlook for the HLHS patients, and indeed for all children with SV defects, improved locally and as these improvements spread and were amplified by work done in other centers, the improvement became national and international. In some institutions, the preferred treatment was and is neonatal transplantation. Its limits are the long waiting time for a transplant, the unavoidable mortality during the waiting period and the ongoing morbidity of neonatal heart transplants, a lifetime of immunosuppression therapy, and the accelerated risk of coronary artery disease seen in heart transplants, even in young children.

The collaboration with pediatric cardiologists around postoperative care of HLHS, Fontan patients, and others spread naturally to the cardiac catheterization laboratory. As pediatric cardiologists began to develop interventional procedures, the need for more control and support of vital functions became apparent. Previously, nurses operating under the supervision of the cardiologist performing the catheterizations had sedated the children for the procedures. In many institutions, this involved high volumes of cases sedated by specially trained nurses, while in others with smaller pediatric caseloads the practice of using general anesthesia for children undergoing cardiac catheterizations had been routine.

The interventional cardiologists turned to pediatric cardiac anesthesiologists for help in managing these patients while the cardiologists themselves were dealing with the complex demands of carrying out interventional procedures in infants and children with CHD. As was the case with newly devised pediatric cardiac surgical procedures, the development of interventional procedures

for CHD in the cardiac catheterization laboratory posed a whole new set of problems and challenges for pediatric cardiac anesthesia. Not the least of these was providing anesthesia and vital function support in the dark and difficult environment of the cardiac catheterization laboratory. The introduction of dilation techniques for pulmonary arteries and veins, and mitral and aortic valves, and, most recently, the dilation of fetal atretic aortic valves *in utero* along with device closure of the PDA, ASD, and VSD all placed progressively greater demands on the anesthesiologists, who became more and more involved in these procedures.

The development of another set of interventional procedures, the use of radiofrequency ablation to deal with arrhythmias in the pediatric patient, illustrates the progressive complexity and difficulty of anesthesia care in these patients. Initially employed only in healthy teenagers with structurally normal hearts but with paroxysmal atrial tachycardia (PAT), anesthesia care was quite straightforward. Now, in contrast, many of these radiofrequency ablation procedures are done in children with complex CHD, repaired or unrepaired, and frequently the children (or adults) may be quite cyanotic or have low cardiac output [49]. At present, in Boston Children's Hospital, the cardiac catheterization laboratory and the cardiac magnetic resonance imaging (MRI) unit perform close to 1,500 anesthesia cases per year.

But despite all those developments, the defects remain the same. If we look at the relative distribution of cases in 1982, 2008, and 2013, we see the same diagnoses and a similar numerical relationship between the major groups. As Helen Taussig remarked in her paper about the global distribution of cardiac diagnoses, only surgical interventions change the numbers [53] (see Table 1.1).

Table 1.1 Cardiovascular surgery at Boston Children's Hospital

	Total cases		
	1982 (*N* = 538)	2008 (*N* = 942)	2013 (*N* = 1,065)
Septal defects	27%	20.1%	23.5%
VSD repair	12%	7.5%	10.4%
ASD repair	9.6%	8.6%	10.1%
CAVC	5.9%	4%	3%
Cavopulmonary connection	3%	8.5%	6.2%
Fontan procedure	3%	5.4%	3%
Bidirectional Glenn		3.1%	3.2%
Systemic outflow obstruction	29%	27.1%	25.8%
Coarctation	7.7%	5.1%	3.4%
Transposition of great arteries		5.6%	3.5%
LVOT repair	11.7%	13.8%	13.4%
Norwood procedure	3%	2.5%	2.3%
Biventricular repair			3.1%
Pulmonary outflow obstruction	13%	18.2%	17.2%
Tetralogy of Fallot repair	7.6%	6.8%	3.9%
Conduit placement/revision	2.8%	2.3%	3.8%
Other RVOT reconstruction	1.6%	9%	9.5%
Pacemaker, AICD placement	5%	3.8%	4.5%
Patent ductus arteriosus	8%	6.2%	7.2%
Miscellaneous	15%	16.1%	15.6%

VSD, ventricular septal defect; ASD, atrial septal defect; CAVC, complete atrioventricular canal; LVOT, left ventricular outflow tract; RVOT, right ventricular outflow tract; AICD, automatic internal cardiac defibrillator.

Emergence of technology, including imaging (TEE, MRI) and ECMO: 2000–2010

The first decade of the 21st century saw many changes driven by the availability of new technology, including transesophageal echocardiography (TEE) and cardiac MRI; these, too, provide new challenges for the pediatric cardiac anesthesiologist.

The utility of TEE in congenital heart surgery was demonstrated in the late 1980s by studies of several groups in Japan and the USA, including Russell and Cahalan at the University of California, San Francisco. The use of two-dimensional echocardiography as well as three-dimensional echocardiography improved diagnosis both within and outside the OR and provided more challenges and opportunities for the pediatric cardiac anesthesiologist.

The TEE interpretation of complex CHD and judgment of the adequacy of intraoperative repairs are considerably more challenging in CHD than in adult acquired heart disease. Many centers have called upon pediatric echocardiographers to make such judgments, rather than the pediatric cardiac anesthesiologist being responsible for that as well as for managing the patient in the post-bypass period. In addition, use of TEE has expanded to the cardiac catheterization laboratory where it is used in parallel with fluoroscopy for device closure of septal defects, allowing confirmation of the placement and location of the device [54]. It has been useful in guiding the mechanical support devices, especially the ventricular assist devices (VAD), confirming cannula placement and the absence of obstruction [55]. The main concerns for the anesthesiologist when using TEE remain airway obstruction, altering left atrial pressure, or even extubating the child in the middle of an operation "under the drapes".

Similarly, the emerging availability of cardiac MRI for diagnosis and follow-up of CHD patients has compounded the difficulties of providing anesthesia and monitoring in an intense magnetic field with limited patient access, but requiring anesthesia to be delivered to patients with severe, complex CHD under difficult conditions. Such technological advances come at a high price and it is hard to see how innovations like the long and expensive search for a method of treatment of HLHS would be justified today.

That decade saw another technical innovation of great importance to pediatric cardiac anesthesia: ECMO (Figure 1.2). Use of rapid-response ECMO for children

Figure 1.2 Infant on extracorporeal membrane oxygenation in the cardiac intensive care unit.

with CHD who suffer cardiopulmonary collapse postoperatively, who cannot be weaned from CPB, or who need to be supported as a bridge to heart transplantation has proved very effective in reducing mortality rates to astonishingly low levels. In the history of the development of pediatric cardiac anesthesia, we have come a long way from the baby in the ice bath being prepared for DHCA to the complex technology necessary for ECMO resuscitation.

This past decade has also seen a pushing of the envelope to devise new surgical and interventional catheterization approaches that cross the boundaries of the traditional care of patients with CHD and these continue to evolve. Two such approaches are transuterine fetal cardiac catheter intervention (see Chapter 15) and hybrid stage I Norwood palliation (see Chapter 25). The hybrid stage I palliation in the catheterization laboratory requires the anesthesiologist to anticipate and treat significant hemodynamic perturbations, blood loss, and arrhythmias during the procedure, while managing neonatal SV physiology without CPB and providing an anesthetic technique that offers the possibility of early tracheal extubation [56,57]. Hybrid procedures are extending in the catheterization laboratory and include VSD closure, HLHS management, and percutaneous valve implantation. They require a multidisciplinary approach and availability of the cardiac interventionists, cardiac surgeon, and anesthesiologist [58].

2011–2015 and the future

With the understanding that certain cardiac lesions are progressive in nature, prenatal intervention is believed to halt the process *in utero* and improve the postnatal outcome of these patients. Since the initiation of fetal cardiac interventions, the number of these procedures has been increasing and includes valvuloplasty of the aortic and pulmonary valve, balloon atrial septostomy for restrictive or intact interatrial septum in cases of HLHS and TGA, and fetal pacing in complete heart block. More than 120 cases have been done at Boston Children's Hospital since 2000 (see Chapter 15). Improving delivery of oxygenated blood to the brain *in utero* may affect neurodevelopmental outcomes of patients with congenital disease – an area of interest and research [59,60]. Pediatric cardiac anesthesiologists have an integral role in designing and carrying out these procedures. Fetal cardiac intervention for aortic valve stenosis or HLHS with intact atrial septum requires the anesthesia team to induce general anesthesia for the pregnant mother, and also analgesia and muscle relaxation for the fetus, with fetal monitoring by ultrasound [61]. The success of the intrauterine procedures allows potential growth of the ventricle with the goal of a biventricular repair during infancy. However, although the reported success of these procedures is promising, the number of cases and series published is small and does not allow us to conclude superiority over neonatal surgeries and discuss long-term outcomes [62,63].

During fetal interventions, anesthesia is most commonly provided to the fetus by intramuscular injection of opioid, muscle relaxant, and atropine. Most studies comparing anesthetics have been done in animal models. Undergoing a prospective clinical trial in a human fetus has multiple limitations, including the limited number and type of procedures, and their associated complications, the maternal condition, and the lack of time to assess the fetal outcomes during the procedure itself [64].

In the past few years, mechanical circulatory support (MCS) has evolved. Although ECMO remains the most widely used MCS among centers, additional ventricular support devices have been used as a bridge to transplant, leading to an increase in the pediatric cardiac transplant waiting lists [65]. The EXCOR® pediatric VAD (Berlin Heart GmbH, The Woodlands, TX, USA) was recently approved by the US Food and Drug Administration (December 2011).

A study database from 2007 to 2011 (the date of approval of the device) compared the 1-year post-transplant survival between patients who underwent heart transplant without VAD support and those who were bridged with EXCOR to transplant. Pediatric patients supported with EXCOR have similar survival rates to Open Procurement and Transplantation Network status 1A patients supported on either inotropes or ventilator [66].

Children with MCS waiting for cardiac transplant may present for multiple surgeries such as line placements, changes of VAD chamber, chest exploration, and laparotomies. Therefore, an understanding of these devices becomes a must and mandates the presence of a pediatric cardiac anesthesiologist in institutions where surgical care is provided to these patients. Challenges include anticoagulation, thromboembolic and cerebrovascular events, and hemodynamic stability [67]. It is important to be familiar with the device and the adjustment of the settings in order to maintain hemodynamic stability. The VAD output is fixed and dependent on volume. Therefore, hypotension is a concern on induction and maintenance of anesthesia, and the most effective therapy is fluid bolus and alpha-receptor agonist. Cave et al.

recommend ketamine as the drug of choice for patients with assist devices [68,69]. A team approach, including surgical, intensivist, anesthesiologist and the mechanical support team, is of the utmost importance for managing these patients and for coordination during the transport to the operating room or the cardiac catheterization laboratory.

As new treatments in CHD are developed by surgeons and cardiologists, and new technology emerges, the pediatric cardiac anesthesiologist faces new challenges. One significant challenge for the current generation of pediatric cardiac anesthesiologists is to help reduce the cost of care. One of the primary ways to reduce perioperative cost is limit ICU and ventilator time. This translates into increased demands and expectations for early extubation, preferably in the OR. Such changes in care have risks associated with them that will require careful assessment considering the advantages achieved with postoperative ventilation and sedation. For example, arrhythmias and cardiac arrest following endotracheal suctioning in the ICU postoperatively almost disappeared when heavy sedation with fentanyl prevented major swings in PA pressure with suctioning [70,71]. Careful selection of patients for early extubation and judicious use of shorter-acting anesthetic agents may allow lengths of stay to be shortened without increasing risks. In some studies, early extubation after relatively simple operations has, in fact, proved to be safe when using new short-acting anesthetic agents such as sevoflurane and remifentanil, particularly when better pain control is also employed. Other advances, such as limiting the total dose of anesthetic agents by developing ways to monitor depth of anesthesia, so as to give sufficient doses to prevent awareness and attenuate stress responses during CPB, are being explored, but remain elusive [72].

In the past, the outcome criterion most emphasized for treatment of CHD was survival. Now that survival rates are very good and getting better for almost all forms of CHD, attention has turned to the quality of that survival. Recent concerns about the effect of anesthetic agents on the developing brain have prompted extensive efforts to study the magnitude of the effect of these agents, the mechanism of the effect, and whether alternative agents or protective strategies are warranted [73]. Neonatal cardiac surgery patients must have surgery at a vulnerable age and also potentially suffer from brain injury from cyanosis, bypass techniques, inflammation, or low cardiac output, and mechanical support devices are a particularly important focus of study. It has been shown that neurodevelopment is impaired in approximately one-third of children who underwent surgery at a neonatal age [74]. As seen on MRI, 23–40% of neonates presenting with a complex cardiac defect show evidence of cerebral injury preoperatively [75–79]. After surgery, 36–73% of patients have evidence of new cerebral lesions on MRI [75–81]. This suggests that much of the injury develops preoperatively. Therefore, cardiac anesthesiologists may play a key role and are involved in research to ameliorate these effects, including brain imaging and long-term neurodevelopmental outcome studies [82–84]. The new American Heart Association/American Academy of Pediatrics guidelines on the evaluation and management of neurodevelopmental outcomes in children with CHD identifies brain biomarkers and EEG measurements that could be useful in managing patients during the perioperative period [85,86].

CHD – a growing specialty from the fetus to the adult patient

Tempora mutantur et nos in illis – "Time changes and we develop with time." It has been 71 years since Robert Gross first ligated a PDA and we have seen amazing developments in the treatment of CHD. Concomitantly, anesthesiology has evolved and slowly defined pediatric anesthesia, and then cardiac anesthesia, and now, in the past two decades, pediatric cardiac anesthesia has developed as a distinct and separate area of subspecialization.

In 2005, the Congenital Cardiac Anesthesia Society (CCAS; www. pedsanesthesia.org/ccas/) in the USA was formed and now has more than 1,100 members. It provides a forum for subspecialized educational meetings, a national database of congenital cardiac anesthesia cases (see Chapter 3), and has initiated an effort to define adequate postgraduate training in pediatric cardiac anesthesia [87] (see Chapter 2). CCAS is a society organized within the larger Society for Pediatric Anesthesia, indicating that this specialty has chosen to align itself more closely with pediatric anesthesiology than with adult cardiac anesthesiology, although there are important common interests and principles in all three of these specialties caring for patients with CHD.

As part of the trend of increasing long-term survival, the patient care group growing most rapidly at most centers is the adult with CHD. The prevalence of adults in the year 2000 was 49% of patients with CHD [88]. This is the somewhat unexpected result as care in childhood improves and more and more of these patients survive to adulthood and even into old age. At many institutions, special programs have been created to treat these patients and the problems they face. These problems include complications, reoperations, and socioeconomic barriers to normal education, employment, and creation of families. The question of pregnancy and anesthetic management of delivery for these patients is also evolving. It is unclear who is most qualified to provide anesthesia for such patients during labor and delivery. But suddenly the pediatric cardiac anesthesiologist may find themselves having to care for adults [89] (see Chapter 16).

Although there has been much progress in pediatric cardiac anesthesia in providing safe anesthetic care and improving the outcome of treatment of CHD in the OR and catheterization laboratory for patients of all ages, much remains to be done. One can say with certainty that the intimate connection between advances in therapy, surgical or medical, and the anesthesia support services

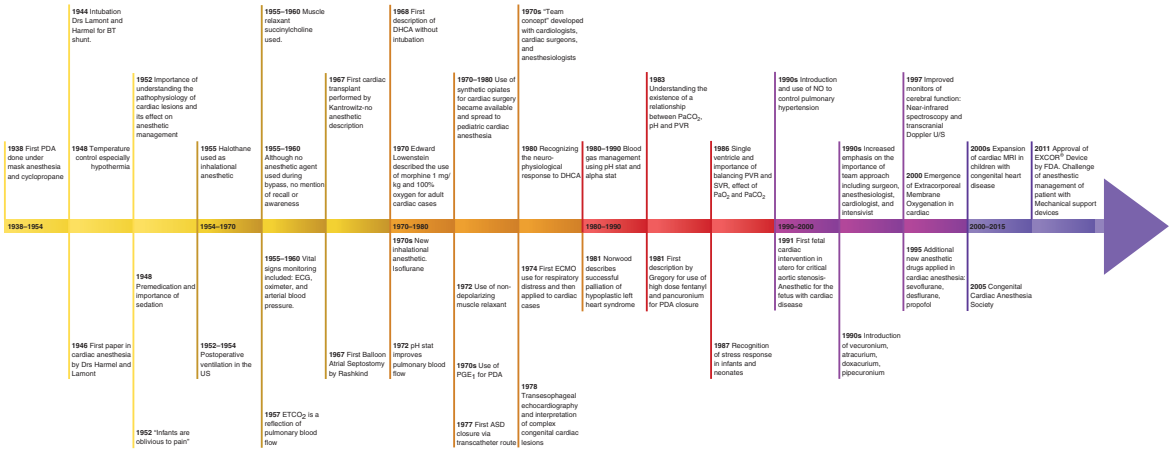

Figure 1.3 Milestones in the anesthetic management of patients with congenital heart disease. BT, Blalock–Taussig; PDA, patent ductus arteriosus; ASD, atrial septal defect US, United States; DHCA, deep hypothermic circulatory arrest; ECG, electrocardiogram; $EtCO_2$, end-tidal carbon dioxide; ECMO, extracorporeal membrane oxygenation; PCO_2, partial pressure of carbon dioxide; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance; NO, inhaled nitric oxide; U/S, ultrasound; MRI, magnetic resonance imaging; EXCOR, extracorporeal ventricular assist device; FDA, Food and Drug Administration.

required to make those therapeutic advances possible will continue to present new challenges to the pediatric cardiac anesthesiologist. (Figure 1.3) The pediatric cardiac anesthesiologists will, in turn, meet those challenges and in the process find ways to make yet more improvements. Thus we progress in our art and science.

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A full reference list for this chapter is available at:
http://www.wiley.com/go/andropoulos/congenitalheart

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CHAPTER 2

Education for Anesthesia in Patients with Congenital Cardiac Disease

Sugantha Sundar[1], *Lori Newman*[1] *and James A. DiNardo*[2]

[1]Harvard Medical School and Beth Israel Deaconess Medical Center, Boston, Boston,, MA, USA

[2]Department of Anesthesia, Boston Children's Hospital and Harvard Medical School, Boston MA, USA

Introduction

Advances in diagnosis in pediatric cardiology, medical management, cardiac surgery, and cardiac anesthesia throughout the world have drastically increased the survival rate of children with congenital heart disease (CHD) to over 90% and, as a result, there are more adults than children living with CHD today. However, although the heart condition is treated at a young age, the defect is usually considered chronic due to the possibility of increased health issues as a result of experiences or restrictions related to the heart disease itself. The need for greater coordination and integration between pediatric and adult services and a long-term healthcare delivery system is obvious for this patient population. Unfortunately, after leaving pediatric cardiology, many patients are lost to follow-up errors. The specific type of program needed to better ensure all of these patients are "found" and better treated is yet to be discovered, but structured education for adolescents (and their parents), explaining the importance of follow-up, is a vital component.

Anesthesiologists, as an integral part of any system caring for patients with CHD, are often called upon to care for patients ranging in age from neonates to adults. Before the advent of the Congenital Cardiac Anesthesia Society (CCAS) in 2005, there were very few resources in terms of providing training and experience in the specific field of pediatric cardiac anesthesia. The board of directors along with other pediatric anesthesiologists addressed the lack of training criteria in congenital cardiac anesthesia both in the United States and internationally and have developed the resources that we have today.

Why teach and learn congenital cardiac anesthesia?

Only very recently has a curriculum for education in the care of patients with CHD been suggested [1]. Establishment of a curriculum had been complicated by the fact that very few anesthesiologists engage in a practice limited solely to the care of pediatric patients undergoing cardiac surgery. By necessity, most pediatric cardiothoracic anesthesiologists devote some portion of their time to the care of general pediatric patients or to the care of adult cardiothoracic surgical patients. Furthermore, while it has been widely regarded since the 1990s that intraoperative transesophageal echocardiography (TEE) is an accepted standard for the adult cardiac anesthetist, at present there is no formal examination or certification process for pediatric TEE and there is a debate about who (cardiologist or anesthesiologist) is best qualified to perform perioperative pediatric TEE.

The current model

Currently, teaching and learning in congenital cardiothoracic anesthesia more closely resemble an apprenticeship

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model than an established training program. This model has not changed over recent years. Most of this training occurs in a few centers across the US. The type of training received and quality of education are not yet standardized in spite of the efforts taken by these centers of excellence. The "apprenticeship model" as currently practiced does not utilize a structured approach that involves advocating teaching behaviors such as modeling, creating a safe learning environment, coaching, knowledge articulation, and exploration.

A recent publication by the Johns Hopkins group looked at pediatric urology training across the US. This specialty has traditionally used the apprenticeship model. They surveyed 44 pediatric urologists who had completed the 2-year Accreditation Council for Graduate Medical Education (ACGME) approved fellowships and concluded that pediatric urologists feel prepared in commonly performed procedures and perioperative care. The surgeons surveyed reported that faculty feedback/supervision, independent reading, and conferences were rated as a very effective method of teaching.

Saperson discusses the value of changing an apprenticeship model of teaching and educating in psychiatry in Canada to a more competency-based education with explicit expectations. Magen et al. discuss the importance of restructuring training in psychiatry in the US in relation to the healthcare environment. They speculate that funding for graduate medical education programs may be determined by quality measures.

Leong et al. recently completed a survey of pediatric pulmonologists to determine how flexible bronchoscopy is taught to trainees. Based on their survey results, they plan to build a formal competency-based curriculum. Pediatric cardiac surgeons have also recognized that the model to teach trainees to successfully cannulate a pediatric patient for extracorporeal membrane oxygenation (ECMO) based on the apprenticeship model is inadequate. Allan et al. have developed a simulation-based curriculum where they used time to cannulation as a primary endpoint to measure competency [7].

Most trainees also learn from their "role models" in the operating room (OR). In role modeling, faculty members demonstrate clinical skills, and model and articulate expert thought processes. Passi et al. question the value of role modeling in medical education and have conducted an extensive review of the literature to assess the effectiveness of this technique.

Curriculum for learning and teaching congenital cardiac anesthesia

Curriculum development should employ a logical, systematic approach linked to specific healthcare needs. The Kern model of curriculum development for medical education could be used to develop a curriculum to teach and learn congenital cardiothoracic anesthesia [9]. This is a six-step approach and consists of the following:

1. Problem identification and general needs assessment
2. Targeted needs assessment
3. Goals and objectives
4. Educational strategies
5. Implementation
6. Evaluation and feedback.

Problem identification and general needs assessment

This comprises identification and characterization of the healthcare problem:

- Whom does it affect?
- What does it affect?
- What is the qualitative and quantitative importance of the effects?

Education in anesthesia for CHD covers a wide range of lesions – uncorrected, corrected, and palliative therapies. The trainee needs to be educated in all aspects of the six core competencies related to these topics. This is often a daunting task for the educator as well as the trainee. Most traditionally trained pediatric anesthesiologists and adult cardiothoracic anesthesiologists do not have the expertise to manage the unique set of problems presented by this diverse patient population. Although a relationship of clinical outcomes to the training and education level of the healthcare provider has yet to be demonstrated, there is still the potential for a structured curriculum to positively impact quality of care and allocation of healthcare resources. van der Leeuw et al. completed a systematic review of the effect of resident training on patient outcome. They concluded that with adequate supervision, contingencies for additional OR time, and evaluation of and attention to the individual competence of residents throughout residency training could positively serve patient outcomes. There is limited evidence available on the effect of residency training on later practice.

The following points should be addressed to obtain adequate needs assessment:

- What proficiencies (cognitive, affective, and psychomotor skills) currently exist among learners?
- Previous training and experiences of fellows and residents in congenital cardiac anesthesia
- Current training and experiences already planned for trainees
- Resources available to learners (patients and clinical experiences, information resources, computers, audiovisual equipment, role models, teachers, mentors)
- Perceived deficiencies and learning needs
- Characteristics of the learners and barriers to learn and teach.

The current state of anesthesiology training in CHD has recently been characterized in a telephone and email survey performed in 2008 of anesthesia residency program directors (n = 131), ACGME-accredited pediatric anesthesia fellowship directors (n = 45), adult cardiothoracic anesthesia fellowship directors (n = 71; 44 ACGME-accredited, 27 non-ACGME-accredited), and

12-month pediatric cardiac anesthesia fellowship training program directors (n = 3). The following responses summarize training in the USA [1]. Hands-on experience with pediatric cardiac anesthesia during basic anesthesia training is described as "nonexistent" or "rare" in 50% of ACGME-accredited residency programs. In the remaining programs, typical exposure is during the CA-2 and CA-3 years, with residents caring for five to 10 patients requiring procedures with cardiopulmonary bypass (CPB). In a few programs, residents care for as many as 20–30 such patients. Pediatric anesthesia fellows in all 45 ACGME-accredited programs have at least a 2-month cardiac experience during the 12-month fellowship. The typical fellowship experience involves 30–50 CPB cases. In two-thirds of the programs this exposure occurs in 1-month blocks, and in the remainder the experience is distributed throughout the year. Approximately one-quarter of the pediatric fellows use elective time to obtain an additional month or two of experience. Presently, only 13 of the 44 ACGME-accredited and one of the 27 non-accredited fellowships in adult cardiothoracic anesthesia have a mandatory exposure to pediatric cardiac anesthesia, with the remaining programs offering an elective experience of varying duration. Typical mandatory exposure is 1–2 months with 20–30 CPB cases. The words "rarely" or "occasionally" were most commonly used by the individuals surveyed to describe the frequency with which adult cardiothoracic anesthesia fellows use available elective time to pursue training in pediatric cardiac anesthesia. Besides the three known 12-month pediatric cardiac anesthesia fellowships (two in the USA, one in the UK), there were several programs in the USA that offer additional training in pediatric cardiac anesthesia for intervals of 3–12 months on an ad hoc basis.

By 2012, a Second Year Advanced Pediatric Anesthesiology Fellowship Network had been formed in the US, through the efforts of the Pediatric Anesthesia Leadership Council and the Pediatric Anesthesia Fellowship Program Directors' Association. Pediatric cardiac anesthesia advanced fellowships were included, and a 12-month training period was specified. As of that time, 18 programs were offering these fellowships with a total of 22 available positions.

There is no formal education in TEE at this time for a fellow training in pediatric cardiac anesthesia. This is a skill that is mandated of an adult cardiac anesthesiologist. The model as it stands today in most centers in the US calls for the cardiologist to be in the OR providing the expertise necessary to make intraoperative decisions. It is not currently an expectation that the pediatric cardiac anesthesiologist will have this skill. The question arises as to who is best suited to perform the TEE in the OR. The other question that needs to be answered is how perioperative TEE education will be incorporated into the training model. Will the National Board of Echocardiography devise goals and objectives and a formal assessment of competency?

Targeted needs assessment

For the needs assessment to be an accurate reflection of what is required, it must involve the current trainees (learners) in pediatric cardiac anesthesia. Attempts should be made to assess the current strengths and weaknesses in knowledge, skills, and performance [13]. The environment in which the education is currently happening needs to be evaluated as well. Is the OR conducive to education of some of the complex physiology or should the initial education happen in a simulated environment where the stress level of all concerned is much lower? It is vital that all the stakeholders (trainees, program directors, cardiologists, intensivists and pediatric cardiac surgeons) are involved in the development at an early stage. Barriers and reinforcing factors that affect learning should be identified early on. Faculty development programs may be necessary to improve the quality of teaching and education in congenital cardiac anesthesia. Needs assessment should also include what resources are currently available to the trainees to facilitate learning in congenital cardiac anesthesia. The case mix in the training programs, multidisciplinary faculty educators, and access to online journals and educational materials, including the availability of audiovisual equipment, are vital to the success of curricular delivery. The value of the hidden and informal curriculum that is currently in place should not be underestimated.

To date, there have been no reports of needs assessment for curriculum development in congenital cardiac anesthesia in the medical literature. Such an initial needs assessment could be accomplished in the form of a Delphi system, in which global expert opinion as to curriculum needs is sought. This would be an economical method of accessing experts in the field and imposes few geographical limitations. Schinasi et al. used a simulation-based model to perform a needs assessment in procedural sedation among pediatric residents. A study by Haji et al. reported needs assessment for simulation training in neuroendoscopy. The nominal group technique (also known as the expert panel) and the consensus development conference could also be utilized; however, these methodologies are more difficult to organize and are time consuming. Focused group discussions at the annual meeting of the Society for Cardiovascular Anesthesiologists or Society for Pediatric Anesthesia will help deepen information obtained. However a skilled facilitator and note taker are essential so everyone is allowed to voice their opinion and accurate information is recorded. Consideration should be given to the use of the Curriculum Management and Information Tool that is made available by the American Association of Medical Colleges to all medical school faculty. The ultimate goal of the developed curriculum would be to reference objectives, competencies and/or learning outcomes in congenital cardiac anesthesia.