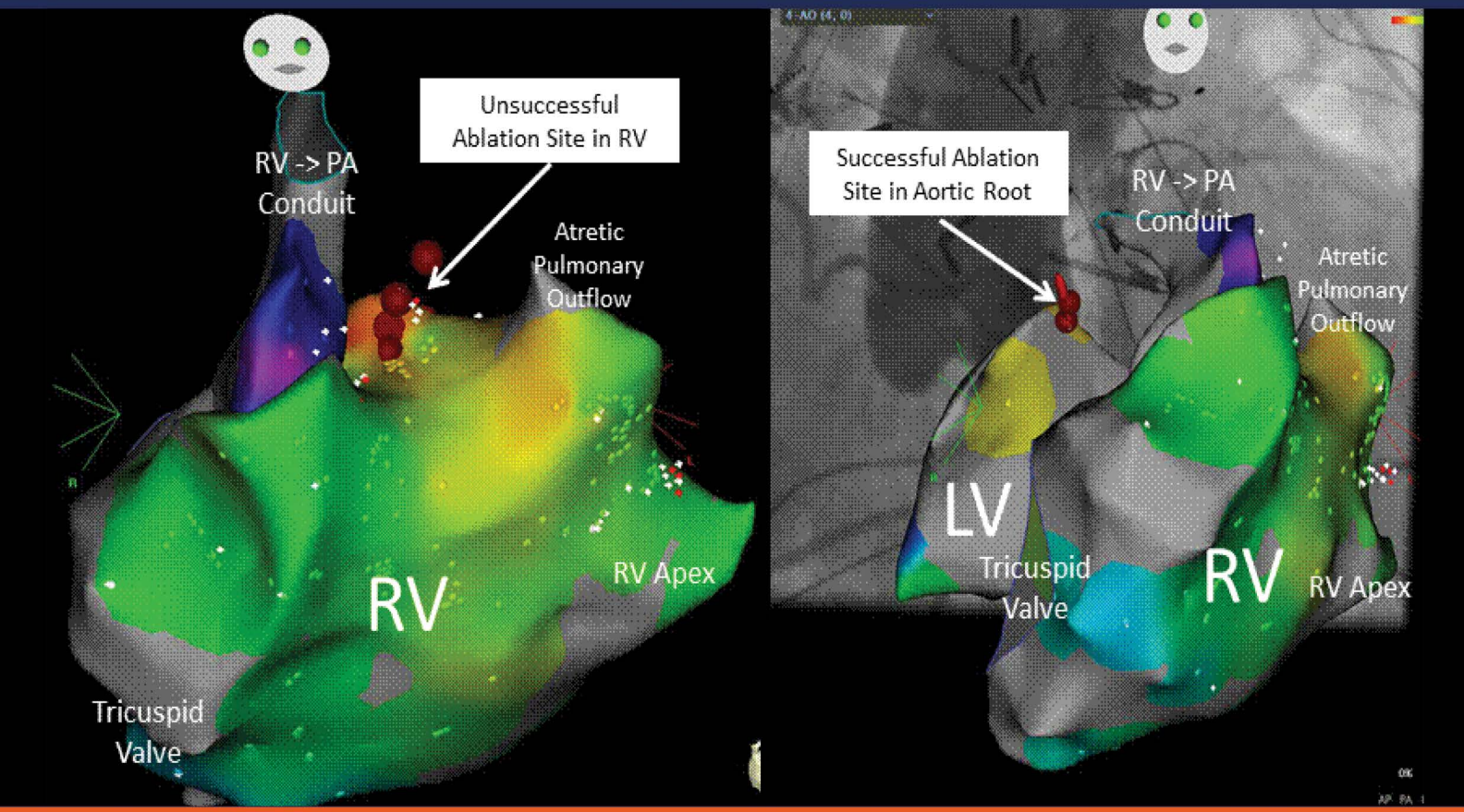
CATHETER ABLATION OF CARDIAC ARRHYTHMIAS IN CHILDREN AND PATIENTS WITH CONGENITAL HEART DISEASE



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Catheter Ablation of Cardiac Arrhythmias in Children and Patients with Congenital Heart Disease

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This work is dedicated to:

Our teachers, trainees, and patients

—and—

Our families, who have supported us throughout our careers.

CONTENTS

FOREWORD

When the groundbreaking cure of catheter ablation became a reality for patients with tachyarrhythmias in the late 1980s, it was an inspiring turning point in electrophysiology and an incredibly opportune time to be a young pediatric electrophysiologist. Not long after that, I had the privilege of working with other members of the Pediatric & Congenital Electrophysiology Society (PACES) to quickly organize the pediatric catheter ablation registry and successfully publish the multicenter 1991–1992 early experience in the *New England Journal of Medicine*. Many of the electrophysiologists involved with organizing the registry are the editors and chapter authors of this amazing new textbook. They, along with their trainees (who have become notable experts in the field and are also chapter authors), have written numerous important peer-reviewed articles and chapters in electrophysiology and cardiology textbooks during the 30 years since the inception of catheter ablation.

Until now, surprisingly, there has not been a pediatric and adult congenital heart textbook dedicated to catheter ablation. Although well overdue for our field, the wait was very worthwhile because of the extraordinary outcome. The highly regarded editors should be congratulated on assembling an experienced and esteemed group of international authors to write chapters on an exhaustive list of all the important catheter ablation topics. They even added significant related subjects such as surgical therapy and cost concerns. Together, they have produced a magnificent textbook that is a concise, yet comprehensive collection of the critical components and issues involved. Each chapter provides the essential basic foundation elements from which the latest important developments are built and expanded. Great textbooks are well illustrated with state-of-the-art examples supported by pertinent key references. This textbook meets and exceeds these criteria. It will become a close and treasured companion for trainees and novice electrophysiologists as well as an updated invaluable reference for established electrophysiologists.

This textbook will stimulate excitement in the field. Pediatric and congenital electrophysiology will be enhanced tremendously because this textbook will advance catheter ablation knowledge and inspire research and education by new pioneers who will become experts in our electrifying discipline.

Finally, and most importantly, patients and their families will benefit enormously from this textbook because their care will be enhanced by the knowledge gained and applied toward the goal to cure them of their tachyarrhythmia.

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PREFACE

The ablation of arrhythmia substrates has been a part of pediatric cardiology practice for many decades. Techniques for surgical ablation for Wolff-Parkinson-White syndrome, atrial and ventricular tachycardia, and other substrates began in the 1970s and 1980s. Techniques for direct current transcatheter ablation developed in adults were translated to pediatric practice, most prominently by Dr. Paul Gillette, but such procedures were certainly infrequent. Starting in 1989, however, the availability of radiofrequency ablation quickly and completely revolutionized the field of pediatric arrhythmia management. There are in fact very few examples of such a rapid and complete transformation driven by technology in pediatric medicine, and those of us who were present at the birth of transcatheter ablation in children have many stories to tell.

We offer this textbook covering catheter ablation techniques in children and patients with congenital heart disease, recognizing that catheter ablation is only one tool available for the management of such patients. We are entirely in agreement with the expectation that our trainees must become fully skilled in all aspects of diagnosis and management of arrhythmias, as opposed to becoming "ablationists." It is true that ablation techniques have been covered as chapters in the larger prominent textbooks which cover the entire field of electrophysiology or the field of pediatric and congenital arrhythmia management. In our view, however, these chapters provide an overly superficial treatment of these techniques, and do not do justice to the importance of catheter ablation in modern pediatric and congenital heart disease practice. Thus, we have endeavored to present a more comprehensive deep dive into the field, recognizing that despite its importance, catheter ablation is only one tool in the toolbox.

Our intention in offering this text is to present the latest and best advice for those undertaking catheter ablation procedures in children and those with congenital heart disease. We recognize that models of care differ quite a bit around the world. In some countries, it is pediatric electrophysiologists who undertake these procedures, while in other parts of the world it may be adult electrophysiologists or even cardiac surgeons who are called upon to perform these procedures. We do not take a position concerning training and credentialing but only point out that anyone performing these procedures, particularly in small children and those with complex congenital defects, needs to be well trained and highly experienced in these procedures.

We have organized the table of contents in a way that we hope will be the most useful to the reader. After an introductory section that covers basic concepts of arrhythmia mechanisms, ablation physics, indications, and principles of mapping, the rest of the text is organized around two principles. Firstly, we cover each of the arrhythmia mechanisms and the approach to ablation, but we then move to specific congenital defects and the ablation techniques needed to achieve success with the substrate seen most commonly in those defects. Finally, we look to the future, to try to foresee what the next 10 or 20 years will bring to this field. It is our hope that as these developments come to fruition, they can be incorporated into future editions of this textbook.

Videos in chapters can be accessed at: **www.routledge.com/9780367534752**

ABOUT THE EDITORS

Edward P. Walsh, MD, attended the University of Pennsylvania School of Medicine, and completed his pediatric residency at Children's Hospital of Philadelphia. This was followed by a cardiology fellowship at Boston Children's Hospital, which included a year of specialized training in cardiac electrophysiology at Massachusetts General Hospital. He joined the staff at Boston Children's in 1985 to establish a cardiac arrhythmia service that has expanded under his direction to become one of the largest programs of its kind. His primary clinical interest has been catheter ablation for complex arrhythmias in patients with congenital heart defects. He is the senior editor and main contributor to one of the standard textbooks in the field and has trained over 50 fellows in his specialty. He has served as president of the Pediatric and Congenital Electrophysiology Society and was honored with the Distinguished Teacher Award from the Heart Rhythm Society in 2008.

Dr. Walsh is currently the Associate Chief of Cardiology for Clinical Affairs, and Division Chief for Cardiac Electrophysiology at Boston Children's Hospital. He is Professor of Pediatrics at Harvard Medical School, and the LJ Sloss Professor of Cardiology.

George F. Van Hare, MD, attended the University of Connecticut School of Medicine and completed his pediatric residency at Case Western Reserve University where he served as chief resident. This was followed by a pediatric cardiology fellowship at the University of California San Francisco (UCSF), with an additional year of specialized training in cardiac electrophysiology at UCSF. He joined the staff at UCSF in 1989, where he performed the first ever radiofrequency catheter ablation in a pediatric patient. He has served on the faculty of Case Western Reserve University, UCSF, and Stanford University, and moved to Washington University in St. Louis in 2008 as Chief of Pediatric Cardiology, a position that he held for 10 years. Dr. Van Hare is Professor of Pediatrics at Washington University in St. Louis, and also serves as a Medical Officer for the US Food and Drug Administration's Office of Cardiovascular Devices.

Dr. Van Hare has a longstanding clinical interest in outcomes from catheter ablation and led the NIH-funded 5-year multicenter prospective observational clinical trial, "Prospective Assessment after Pediatric Cardiac Ablation (PAPCA)." He is interested in the ways that catheter ablation allows us to define fundamental arrhythmia mechanisms, and in particular those responsible for reentrant tachyarrhythmias after repair of congenital heart disease. He is a past president of both the Pediatric & Congenital Electrophysiology Society and of the Heart Rhythm Society.

Paul Khairy, MD, PhD, attended medical school at McGill University in Montreal and completed his internal medicine residency at the University of Montreal. This was followed by fellowships in cardiology and adult electrophysiology at the Montreal Heart Institute, with additional fellowship training in adult congenital heart disease and pediatric/congenital electrophysiology at the Brigham and Women's Hospital and Boston Children's Hospital. Dr. Khairy holds an MSc degree in epidemiology and biostatistics from McGill, with a subsequent PhD in this discipline from the University of Montreal. He joined the staff of the Montreal Heart Institute in 2004. His primary clinical interest has been the management of arrhythmias in adults with congenital heart disease. Dr. Khairy co-founded the North American Alliance for Adult Research in Congenital Cardiology (AARCC), served as president of the International Society for Adult Congenital Heart Disease (ISACHD), and chaired an international panel that elaborated the first guidelines on the recognition and management of arrhythmias in adult congenital heart disease. He has supervised over 80 trainees and has co-authored more than 370 manuscripts in peer-reviewed journals. Dr. Khairy was honored by the Canada Top 40 Under 40 Award in 2010 and was inducted as a founding member of the Royal Society of Canada's College of New Scholars, Artists, and Scientists in 2014.

Dr. Khairy is currently Professor of Medicine at University of Montreal, the André Chagnon Research Chair in Electrophysiology and Adult Congenital Heart Disease, Scientific Director of the Montreal Heart Institute Adult Congenital Centre, and Director of Clinical Epidemiology and Outcomes Research at the Montreal Health Innovations Coordinating Centre (MHICC).

Mohammad Shenasa, MD, attended the University of Tehran School of Medicine and completed his internal medicine training at the University of Pennsylvania (where he was awarded a scholarship), Shiraz University in Iran, and Guy's Hospital in London. This was followed by a fellowship in adult cardiac electrophysiology at Mount Sinai Medical Center in Milwaukee, Wisconsin. He has subsequently practiced as a staff electrophysiologist at the University of Wisconsin, University of Montreal, McGill University, and the University of Pittsburgh. He spent 9 months in the Department of Pediatric Cardiology at Cornell University under Dr. Mary Allen Engle. He is currently a member of the Heart & Rhythm Medical Group at O'Connor Hospital in San Jose, California, and Professor Emeritus at the University of Pittsburgh Department of Medicine.

Dr. Shenasa has received both national and international awards, including teacher of the year. He has published extensively in cardiac electrophysiology and is the leading author of the only textbook on cardiac mapping, of which the fifth edition was published in 2019. He has also edited several other textbooks on electrocardiography and cardiac electrophysiology.

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Part I
Introductory Concepts

Chapter 1
DEVELOPMENT AND MORPHOLOGIC ASPECTS OF THE CARDIAC CONDUCTION SYSTEM IN NORMAL HEARTS AND CONGENITAL HEART DEFECTS

Alan Sugrue, Ilya Y. Shadrin, and Samuel J. Asirvatham

Introduction

There is an inherent beauty to the cardiac conduction system. Its journey to creation is a remarkably complex process beginning in the second week of embryological development. By birth, there is a mature network of conduction tissue responsible for initiating and maintaining the cardiac heartbeat. Abnormalities in cardiogenesis, which result in congenital heart defects, produce various conduction system anomalies. Cardiologists, electrophysiologists, and surgeons must have an in-depth knowledge of the cardiac conduction system in normal and congenital hearts. In the following chapter, we provide insight into this complexity as we discuss the embryological origins and morphological aspects of the conduction system in both normal hearts and those with congenital heart defects.

Embryological Development of the Cardiac Conduction System

Cardiac development is initiated at the end of the second week of embryological development, and by approximately 3 weeks, fusion of two endocardial tubes occurs to create the primary heart tube. This primary tube is a single endocardial tube with two caudal inlets (often referred to as venous poles) and one cranial outlet. The primary heart tube is composed of five key components; the sinus venosus, primitive atrium, primitive ventricle, bulbus cordis (conus), and truncus arteriosus (Figure 1.1). The sinus venosus receives inflow from both sinus horns (left and right), with the right horn incorporated into the right atrium and the left horn developing into the coronary sinus. The primitive atrium develops into the definitive left and right atria, with the left ventricle formed from the primitive ventricle. The right ventricle is formed from the bulbus cordis, which also contributes to the aortic outflow tract. The truncus arteriosus creates the ascending aorta and pulmonary trunk. As this primary tube develops, it elongates by adding cells to the heart tube from the secondary heart field. The secondary heart field is critical for establishing the cardiac outflow tract and right ventricle. It also contributes to the formation of the proepicardium. Later in development, the cardiac neural crest cells travel from the neural tube through the aortic arches and terminally arrive at the outflow tract. These cells are critical in ensuring the septation of the ventricles and outflow tract. Further, they serve a critical role in forming the anterior parasympathetic plexus. This plexus contributes to cardiac innervation and, subsequently, the regulation of heart rate. Although previously an area of debate, it is essential to recognize that the cardiac conduction system arises from the myocardium and does not show any lineage to cardiac neural crest cells.

At 3 weeks, the heart tube is rather primitive in its electrical conduction. Critical components of mature conduction in the normally developed heart are not present, and consequently, pacemaker activity is slow and unidirectional, and results in a peristaltic-like contraction, traveling cranially

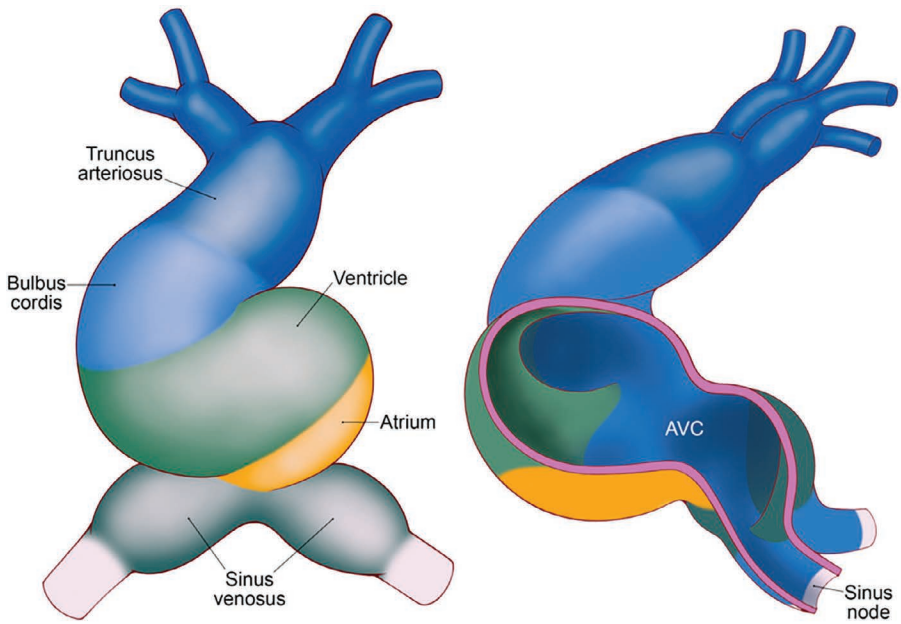

FIGURE 1.1 The primary cardiac tube. In this illustration we see the five key components; the sinus venosus, primitive atrium, primitive ventricle, bulbus cordis (conus), and truncus arteriosus. The image on the right depicts the location of the atrioventricular canal which becomes the AV node and the right sinus venous which becomes the sinus node.

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from the venous pole of the cardiac tube. Recording of electrical activity at this stage reveals a sinusoidal ECG. However, as the myocardium begins to evolve and develop, conduction velocity increases differentially, and conduction in the cardiac tube is no longer uniform. Areas of slow, primitive conduction velocity remain (sinus venous, the atrioventricular canal, and the outflow tract), enabling sphincter-like antegrade blood flow without the need for valves, which develop later from the endocardial cushions.

Three proposed models have described the contribution of cardiac myocytes to the cardiac conduction system (Figure 1.2). The first was the ring theory based upon the early observation that the conduction system tended to form within the four constriction points in the normal looped heart (D-loop). This model postulated that these four rings existed in the heart before looping and subsequently developed into the sinus node, atrioventricular node, His bundle, and bundle branches.[1,2] However, this model has since been discredited. Two other similar models are termed the "recruitment model"[3] and the "early specification model."[4] In the recruitment model, cardiac progenitor cells create a conduction or myocyte cell. As embryological growth continues, these cells hold bipotential traits and can continue to create conduction cells, resulting in ongoing recruitment. Conversely, in the early specification model, a cardiac progenitor cell can separate into a conduction or myocyte cell, but once a cell becomes dedicated to one of these outcomes, they remain divergent from each other. The early specification model is favored presently.

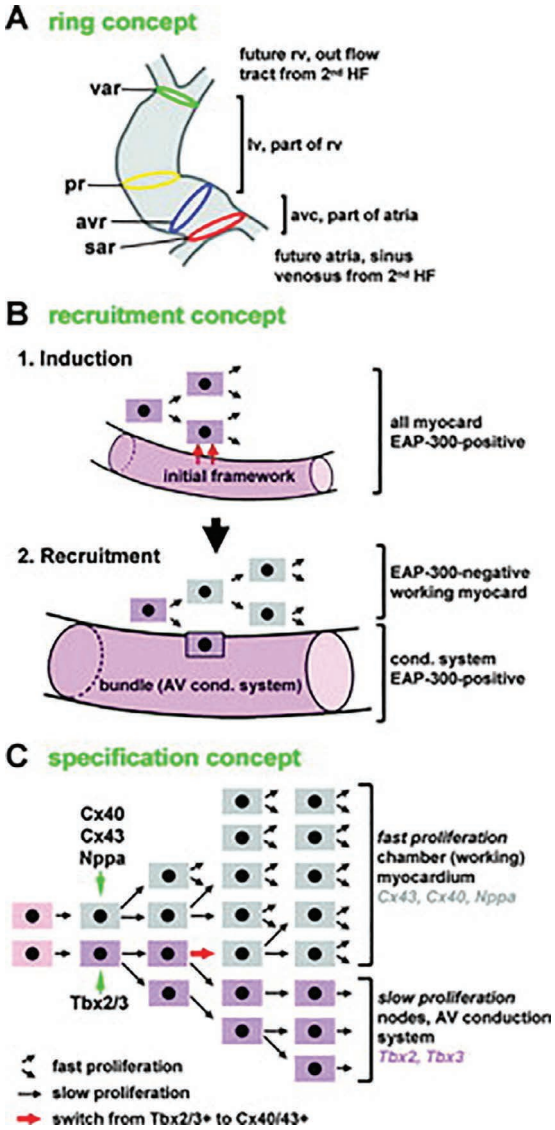

FIGURE 1.2 Three proposed models that describe the embryological lineage of the cardiac conduction system. (A) The ring theory (sar indicates sinuatrial ring; avr, atrioventricular ring; pr, primary ring; var, ventriculoarterial ring). (B) The recruitment model. (C) The early specification model.

(Reprinted with permission from Christoffels VM, Moorman AF. Development of the cardiac conduction system: why are some regions of the heart more arrhythmogenic than others? Circulation: Arrhythmia and Electrophysiology. 2009 1;2: 195–207.)

The genetic transcription of the cardiac conduction system is complex and well beyond the scope of this book chapter. However, the following sections will provide a brief review with further detailed information found in well-written reviews.[5–7]

Sinus Node

The dominant pacemaker originates from the venous pole, and this continues until the formation of the sinus node (SN), which is readily identified by the eighth week of fetal life.[8] Specifically, the sinus node arises from the sinus venous right horn. The genetic transcription that leads to SN development is a complex pathway of signaling and regulation. It is the most extensively studied process compared to the other conduction system elements. This SN arises from specialized *Tbx18+/Nkx2.5-* progenitors within the venous pole. These progenitor cells express *Isl1*, *Shox2*, and *Tbx3*, which play a critical role in regulating and expressing other transcription factors. In particular, they ensure pacemaker activity is confined to the venous pole (particularly restricting to the right side) and suppress atrialization of tissue, particularly preventing the differentiation towards a working myocardium phenotype.

Atrioventricular Node

Unlike the sinus node, the mechanistic development and transcription pathways for the atrioventricular node (AVN) are poorly delineated, largely because it is a heterogeneous structure composed of transitional cells, atrial inputs, and compact nodal cells. Lineage tracing studies of the AVN show that it is created from the embryonic atrioventricular canal (AVC). Primitive AVN cells appear as early as embryonic day 9.5, shortly after chamber differentiation. The AVC retains its slow conducting phenotype throughout development. *Tbx2*, *Tbx3*, and *Bmp2* are among the most important regulators of the AVC and play a critical role in developing the AVC and AVN. Like the SN, these factors regulate and express other factors that ultimately prevent myocardial gene programming, ensuring the AVC retains its primitive, slowly conducting phenotype. It is the formation of the annulus fibrosis (approximately embryonic day 12) that insulates the atrial and ventricular myocardium.

Proximal Ventricular Conduction System (His and Left and Right Bundles)

The peripheral conduction system is derived from ventricular myocardial precursors and specifically arises from the ventricular septum crest. In contrast to the AVN, proximal conduction tissue is not created from the *Tbx*$^+$ cells of the AVC. The His bundle originates from the *Tbx3*$^+$ primary interventricular

ring, specifically the ventricular septal part with the bundle branches created from the *Tbx3*+ subendocardial trabeculae. *Tbx5* and *Nkx2–5* are critical regulators in the proximal conduction system and bundle branch formation. These factors are critical in creating fast conduction properties of the conduction tissue and ensuring there is inhibition of myocardial gene programming.

Purkinje Fibers (Peripheral Conduction System)

Beginning with early studies in avian embryos, there has been considerable debate about whether the Purkinje network originates from specialized precursor tissue within the ventricles or by differentiation from a common ventricular myocardium. While evidence has been presented for both, the majority of evidence suggests that the Purkinje fibers (PF) share a common progenitor with contractile cardiomyocytes, and they are derived from the trabecular myocardium. It was demonstrated in avian models that PF share a common cellular progenitor with the working myocardium and that the recruitment only occurs in direct proximity to the coronary arteries. Evidence for this was reasonable, since myocytes exposed to endothelin (ET-1) formed a Purkinje fiber-phenotype.[9] However, the application of this belief to mammalian hearts was questioned because PF in avians are located deep in the myocardium, often in proximity to coronary vessels, contrary to human PF, which drape the subendocardial ventricular wall. Subsequently, a study in mice contradicted this theory and showed that the cardiac conduction tissue abnormalities did not occur in those lacking endothelin signaling. Regardless of these potential differences, it has been established more recently that the ventricular trabeculae are critical in containing the PF progenitor cells and that there is a biphasic development with lineage restriction mostly complete by embryonic development day 16.5.[10] Similar to the rest of the conduction system, a few key transcription regulators help define the conduction system fate. The PF are derived from the early ventricular chamber myocardium cells that express *Bmp10, Gja5, Irx3*, and *Nppa*. *Nkx2–5* ensures trabecular cells differentiate towards a PF phenotype.

Familial Cardiac Conduction Disease Syndromes

SCN5A Mutation

The SCN5A gene encodes the SCN5A alpha subunit of the $Na_v1.5$ cardiac sodium channel. Numerous mutations have been identified, which cause both loss and gain of function of the channel. In particular, loss of function results in difficulties with impulse initiation and propagation, while a gain of function (LQT3) is associated with bradycardia. SN dysfunction is often part of the clinical picture because this defect can also occur with other conduction system abnormalities.

HCN4 Mutation

HCN4 channels play a critical role in the hyperpolarization-activated funny channel (I_f), which is essential for SN automaticity. Mutations in the *HCN4* gene have been linked to inherited sinus bradycardia and, more recently, atrial fibrillation, ventricular arrhythmias, and left ventricular non-compaction.

TRPM4 Mutation

Mutations in the transient receptor potential channel, subfamily M (elastatine), member 4 [TRPM4] are linked to several patients with right bundle branch block (RBBB) and AV block. The mechanism behind conduction abnormalities is not clear, but elevated density of TRMP4 may alter the propagation of the action potential down the Purkinje fibers.

Tbx5 and *Nkx2–5* Mutations

These transcription factors play a critical role in conduction system development. Defects in *Tbx5* have been classically related to Holt-Oram syndrome (secundum atrial septal defects, progressive AV block, and radial ray deformities), with mutations in *Nkx2–5* resulting in a variety of congenital heart defects and hypoplasia of the cardiac conduction system.

LMNA Mutation

Mutations in the nuclear envelope *lamin A/C* (LMNA) are typically associated with muscular dystrophies and a wide variation of conduction abnormalities (with and without cardiomyopathy).

PRKAG2 Mutation

PRKAG2 gene encodes the γ2-subunit of an AMP-activated protein kinase (AMPK). Mutations in this gene result in various phenotypic features including glycogen storage disease, progression conduction system anomalies, and ventricular preexcitation.

Conduction System Anatomy in Normal Hearts

The Sinus Node

Gross Anatomy: The sinus node (SN) is a subepicardial comma-shaped structure located at the sulcus terminalis (Figure 1.3). The sulcus terminalis is a natural groove between the superior vena cava and the right atrium. It is the epicardial manifestation of the endocardial crista terminalis, which demarcates the embryologic sinus venous from the muscular right atrium. The body is often located cranially towards the orifice of the SVC, and the tail extends toward the eustachian ridge and inferior crista

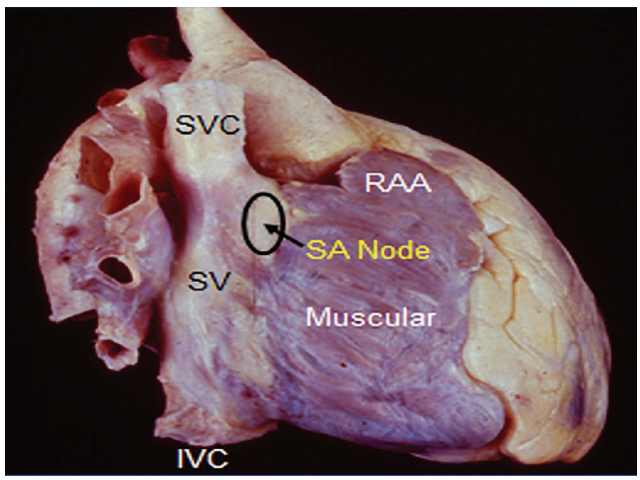

FIGURE 1.3 Sinus node location. This image highlights the location of the sinus node. It is located epicardially at the sulcus terminalis—the natural groove between the super vena cava and the right atrium.

(Courtesy of Dr. William D. Edwards, Mayo Clinic, Rochester, MN.)

terminalis. The length of the node is approximately 13.5 mm (range 8 to 21.5 mm).[11] The body is subepicardial, primarily located at 0.1–1.0 mm below the epicardial surface, and is usually covered with fatty tissue. As one moves closer to the tail, the node penetrates the myocardium, and consequently, the tail portion is closer to the subendocardium. Anatomical variations do exist, which often account for the SN's varying anatomical descriptions in early years, with the most common being a horseshoe arrangement (10%) in which the SN is situated anteriorly and draped over the right atrial appendage.[12]

Histology: Although the SN is often drawn as a demarcated structure, it has a heterogeneous appearance on histology. The demarcation between nodal tissue and atrial tissue is indistinct, and there is no discrete fibrous border. The node's center contains a tightly packed cluster of cells in a dense connective tissue matrix. These cells are small and parallel, contain a single central nucleus, and have poorly developed microfilament cytoskeleton—often referred to as P cells.[13] As one moves towards the node's tail, the cells become elongated and less discrete, and show intermediary characteristics between the central nodal cells (P cells) and atrial tissues. These cells are called transitional cells (T cells) and become interwoven with atrial tissue. This transition from sinus node tissue to atrial tissue is often called the transitional zone, which is usually large and extensive. This zone corresponds with electrophysiology mapping studies of the SN, which show a sizeable anatomical area for the SN, larger than the histological discrete P cells. More recent studies have identified a discrete paranodal area with cells that are an intermediate between cardiomyocytes and sinus node tissue. This area is not continuous but in proximity to the sinus node.

Many anatomical drawings of the right atrium and sinus node often identify discrete intra-atrial tracts that travel from the sinus node to the AVN. However, unlike canine hearts, which have discrete exit pathways, no tracts have been identified in the human SN. Radiations that travel to the atrial wall from the sinus node (0.2–2mm in length) have been described extending superiorly towards the superior vena cava, subepicardium, and terminal crest.[11] Although these are described as discrete histological radiations, they are not isolated from the atrial myocardium. Therefore, they do not fulfill the third criterion for a specialized track (being insulated from the adjacent myocardium[14]). There is no doubt that preferential conduction in a superior-inferior direction exists, which one could assume is a consequence of discrete SN exits. However, the observed preferred conduction is 'functional' and a consequence of right atrial anisotropy and anatomy. There is no one dominant breakout site based on the node's heterogeneous nature and its fragmented intersection with atrial tissue. As mentioned, during sinus rhythm, it has been noted that the electric breakout from the SN occurs well beyond the length of the compact SN cells. More recently, simultaneous epicardial-endocardial mapping of the human SN has provided additional 3D insights.[15] There was a caudal shift in exit and evidence of multicentricity with epi-endo dissociation of exit sites with overdrive suppression.

Arterial Supply: In 1961, James proposed that the node is critically positioned around its vascular supply;[16] however, further studies have failed to confirm this initial finding. The SN artery is derived from the right coronary artery in 60% and from the left circumflex artery in 40%, with some having a dual supply. The SN artery has been shown to travel retrocaval, pericaval, or precaval.[17] The SN artery is larger than the surrounding tissue, which plays a role in controlling its pacemaker function, with an increase in perfusion pressure associated with a slower heart rate.

Innervation: The autonomic nervous system heavily innervates the sinus node. Its automaticity is sensitive to subtle nervous system changes that influence pacemaker spontaneous depolarization and shift the SN's principal pacemaker site. Parasympathetic inputs are received via the vagal nerve and sympathetic inputs via fibers from the T1-T4 spinal nerves. Sympathetic and parasympathetic effects are not created equal, and the concept of accentuated antagonism has been proposed. In essence, with greater sympathetic activity, the inhibitory effect for a given level of vagal activity becomes more pronounced, resulting in the shifting of the SN's main site of pacemaker activity more inferiorly.

The Atrioventricular Node

Gross Anatomy: The atrioventricular node (AVN) is located in the right atrium and can be found in Koch's triangle (Figure 1.4). Koch's triangle is defined by the septal leaflet of the tricuspid valve, the coronary sinus ostium, and the tendon of Todaro. The floor of the triangle contains atrial myocardium. This floor and atrial wall are separated from the crest of the muscular ventricular septum by the superior extension of the inferior atrioventricular groove and the fibro-adipose tissue of the inferior pyramidal space, respectively. The membranous septum defines the apex of the triangle. The AVNs location within the triangle of Koch is not completely predictable; in 76% the compact node is located on the atrioventricular component of the membranous septum, while in 24%, it is located inferiorly within the triangle.[18]

Histology: The AVN histologically has been divided into three groups; atrionodal, compact nodal, and nodo-His. The atrionodal and nodo-His regions represent a hybrid region between nodal cells and their respective tissues (atrial or His). The mean length, width, and thickness of the compact AVN is 3.5 ± 1.2 mm (2.5–5.5), 4.5 ± 1.1 mm (2.5–7.4), and 1.2 ± 0.3 mm (0.8–1.8), respectively.[18] The AVN can be oval or sloping in shape, with its cells small, spindle-shaped, and lacking cellular orientation. Nodal extensions have been an area of considerable debate and, more recently, the focus of noteworthy

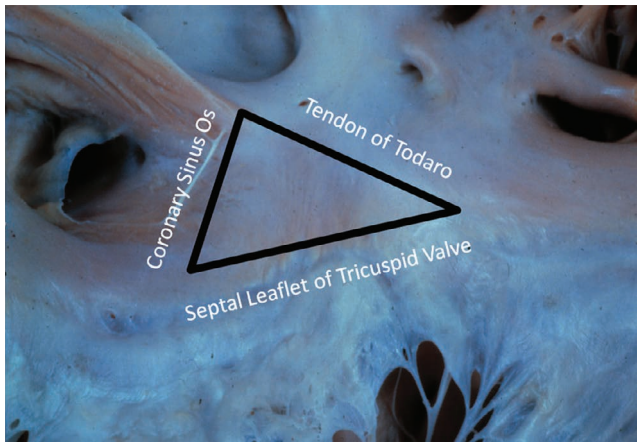

FIGURE 1.4 Triangle of Koch. The atrioventricular node (AVN) is located in the right atrium and can be found in Koch's triangle (black triangle). Koch's triangle is defined by the septal leaflet of the tricuspid valve, the coronary sinus ostium, and the tendon of Todaro.

(Courtesy of Dr. William D. Edwards, Mayo Clinic, Rochester, MN.)

anatomical studies. It is important to recognize that many of the proposed models of nodal inputs are based on animal studies with a different atrioventricular axis from that of humans. There is considerable evidence suggesting that nodal extensions exist in humans and provide the potential anatomical substrate for the slow pathway. There are two inferior extensions, a right and a left. The right extension passes parallel to and nearby the hinge of the tricuspid valve and is related closely to where slow pathway ablation is performed, while the left extension projects towards the vestibule. The right inferior extension is proposed to be derived from the original primary ring, with the left extension from the atrioventricular canal myocardium. There is considerable anatomical variability in the inferior extensions, with evidence of extensions into the tricuspid and mitral vestibules, but this is not consistently observed.

Furthermore, there is variation in whether the leftward or rightward extension is dominant in forming the node's base, with rightward the most common. In rare cases, the nodal extensions can be found at the basal inferolateral part of the left atrium in close proximity to the mitral annulus. Superior inputs have been an area of considerable debate and evidenced largely by observations from animal studies; more recently, Anderson has provided human histological evidence that one potentially exists.[19] Towards the apex of Koch's triangle, they noted that the AV nodal tissue received an input from the central layer of the atrial septum. This is often seen as the 'last connection' to the AVN before it becomes insulated, before entering the membranous septum.

Arterial Supply: The AV nodal artery originates from the right coronary artery in 83% and the left circumflex artery in 17%.[18] The artery's length ranges from 14–28mm, with its anatomical course depending upon its origin. In 54% of cases, the RCA extends beyond the posterior interventricular groove, and the artery arises distal to the U loop. It then passes through the pyramidal space towards the base of the triangle. In 21% of cases, the artery arises as a final branch of a dominant RCA and emerges distal to the interventricular septum, traveling in an oblique direction along the hinge of the tricuspid valve septal leaflet to the triangle of Koch. Dual blood supply has also been reported. In a left-dominant system, the AV nodal artery originates from the left circumflex artery prior to the transition to the posterior interventricular artery. At the triangle base, it is closest to the CS floor rather than the septal leaflet. Alternative sources of arterial supply have been described, including the anterior atrial branches and the first septal artery. Rarely it can be supplied from the Kugel anastomotic artery (an atrial artery that arises from the proximal left circumflex and can anastomose with the distal right coronary).

Innervation: Cholinergic and adrenergic fibers richly innervate AV nodal area. An epicardial fat pad provides parasympathetic innervation of the AVN. This is situated at the connection of the right inferior pulmonary vein and inferior left atrium.[20]

The His Bundle

Gross Anatomy: The His bundle (HB) represents a continuation of the AVN, and anatomically begins at the penetration of the central fibrous body (CFB). It measures 4 x 20 mm and is primarily composed of longitudinally oriented Purkinje type cells. The HB passes in a leftward direction through the CFB towards the ventricular septum. It then penetrates the membranous septum before separating into left and right bundle branches. Kawashima divided the HB into three elements: Nonpenetrating—as it transverses through the annulus fibrosis; Penetrating—as it is located within the fibrinous tissue of the CFB; and a Branching portion—when it bifurcates into the bundle branches. More recently, as we discuss in the next section, histological analysis has further refined these elements.

Histology: While the AVN's anatomical border to HB is defined as in the previous section, histologically, it is more subtle, and it is the collagen longitudinal division of the HB that provides a discrete histological differentiating factor from the AVN. The site of the His bundle penetration into the central fibrosis body occurs superiorly within Koch's triangle in 59% and 41% inferiorly. The penetration site was most commonly within the atria (54%), followed by the tricuspid valve septal leaflet hinge point (32%). In 15%, the ventricular component of the membranous septum was the penetration site (with a mean length of 4.6 ± 1.5 mm, and a range from 1 to 9 mm).[21] Interestingly, there is reported to be a histological lack of interventricular septum in 59% of cases, and in this situation, a rapid beginning of the LBB fascicles at the hinge of the septal leaflet of the tricuspid valve occurs. The distance between the HB and the right atrial endocardial surface is variable, ranging between 0.3–2.5 mm (mean 0.81 ± 0.46 mm).

Arterial Supply: It has a dual arterial supply receiving blood from the atrioventricular nodal artery and the first septal branch of the LAD.

Innervation: HB innervation has not been well studied in human hearts. It has relatively sparse autonomic innervation but contains both cholinergic nerve and adrenergic fibers. Sympathetic and vagal stimulation does not affect conduction.

The Right and Left Bundle

Gross Anatomy: After penetrating the membranous septum, in 75% of cases, the HB becomes a common infranodal bundle because there is a non-branching element that travels 1 to 3 mm on the septal crest before the bundles arise. The right bundle branch (RBB) is a straight continuation of the HB. It is a cord-like structure that takes an intramural course after the left bundle branch (LBB) takes origin. It then emerges subendocardially at the medial papillary muscle base. It passes towards the apex as a narrow cord, crossing the cavity in the moderator band before it subdivides into the distal Purkinje fibers that supply the RV subendocardium.

Before describing the anatomy of the LBB, it is critical to note that the LBB has marked variability. The LBB originates at the membranous septum (inferior portion) close to the right and non-coronary sinus. It can be both broad and narrow (margin in size from 1–14 mm) and is usually subendocardial. The branching of the LBB is an area of debate, and our current understanding is based mainly upon Rosenbaum's work, who proposed a bifascicular division of the LBB (left anterior and posterior fascicle) and subsequently described the ECG features of these. Nevertheless, pathological analysis shows that the size, number, location, and configuration of the LBB subdivisions are unpredictable. For example, some hearts showed numerous anterior subdivisions, and some only a single subdivision. That said, these "branches" do provide anterior and posterior activation of the LV. The left anterior fascicle originates under the inferior boundary of the membranous septum and is a long thin structure that navigates to the anterolateral papillary muscle. The left posterior fascicle is usually the first fibers to originate from the LB and is thick and broad, traversing towards the posteromedial papillary muscle. This bundle gives off two primary fibers, one to the posterior papillary muscle base and the other to the left septal surface. Sometimes, septal fibers have been reported to be their own distinct third division

of the common bundle. When the bundles reach the papillary muscles, they fan out into a dense, rich Purkinje network.

Histology: The bundle branches' cells are conventionally described as Purkinje cells in that they are large and vacuolated. Proximally, the bundles tend to contain long strands of Purkinje cells separated by a collagenous skeleton.

Arterial Supply: The LBB derives a large bulk of its supply from the LAD, with the anterior fascicle receiving its blood supply from the septal perforators in 50% of cases and AVN artery in the remaining 50%. Septal perforators proximally supply the posterior fascicle. A dual blood supply from both the anterior and posterior septal perforators supplies the distal portion. The RBB proximal part is supplied by the LAD or AVN artery. The branches of the LAD mainly supply the distal part.

Innervation: There is minimal autonomic innervation to the BB.

The Purkinje Fibers

Gross Anatomy: The Purkinje fibers (PF) are terminal branches of the bundles that form an interwoven network within the subendocardium. They are responsible for ensuring rapid excitation spread to a large ventricular mass to ensure synchronic ventricular contraction. They cover a large area of the ventricle but are less focused at the ventricular base. The PF are subendocardial, but some have proposed intramural elements (as observed in other species); studies have not yet shown this to be true in humans.

Histology: Histological findings regarding Purkinje cells are species-dependent, but they are generally larger and lack the transverse tubules present in myocardial cells. They have a larger amount of glycogen and appear lighter microscopically since they have fewer myofibrils.

Arterial Supply: No specific artery is identified that supplies the peripheral subendocardial PF network, but it is presumed to be extensive from both the left and right coronary systems. It is important to note that PF are more resistant to ischemia than myocardial cells since they likely receive adequate oxygen via diffusion from cavity blood and the capillary network.

Innervation: There is minimal autonomic innervation of the Purkinje system.

Additional Structures

Dead-End Tracks: In some hearts, dead-end tracts have been described as a continuance of the branching atrioventricular bundle[22] (Figures 1.5 and 1.6). These terminate past the septal crest towards and around the aortic valve annulus before fading.

Retroaortic Node: The retroaortic node is a growing area of interest[23,24] (Figures 1.5 and 1.6). Although to date it has not been fully delineated, there is growing histological evidence for its existence. It represents a remnant of the primary ring and is found in the atria directly posterior to the non-coronary sinus. This area has nodal phenotypic features with *HCN4* expression and *Cx43* absence. It has been identified as a possible substrate for non-coronary sinus arrhythmias.

The Conduction System in Congenital Heart Disease

Ventricular Septal Defects

Classification: Ventricular Septal Defects (VSDs) describe an interventricular communication between the right and left ventricle. VSDs usually occur with other congenital heart diseases (which are discussed further in the chapter), but we explore them in isolation in this section. There is significant discrepancy in the classification of VSDs, which has led to some confusion in the literature. For this chapter, we have employed the classification outlined in the consensus report

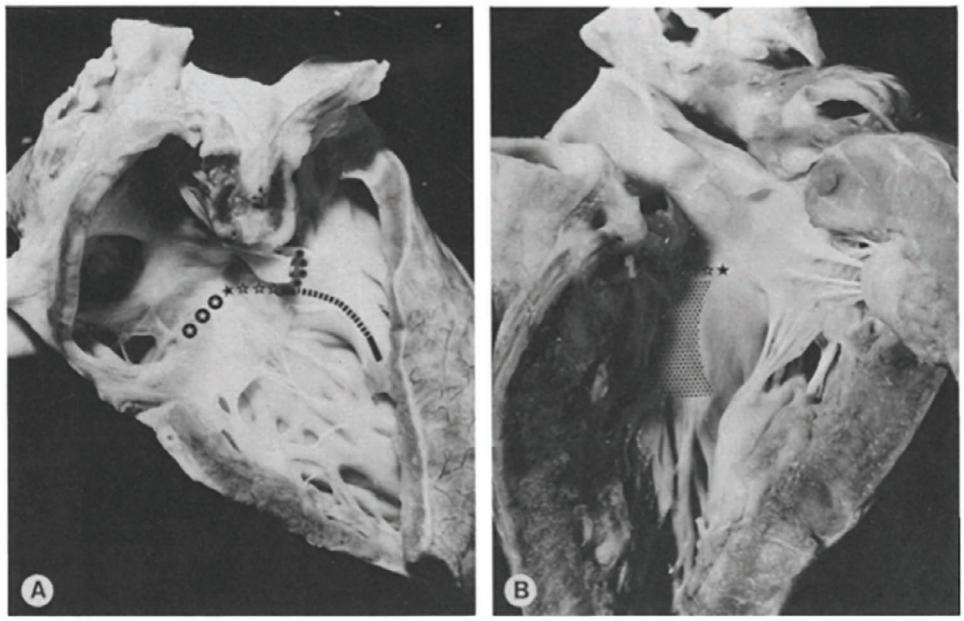

FIGURE 1.5 Dead-end tract in right (A) and left (B) ventricular views. The dead-end tract courses beneath the aortic valve and disappears.

(With permission from Kurosawa H, Becker AE. Dead-end tract of the conduction axis. International Journal of Cardiology. 1985;7(1):13–8.)

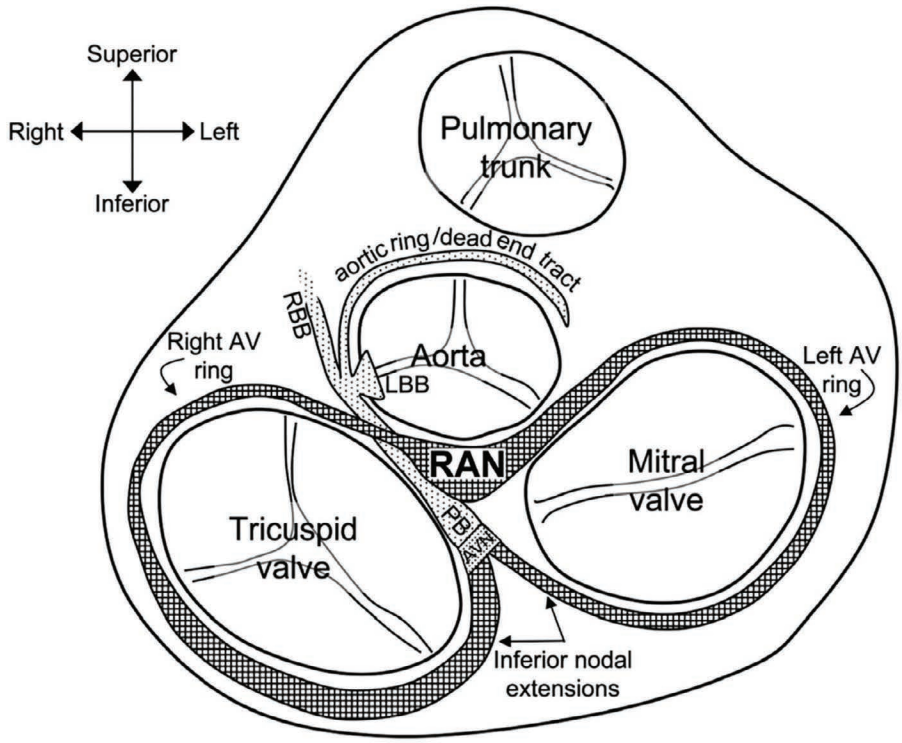

FIGURE 1.6 Schematic diagram shows the location of the atrioventricular and aortic rings and the retroaortic node in the hearts. *Abbreviations:* AVN: atrioventricular node; BB: branching bundle; PB: penetrating bundle; RA: right atrium; RAN: retroaortic node; RBB: right bundle branch; RV: right ventricle.

(With permission Yanni J, Boyett MR, Anderson RH, Dobrzynski H. The extent of the specialized atrioventricular ring tissues. Heart Rhythm. 2009;6(5):672–80.)

from the International Society for Nomenclature of Paediatric and Congenital Heart Disease.[25] There are four types of defects defined in the consensus statement:

1. *Outlet VSDs*: These defects are located in the RV between the septal band's two limbs—anterosuperior and posteroinferior. They are separated into perimembranous outlet defects, doubly committed juxta-arterial defects, or outlet muscular defects. Outlet perimembranous defects can be differentiated from central perimembranous defects because they are neighboring the tricuspid valve's anterior leaflet, with central defects related to the septal leaflet.
2. *Central Perimembranous VSDs*: These are located at the space occupied by the interventricular part of the membranous septum, below and behind the septal band's posterior inferior limb.
3. *Inlet VSDs*: These open into the RV inlet. The consensus report subclassifies this group as either inlet perimembranous or muscular, since these defects are usually reclassified upon surgical inspection as perimembranous with inlet extension or muscular inlet defects. Inlet muscular defects have exclusively muscular borders.
4. *Trabecular Muscular VSDs*: These have a muscular border exclusively and are located in the trabecular portion of the muscular septum. Their geographic location allows for subclassification as either apical (distal to moderator band), midseptal (middle of the apical muscular septum, and not involving the base of the ventricular mass), posterior-inferior, or anterosuperior (anterior to the septal band).

Sinus Node: The sinus node is normally located (subepicardial at the sulcus terminalis) in all four types unless associated with atrial isomerism or situs inversus.

Atrioventricular Node: Central perimembranous, outlet, and trabecular muscular VSDs have an AVN in its usual position within Koch's triangle. In inlet perimembranous defects, the AVN is inferior but located in Koch's triangle in those with an aligned atrial and ventricular septum. When an inlet perimembranous defect is associated with a malaligned septum and a straddling tricuspid valve, there is typically an anomalous AVN inferiorly located at the junction of the right AV groove and muscular interventricular septum.[26] This node is the primary method of conduction to the ventricle. There is a regular node in the Koch triangle in these cases, but it does not connect with the central conduction system.

His-Purkinje System: In all perimembranous VSDs (central, inlet, outlet), the HB travels on the posterior rim of the VSD to the muscular septum crest (Figure 1.7). In the other outlet VSDs, the conduction system is usually protected by a muscular posterior inferior rim formed from the fusion between the ventriculo-infundibular fold and the posterior limb of the septal band. However, if there is no muscle observed and a fibrous ring is seen, its course is similar to perimembranous VSD.[27] In inlet muscular VSDs, the conduction system is found in the anterosuperior quadrant but usually remote from the defect. Muscular defects have no anatomical concerns regarding the

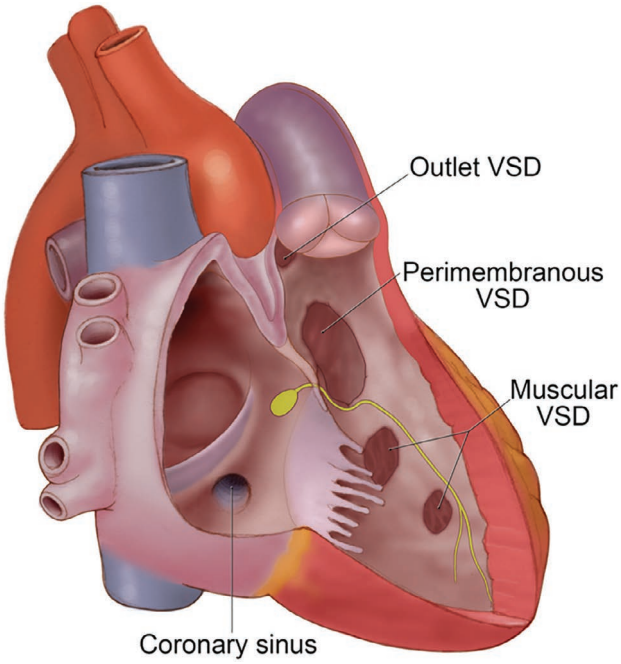

FIGURE 1.7 Relationship of the cardiac conduction system in ventricular septal defects. In all perimembranous VSDs (central, inlet, outlet), the His bundle travels on the posterior rim of the VSD to the muscular septum crest. In the other outlet VSDs, the conduction system is usually protected by a muscular posterior inferior rim formed from the fusion between the ventriculo-infundibular fold and the posterior limb of the septal band. Muscular defects have no anatomical concerns regarding the His bundle, but depending upon their location in the trabecular septum, they can be closely related to the bundle branches.

His bundle, but depending upon their location in the trabecular septum, they can be closely related to the bundle branches.

Atrioventricular Septal Defects

Atrioventricular septal defects (AVSDs) incorporate a wide spectrum of abnormalities, with the anatomic hallmark being a common atrioventricular junction coexisting with deficient atrioventricular septation. They are classified into four main categories; complete, partial, intermediate, and AVSDs associated with ventricular imbalance. Complete AVSDs refer to the situation in which there is a common AV valve (which has five leaflets), and there is an ostium primum ASD with coexisting inlet VSD. Partial AVSDs have an isolated ASD or VSD, most commonly the former. Intermediate AVSDs are on the spectrum of complete defects that comprise a primum ASD in association with a restrictive VSD, a common AV valve with separate right and left orifices.

Sinus Node: The sinus node is normally located in AV canal defects (subepicardial at the sulcus terminalis) unless associated with atrial isomerism.

Atrioventricular Node: The AVN in AVSD is not found in the classical Koch's triangle and is posteriorly and inferiorly displaced in the floor of the RA. It is located in a "nodal triangle" as defined by Thiene.[28] This nodal triangle has an obtuse apex that is delineated by the upper border of the coronary sinus ostium, the posterior insertion of the bridging tendon to the posterior fibrous area, and the posterior attachment of the posterior bridging leaflet. The AVN is displaced because the inferior limbus of the atrial septum does not connect with the ventricular inlet septum, except directly at the heart crux. The node's precise location within this triangle is driven by the degree of septum development—the more deficient, the more posteriorly deviated. The AVN is on average 1 mm deep to the endocardium with a mean distance of 1.7 mm from the coronary sinus orifice.[29] In the rare situation in which there is an AVSD with gross malalignment of the muscular ventricular septum and the atrial septum, the AVN is anomalous and originates from the inferior aspect of the right AV junction rather than at the crux of the heart.[30]

His-Purkinje System: The His bundle travels on the posterior inferior rim (Figure 1.8). It travels on the left side of the ventricular septum crest. The ascending component of the "scooped out" septum is typically lacking conduction tissue. Interestingly, the left bundle branches have marked posterior displacement with relative hypoplasia of the anterior bundle. This posterior deviation of the bundles corresponds with the superior axis that is often seen in AVSDs. Because of the posteriorly displaced branching bundle, the RBB has a long segment that travels very close to the defect's ventricular margin, with the distance from the inferior AV junction to the takeoff of the RBB approximately 12.8 mm. In partial AVSDs, the His is concealed deep under the posterior bridging leaflet and the connecting tongue.

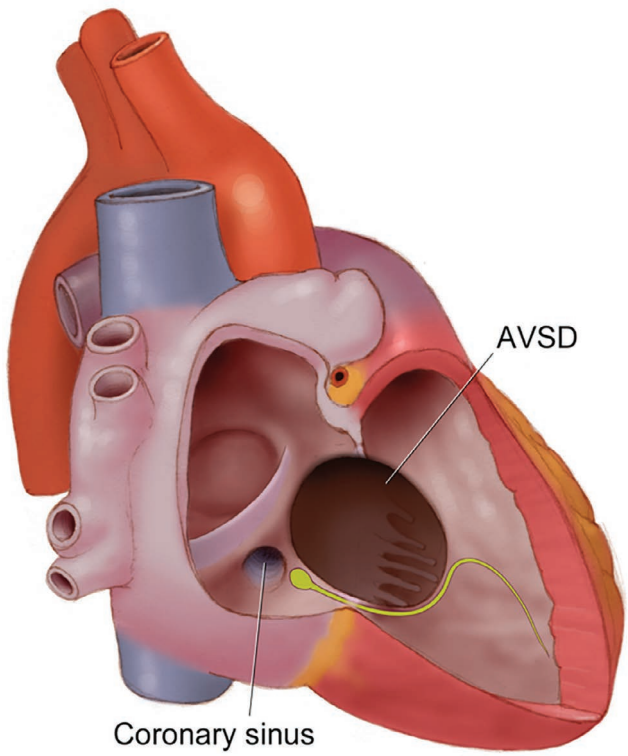

FIGURE 1.8 Relationship of the cardiac conduction system in atrioventricular septal defects. The AV node in AVSD is not found in the classical Koch's triangle and is posteriorly and inferiorly displaced in the floor of the RA—in a nodal triangle described by Thiene. The His bundle travels on the posterior inferior rim of the defect. The left bundle branches have marked posterior displacement with relative hypoplasia of the anterior bundle. Because of the posteriorly displaced branching bundle, the RBB has a long segment that travels very close to the defect's ventricular margin.

Ebstein's Anomaly

Ebstein's anomaly (EA) is defined by the failure of the tricuspid valve (TV) leaflet delamination with apical displacement of the functional tricuspid annulus hinge points. It is most notable for the high incidence of accessory pathways.

Sinus Node: Although EA is classically associated with an abnormal P wave, the sinus node does not deviate from its normal position.

Atrioventricular Node: The AVN is still localized in its classical position in the triangle of Koch. However, Koch's triangle tends to be of a smaller dimension than normal. The true AV junction used to define the triangle is discernible by a fibromuscular ridge in most patients. The nodal body tends to be located further towards the base of the triangle.[31] The AVN body can have an irregular shape (semilunar, ovoid, comma, spindle).

His-Purkinje System: Histologically, in 91%, the His bundle's entry point into the membranous septum tends to occur before the triangle's apex.[32] The right bundle is often intact but shows various histopathological features ranging from the encasement in dense fibroelastic tissue, to high septal connections between the RBB and the septum, to reports of the RBB being narrow and terminating a short distance from its origin.[31] These variations have been associated with the degree of septal leaflet and medial papillary muscle formation. The left bundle is reported to be normal.

Tricuspid Atresia

Tricuspid Atresia is defined by the congenital absence of the tricuspid valve, and consequently, there is no direct connection between the RA and RV.

Sinus Node: The sinus node is normally located (subepicardial at the sulcus terminalis).

Atrioventricular Node: The AVN is located in an underdeveloped and diminutive triangle of Koch.[33] There is no septal leaflet, but in most cases, a right atrial dimple can be identified anterior to the coronary sinus ostium, which indicates the absent tricuspid valve's theoretical site. The AVN lies posterior to the tendon of Todaro's insertion but is in contact with the right atrioventricular sulcus. Rarely, the AVN extends anteriorly beyond the insertion of the tendon of Todaro into the CFB.

His-Purkinje System: The His bundle may course through the myocardium on the left side or immediately become subendocardial on the left side. The presence and location of the VSDs determine the complete course of the His-Purkinje system. The distribution of the LBB typically favors the posterior part of the LV. The RBB tends to be distinctly elongated in its passage to the right septal endocardium, usually on the inferior aspect of the VSD.[34]

Pulmonary Atresia and Intact Ventricular Septum

Pulmonary Atresia and Intact Ventricular Septum is defined by atresia of the pulmonary valve with hypoplastic heterogeneity of the tricuspid valve and right ventricular cavity. The pulmonary valve is classically imperforate. The RV is classically tripartite with an inlet, trabecular, and outlet component, but in this congenital condition, there will be variable intracavitary muscular overgrowth with a bipartite ventricular only having an inlet and outlet portion (34%) and unipartite ventricular only having an inlet portion identifiable (8%). It can coexist with Ebstein's anomaly in approximately 10% of cases, which has conduction system implications. In up to 30% of patients, an RV-dependent coronary circulation exists. In patients with RV to coronary fistula resulting in RV-dependent coronary circulation, potential alteration in hemodynamics could compromise blood flow and lead to conduction system abnormalities.

Sinus Node: The sinus node is normally located (subepicardial at the sulcus terminalis).

Atrioventricular Node: The AVN is situated in the triangle of Koch.

His-Purkinje System: The LBB and RBB take a typical course,[35] but variations may be noticed if other conditions exist, specifically Ebstein's anomaly, as discussed previously.

Truncus Arteriosus

Truncus Arteriosus (TA) occurs because of a failure of neural crest tissue migration, which results in a single vessel providing coronary, pulmonary, and systemic arteries. Different phenotypes exist, ranging from confluent pulmonary arteries or absence of a pulmonary arch to interrupted aortic arch or severe coarctation. Usually, there is a single valve (truncal valve), which can be unicuspid or quadricuspid, but it is usually tricuspid. The atrium and ventricles are normally formed, so there are usually no abnormalities in the sinus and AVNs, as we mention later. The truncus usually overrides a large VSD and straddles the ventricles but may favor one ventricle; extremely rarely, the VSD may be absent, and in these cases, the TA exclusively arises from the RV.

Sinus Node: The sinus node is normally located (subepicardial at the sulcus terminalis).

Atrioventricular Node: The AVN is normally located in Koch's triangle.

His-Purkinje System: The penetrating bundle passes on the left side of the CFB with its subsequent course dependent upon the VSD type observed. The VSD is usually anteriorly located, analogous to the conal (infundibular) ventricular septum. It is located between the two limbs of the septomarginal trabeculation with the truncal valve as the superior boundary and ventriculo-infundibular fold posteriorly. Therefore there is usually a muscular discontinuity between the tricuspid and truncal valves (formed from the fusion of the inferior limb of the septomarginal trabeculation with the ventriculo-infundibular fold). However, there is rarely tricuspid and truncal valve continuity, making the VSD perimembranous. If the defect is perimembranous, then the conduction system travels posterior to the VSD.[36] In these cases, the LBB emerges before reaching the posteroinferior rim of the VSD.[37] The RBB travels on the posterior aspect of the rim and, after a long intramyocardial course, it penetrates the myocardium to reach the septomarginal band. It is of critical importance that if surgical expansion of the VSD is needed, this should comprise only the anterosuperior quadrant with avoidance of the defect's inferior border.

Tetralogy of Fallot

Tetralogy of Fallot (TOF) is classically described as four components; a VSD, an overriding aorta, right ventricular hypertrophy, and infundibular stenosis. These features are a consequence of anterocephalad deviation of the outlet septum. The VSD in TOF is classically an outlet perimembranous (80%), since there is a fibrous continuity between the leaflets and the aortic and tricuspid valves. In 20%, there is the fusion of the caudal limb of the septal band with the ventricular infundibular fold, which creates a muscular rim on the VSD. This rim has implications for the conduction system, as we discuss later. Often deemed an extreme variant of TOF, pulmonary atresia with ventricular septal defect (PA-VSD) differs from TOF

due to severe underdevelopment of the right ventricular outflow tract and proximal pulmonary artery, both of which are largely preserved in TOF.[38] Due to significant pulmonary atresia, PA-VSD often also encompasses major aortopulmonary collateral arteries (MAPCAs) which provide an alternative pulmonary circulation, although they do not appear to carry a mortality benefit.[39,40]

Sinus Node: The sinus node is normally located (subepicardial at the sulcus terminalis).

Atrioventricular Node: The AVN is normally located in Koch's triangle.

His-Purkinje System: In those with the perimembranous defect, the His bundle descends on the posterior rim's left ventricular aspect and is closest to the edge at the aortic-mitral tricuspid valvular continuity[41] (Figure 1.9). It has been reported that the septal crest may support conduction tissue in a minority of hearts. The LBB descends rapidly away from the VSD, and the RBB pierces the septum near the medial papillary muscle. In those cases wherein the defect creates a muscular posterior inferior rim (outlet muscular defect), this protects the conduction system.[42] Rarely a double committed juxta-arterial defect can be observed, and the conducting tissue is separate from the edge of the defect, similar to the outlet muscular defect.

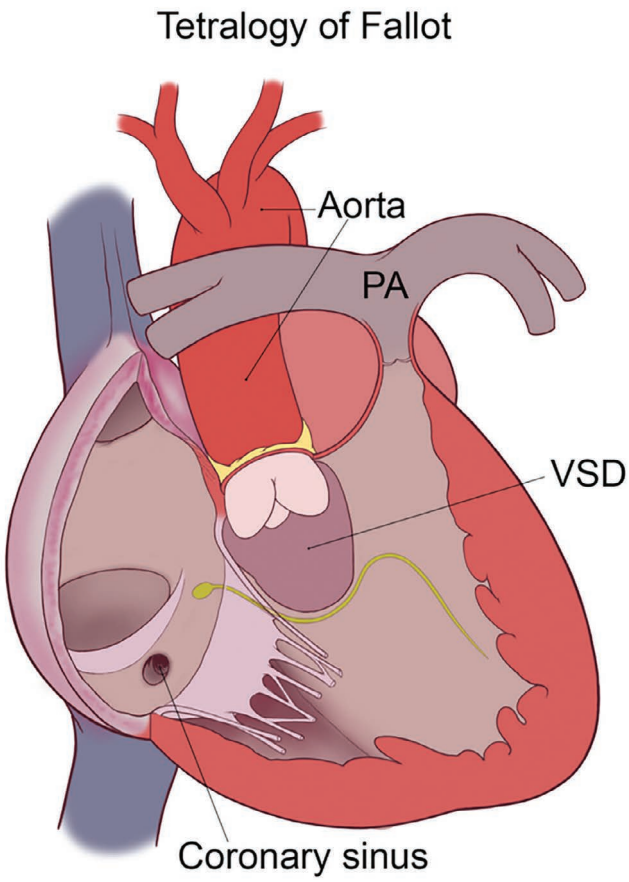

FIGURE 1.9 Relationship of the cardiac conduction system in tetralogy of Fallot. The AV node is usually located in Koch's triangle. In those with the perimembranous defect, the His bundle descends on the posterior rim's left ventricular aspect and is closest to the edge at the aortic-mitral tricuspid valvular continuity.

Congenitally Corrected TGA (cc-TGA) With Situs Solitus

Often referred to as L-transposition, the anatomical essence of this congenital defect is atrioventricular and ventriculoarterial discordance. In cc-TGA, the morphological right atrium is connected to the morphological left ventricle via the mitral valve, which pumps blood to the pulmonary system via the pulmonary valve and pulmonary artery, and the morphological left atrium is joined to the morphological right ventricle via the tricuspid valve, which pumps blood systemically via the aortic valve and aorta. In most cases, there is situs solitus with a left and anteriorly located aorta (in reference to the pulmonary artery), but there can be situs inversus in 10% of cases in which the aorta is located anterior but to the right of the pulmonary artery. There are key differences in the conduction system axis, depending upon whether the patient has solitus or inversus.

Sinus Node: The sinus node is normally located (subepicardial at the sulcus terminalis).

Atrioventricular Node: Two AVNs exist, an anterior and posterior AVN[43] (Figure 1.10). The posterior node is usually located at the apex of Koch's triangle but is hypoplastic and does not connect with the His-Purkinje system. This is a consequence of atrial and inlet ventricular septum malalignment. An anterior AVN is located at the right atrial appendage orifice and in proximity to the fibrous continuity between the pulmonary and mitral valves. The anterior node penetrates the annulus lateral to the pulmonary outflow tract at the fibrous continuity. The pulmonary trunk size is closely related to the degree of septal malalignment; with a small or absent pulmonary trunk, there is good septal alignment, and therefore there will likely be two nodes with a possible conduction tissue sling.[44]

His-Purkinje System: The His bundle, which anteriorly crosses across the pulmonary valve (just inferior to the pulmonary valve ring), descends onto the right side (morphological LV) of the septum. If there is a VSD (mostly perimembranous) present, it will pass along its anterosuperior margin. Upon reaching the ventricular septum, it bifurcates, with the RBB extending leftwards as a cord-like structure (to morphological RV). The LBB usually passes anteriorly down the junction of the anterior and middle portions of the morphological left (right-sided) part of the septum.

Congenitally Corrected TGA (cc-TGA) with Situs Inversus

Often referred to as D-looped ventricles with situs inversus, the conduction system in this condition differs significantly from L-transposition described earlier despite similar "congenitally corrected" hemodynamics.

Sinus Node: The sinus node is normally located but in the left atrium (which is right-sided).

Atrioventricular Node: Two AVNs exist, an anterior and posterior AVN. However, the posterior node is the primary node and normally related to the landmarks of the atrial septum, with the HB arising from this. The anterior node is usually well developed but does not make contact with the ventricular conduction system or myocardium. It is felt that the consequence of the good alignment seen between the interatrial and the interventricular septum is the connecting posterior node.

His-Purkinje System: If a VSD is present, the HB will travel along the inferior rim (in contrast to cc-TGA with situs solitus, which travels anteriorly). The bundle branches descend in the usual fashion.

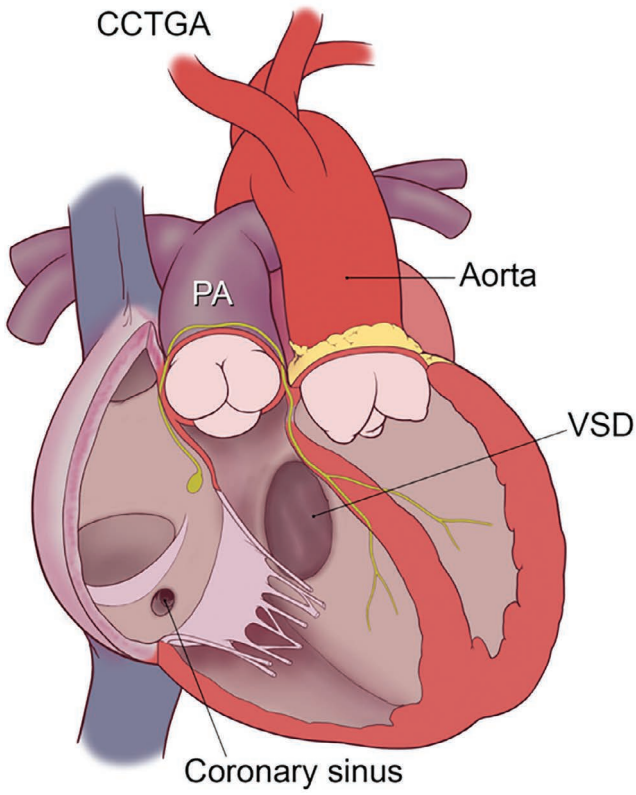

FIGURE 1.10 Relationship of the cardiac conduction system in congenitally corrected TGA (situs solitus). Two AV nodes exist, an anterior and posterior AVN. The posterior node is usually located at the apex of Koch's triangle but is hypoplastic and does not connect with the His-Purkinje system. An anterior AV node is located at the right atrial appendage orifice and in proximity to the fibrous continuity between the pulmonary and mitral valves. The anterior node penetrates the annulus lateral to the pulmonary outflow tract at the fibrous continuity. The His bundle, which anteriorly crosses across the pulmonary valve (just inferior to the pulmonary valve ring), descends onto the right side (morphological LV) of the septum. If there is a VSD (mostly perimembranous) present, it will pass along its anterosuperior margin. In situs inversus, two AV nodes also exist, an anterior and posterior AV node. However, the posterior node is the primary node.

Transposition of the Great Arteries (TGA)

In transposition of the great arteries (TGA), the aorta arises from the RV and the pulmonary artery from the LV. The most significant and frequently occurring lesions are VSDs, which are usually perimembranous defects or muscular defects.

Sinus Node: The sinus node is normally located (subepicardial at the sulcus terminalis).

Atrioventricular Node: The central fibrous body is abnormally shaped, often receiving fibrosis prongs from the mitral, tricuspid, and pulmonary annuli.[45] The CFB often engulfs the AVN.

His-Purkinje System: If a VSD is present, the peripheral conduction system will follow the typical VSD patterns described previously. With an intact ventricular septum, the penetrating HB enters the outflow tract underneath the pulmonary-mitral continuity and is then carried onto the ventricular septum (left side). The LBB is a more compact structure resembling a typical RBB.

Double Inlet Left Ventricle

Occurring in 1% of congenital malformations, double inlet left ventricle (DILV) is defined broadly as when both atrioventricular junctions (more than 50%) are supported by the same ventricle. The AV junction can have significant variation but usually has two separate valves or a common valve. Historically, this was often referred to as a univentricular heart since it was believed anatomically only one ventricle existed. However, we now understand this to be more of a functionally univentricular heart because there is a rudimentary ventricle (usually the right ventricle) that is usually small and redundantly located with the ventricular mass. It is usually found anterosuperior to the dominant ventricle, most frequently to the left and occasionally to the right. If there is a right ventricle dominant variation, the second rudimentary ventricle is posteroinferior, and similar to the LV dominant form, it is usually to the left. Rare cases have identified a purely dominant single ventricle (solitary ventricle of indeterminate pattern), wherein the rudimentary ventricle cannot be appreciated. In these cases, the single ventricle usually has coarse apical trabeculations suggestive that it is an RV, with the incomplete LV so small that it cannot be identified. This variation is found commonly in right atrial isomerism, which has implications in conduction tissue anatomy. The ventriculoarterial connections are usually discordant (transposed great arteries) when there is a dominant LV or an incomplete LV, and VSDs (often multiple) are present. Rarely they can be concordant, and this variant is often referred to as Holmes's heart. When the RV is dominant, there is also usually a double outlet. DILV can exist with any of the four possible atrial arrangements; right isomerism, left isomerism, usual arrangement, and mirror-imaged arrangement.

Sinus Nodes: Please see the discussion on Heterotaxy syndrome in regards to right and left isomerism. In mirror image arrangement, the morphological RA is in a left-sided position but contains the sinus node. The sinus node is normally located within the left-sided RA.

Atrioventricular Node: There are usually two nodes (anterior and posterior) that have developed. The posterior node is in its typical location and associated with the coronary sinus. It is hypoplastic and makes no connection to the conduction system. Meanwhile, the anterior node is well established and is situated at the intersection of the anterior interatrial septum and right atrial appendage. The AVN perforates the right AV valve annulus to enter the main ventricular chamber.

His-Purkinje System: The non-branching part of the bundle is dependent upon the location of the rudimentary chamber.[46] If it is left-sided, the bundle takes a more comprehensive course, and it travels anterior to the annulus of the pulmonary outflow tract and then onto the right margin of the VSD. If it is right-sided, the non-penetrating bundle travels lateral to the outflow tract before traversing the rim of the VSD. Regardless of the rudimentary chamber, the bundle courses along the right-sided rim of the VSD and is located on the left ventricular aspect of the trabecular septum.

Double Outlet Right Ventricle

Double outlet right ventricle (DORV) contains a spectrum of anatomical and physiological variations. The consensus definition states that it is a type of ventriculoarterial connection in which both great vessels arise either entirely or predominantly from the right ventricle, implying that more than 50% of each of the great vessels arise from the morphological right ventricle.[47] Simplistically, it can be categorized as:

1. *Tetralogy of Fallot type*: The VSD is in a subaortic location, with the aorta spiraling from right to left in relation to the pulmonary trunk. There is associated pulmonary stenosis as a consequence of a VSD with infundibular deviation.
2. *Taussig-Bing variant*: The VSD is in the subpulmonary location with the aorta to the right of the pulmonary trunk and parallel to it.
3. *VSD type*: VSD is in the subaortic location with the aorta spiraling right to left relative to the pulmonary trunk, similar to the TOF type, but there is no pulmonary stenosis.
4. *Single-ventricle type*: This is an uncommon variant with a non-committed VSD.

Sinus Node: The sinus node is normally located (subepicardial at the sulcus terminalis) unless there is atrial isomerism.

Atrioventricular Node: In the Taussig-Bing variant, the CFB is small and abnormally formed. It may only consist of the mitral and tricuspid annuli, with no pulmonic or aortic contribution; rarely, there may be a pulmonary prong of tissue to help form the CFB.[48] The AVN is often short but is usually located.

His-Purkinje System: The TOF type conduction anatomy is described earlier. In the Taussig Bing type, the VSD is subpulmonic and usually extends posteriorly to be perimembranous.[49] The His bundle is long and travels through the ventricular septum to the left side, reaching the left posterior wall of the VSD. It travels along this VSD edge at varying distances to the edge. Similar to VSDs previously discussed, if a muscular posterior inferior rim exists from the fusion of the posterior limb of the septomarginal trabeculation with the ventriculo-infundibular fold, the conduction axis is protected. At the distal portion of the defect, the His bundle divides into the RBB and LBB. Rarely this bifurcation can occur at the proximal portion of the inferior wall of the defect. At the distal end of the defect the RBB can come in close contact with the defect as it penetrates the septum to the right side.

Heterotaxy (Isomerism of Atrial Appendages)

Heterotaxy syndrome is a general term that encompasses abnormal lateralization of the abdominal viscera, thoracic organs, and cardiac segments. The conduction system is complex in these patients, given the atrial isomerism and abnormal atrioventricular and ventricular arterial connections.[50] Heterotaxy syndrome can be divided into a right atrial isomerism (RAI) subtype (sometimes referred to as asplenia syndrome) or left atrial isomerism (LAI) subtype (sometimes referred to as polysplenia syndrome). Right atrial isomerism is characterized by appendages, each having the morphology of the normal right appendage. In RA isomerism, pectinate muscles are extensive (the degree of the pectinate muscles is the universal criterion for morphological rightness) and are located around the atrioventricular junction and meet at the crux of the heart. In left isomerism, both appendages have normal left appendages, pectinate muscles only within the appendage, and a smooth atrial vestibule directly confluent with the venous components.

Sinus Nodes: The atrial situs determines the position and number of sinoatrial nodes (Figure 1.11). In right isomerism, bilateral nodes exist and are located at the roots of the SVC. In cases with unilateral SVC, sinus nodes can still be found bilaterally and with the additional sinus node located at the SVC's expected root. Hypoplastic nodes are observed if found in cases of left atrial isomerism and in hearts that can often be difficult to find. If a node is found, it usually lies to the right

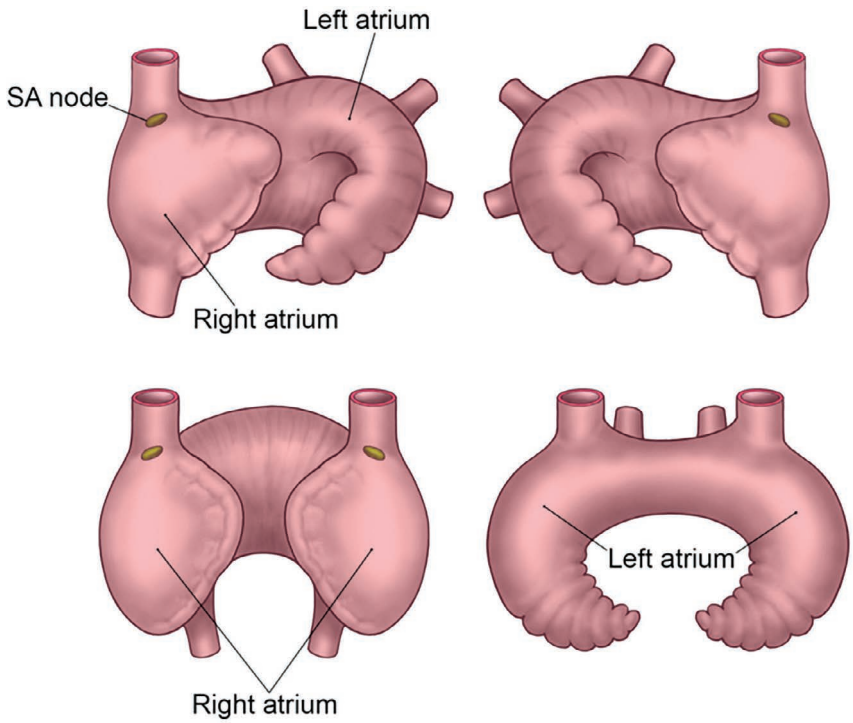

FIGURE 1.11 Impact of atrial isomerization on the number and location of the sinus node. In normal heart (top left image) and mirror image (top right image) the sinus node is located at the sulcus terminalis. In right isomerism (bottom left image), bilateral nodes exist and are located at the roots of the SVC. Hypoplastic nodes are observed if found in cases of left atrial isomerism (bottom right image) and in hearts that can often be difficult to find.

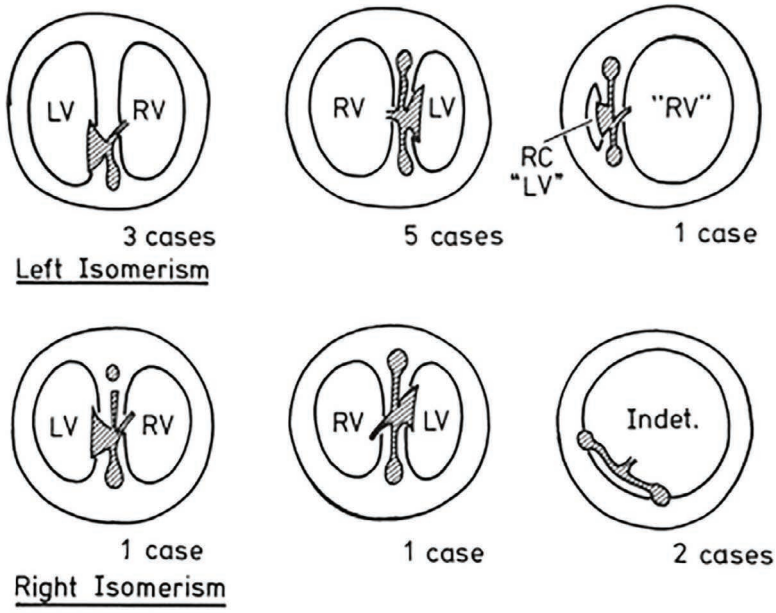

FIGURE 1.12 Impact of left and right isomerism on AV conduction system. In left isomerism, the atrioventricular node is present in its normal position when there is a biventricular connection with normal ventricular morphology (D-looped ventricle), and a single AV node is usual. Dual AV nodes are more common in L-looped morphology or a univentricular heart of predominant right ventricular types. In these cases there is a well-defined sling of specialized conduction tissue that transverses the inferior rim of the VSD. In right isomerism, dual AV nodes are common, with one node in its typical triangle and the second node in the anterior position. Variations have been reported in the second node, and in univentricular hearts, it can be located at the left lateral atrioventricular sulcus.

(With permission from Dickinson DF, Wilkinson JL, Anderson KR, Smith AU, Ho SY, Anderson RH. The cardiac conduction system in situs ambiguus. Circulation. 1979;59:879–85.)

within the right-sided atrium near the appendage. When found in the left-sided atrium, it is usually located inferiorly.

Atrioventricular Node: The disposition of the AVN is complex and relies largely on the atrioventricular connection and the ventricular topology (Figure 1.12). The AV connection can be biventricular or univentricular. RAI has a univentricular morphology commonly (typically double inlet via a common atrioventricular valve). In right isomerism, dual AVNs are common, with one node in its typical triangle and the second node in the anterior position.[51] Variations have been reported in the second node, and in univentricular hearts, it can be located at the left lateral atrioventricular sulcus. These nodes are often linked by a conduction tissue sling (discussed later). In cases with a double inlet to an indeterminate ventricle, the nodes are located inferiorly and left inferolaterally and joined by a sling of conduction tissues. This sling is located within the posteroinferior wall of the solitary ventricular chamber. A solitary strand of conduction tissue arises from this sling, potentially reminiscent of a right bundle branch. Interestingly, a third hypoplastic node was reported in a superolateral position with no connection to the AV conduction axis.

In left isomerism, the AVN is present in its normal position when there is a biventricular connection with normal ventricular morphology (D-looped ventricle), and a single AVN is usual. Dual AVNs are more common in L-looped morphology or a univentricular heart of predominant right ventricular types. In these cases, a second AVN is usually present (in the anterior part of the atrial septum), and there is a well-defined sling of specialized conduction tissue that transverses the inferior rim of the VSD.

His-Purkinje System: The HB travels on the inferior rim of the VSD.[50] Sometimes a prominent trabeculation is observed in univentricular hearts. The sling does not make histological contact with both nodes in some cases (often those with presumed D-looping). A solitary fascicle of conducting tissue arises from the sling in the univentricular hearts. Normal right and left bundle branches are present in the morphologically appropriate ventricles, but in one case, only the LBB was present. In LAI, the sling of conduction tissue is frequently discontinuous with the penetrating bundle. The bundle branches arise from the sling and follow an anatomical course comparable with the ventricle's morphology to which they are related.

Conclusion

This chapter highlights and provides critical knowledge of the cardiac conduction system's development and morphological aspects in both normal and abnormal hearts. The complexity of congenital heart anatomy (and their variations) can result in various conduction system abnormalities. The following basic points will help readers understand and remember when to expect an abnormal or normal conduction system. The sinus node is primarily located subepicardially at the sulcus terminalis, and in congenital defects, it is usually in this position unless atrial isomerization is present. The AVN is classically located in Koch's triangle, but any degree of septal malalignment should raise suspicion for abnormal AVN location or the possibility of two AVNs. Lastly, ventricular conduction tissue primarily runs on the inferior rim of ventricular septal defects.

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Chapter 2
TACHYCARDIA MECHANISMS IN CHILDREN WITH NORMAL HEARTS AND IN PATIENTS OF ALL AGES WITH CONGENITAL HEART DEFECTS

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Introduction

It is reasonable to assume readers of a textbook dedicated to catheter ablation already possess an understanding of basic electrophysiology. This chapter is therefore not intended as a comprehensive review of the topic, but will focus instead on mechanisms and clinical presentations that are most relevant to pediatric patients, as well as patients of any age with congenital heart disease (CHD). Multiple features set these groups apart from the typical adults with cardiac arrhythmias, ranging from differences in cell physiology to variance in body size and cardiac anatomy that can have profound influences on timing and performance of invasive procedures. An overview of such features will be provided here, with more detailed discussion of specific items in chapters that follow.

Unique Rhythm Features in Children and Patients with Congenital Heart Disease

Table 2.1 lists tachycardias found in the pediatric and CHD populations. Although there is considerable overlap with arrhythmia mechanisms seen in adult patients with structurally normal hearts, an understanding of unique challenges presented by young patients and those with CHD is essential for effective management.

Electrophysiology of the Developing Heart

Immature heart cells differ from mature myocytes in terms of enhanced spontaneous depolarization of pacemaker cells to generate faster rates, and shorter refractory periods to allow these rates. The differences are not of major importance during clinical evaluation and treatment, but do confirm that cellular properties change with age, which may explain why certain tachycardias in neonates (e.g. chaotic atrial tachycardia, accelerated idioventricular rhythm) often resolve spontaneously over the first year of life, while others may not become manifest until older ages. Immature myocytes also differ in terms of their higher dependence on extracellular calcium for excitation-contraction coupling, which is the likely explanation behind the profound negative inotropic effect of intravenous verapamil on the infant heart.[1]

Maturational changes also occur at the level of the specialized conduction tissues. It is known from histopathologic study that slow pathway extensions elongate progressively relative to size of the compact AV node between birth and teenage years.[2] The fact that AV nodal reentrant tachycardia (AVNRT) is uncommon before adolescence could be linked to this evolving morphology. Similarly, accessory atrioventricular pathways (APs) can change during early months of life. Benson and colleagues[3] demonstrated that more than 30% of newborns with manifest preexcitation and documented tachycardia will have resolution of the delta wave and be non-inducible with esophageal atrial stimulation by age one year. This may be caused by ingrowth of fibrous tissue along the AV valve or changes in the AP itself, but in all events, the potential for spontaneous regression influences how AP-mediated tachycardias are managed in very young patients. Medical therapy is favored during infancy to allow growth and a chance for natural cure prior to ablation unless there are compelling reasons to proceed early (e.g. tachycardia-induced myopathy, cardiac arrest, multidrug failure, or impending CHD surgery).

TABLE 2.1: Tachycardia Mechanisms in Children and Patients with Congenital Heart Disease

Supraventricular Tachycardia (SVT)
Accessory Pathway (AP)
Bidirectional pathway (WPW syndrome)
Unidirectional retrograde pathway ("concealed")
Permanent junctional reciprocating tachycardia (PJRT)
Unidirectional anterograde pathway
Atriofascicular pathway
AV nodal reentrant tachycardia (AVNRT)
Slow-fast
Fast-slow
Other
*Twin AV node reentry**
Ectopic atrial tachycardia (EAT)
Chaotic atrial tachycardia (CAT)†
Typical atrial flutter (AFL)
*Intra-atrial reentrant tachycardia (IART)**
Atrial fibrillation (AFib)
Junctional ectopic tachycardia (JET)
Congenital
Postoperative*
Ventricular Tachycardias (VT)
Accelerated ventricular rhythm†
Focal VT
LV septal fascicular VT
Macroreentrant monomorphic VT
Polymorphic VT

*Specific to congenital heart disease.
†Specific to neonates.

Influence of Congenital Heart Disease

Congenital heart defects can interfere with development of the sinus node and the AV conduction tissues. The most striking examples involve heterotaxy with abnormalities of atrial situs and discordant connections of the atria and ventricles (see Chapter 17). Heterotaxy can be subcategorized as polysplenia (left atrial isomerism) or asplenia (right atrial isomerism). In the former condition, a true sinus node may be absent and complete heart block is common, while in the latter, there may actually be two separate sinus nodes, and not infrequently, the AV conduction system will be duplicated in an arrangement

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referred to as "twin AV nodes" that can support a variety of reentrant tachycardias.[4]

Even simpler forms of CHD can have abnormalities of conduction tissues. One of these is congenitally corrected transposition of the great arteries (cc-TGA or L-TGA) where the compact node develops outside Koch's triangle in an anterior location near the base of the right atrial appendage. This displaced node can be feeble and deteriorate over time, so that complete heart block is seen in 5% of patients at birth and more than 25% by adulthood. Displacement of the AV node also occurs in patients with endocardial cushion defects. These hearts lack a true triangle of Koch, and the compact node will consequently be found at an inferior location beneath the mouth of coronary sinus.

The incidence of accessory pathways in most forms of CHD is no higher than in the general population, with the notable exceptions of Ebstein's anomaly and some cases of cc-TGA (which can have an Ebstein's-like malformation of the left-sided tricuspid valve). Patients with Ebstein's have an extraordinarily high incidence of accessory pathways in the range of 20–30% that tend to localize to the region where the tricuspid valve is most abnormal.[5]

Apart from congenital conduction abnormalities, the hemodynamic stress of CHD and the tissue injury resulting from surgical repairs can have a negative impact on rhythm status. Fibrosis and hypertrophy in combination with conduction barriers along surgical scars all combine to create a substrate that is highly conducive to development of macroreentrant tachycardias. These occur predominantly at the atrial level, especially after the Mustard/Senning operations for transposition of the great arteries or the Fontan operation for single ventricle. Macroreentrant ventricular tachycardias (VT) can also develop in some CHD lesions, most notably tetralogy of Fallot.

Arrhythmia-Induced Cardiomyopathy in Young Patients

Some incessant tachycardias presenting during childhood can result in severe ventricular dysfunction. Tachycardia-induced cardiomyopathy is well described in all age groups and can be caused by a variety of mechanisms,[6] but among pediatric patients, the most common culprits are ectopic atrial tachycardia (EAT), the permanent form of junctional reciprocating tachycardia (PJRT), and focal automatic VT. These tachycardias must always be considered in the differential diagnosis for any young patient with new onset cardiomyopathy. All are treatable with catheter ablation to allow prompt recovery of function.

Size/Age/Anatomic Considerations

Small size is the most distinguishing feature of the pediatric patient and influences all aspects of arrhythmia management, especially catheter ablation procedures. Equipment must be tailored to patient size, and the level of sedation must be sufficient to ensure comfort and immobility which often necessitates a general anesthetic. Vascular access must be planned carefully within the constraints of vessel caliber, downsizing to 4 or 5 Fr catheters when necessary, and economizing on catheter number by combining functions (Figure 2.1). Compulsive mapping is required to minimize unproductive ablation lesions, and caution is required when ablating within or near the reduced dimensions of Koch's triangle. Finally, radiation exposure must be minimized in young patients who remain at risk for stochastic tissue injury over many decades after procedures.

The distorted anatomy that accompanies complex CHD will confound both ablation and implant of rhythm management devices regardless of patient size. It is imperative that the operator has clear understanding of a specific defect as well as surgical patching and vascular redirection involved with its repair. Clear registration of underlying anatomy with echocardiography, cardiac MRI, cardiac CT, angiography, and/or intracardiac echo is essential (Figure 2.2).

Fetal Tachycardia

Another unique consideration in the pediatric population is tachycardia occurring in the fetus. The most practical approach to rhythm analysis is fetal echocardiography, in which M-mode recordings of atrial and ventricular wall motion are used in conjunction with Doppler flow analysis to provide an accurate construct of rhythm status (Figure 2.3 and Video 2.1). The most common mechanisms for fetal tachycardia are AP-mediated

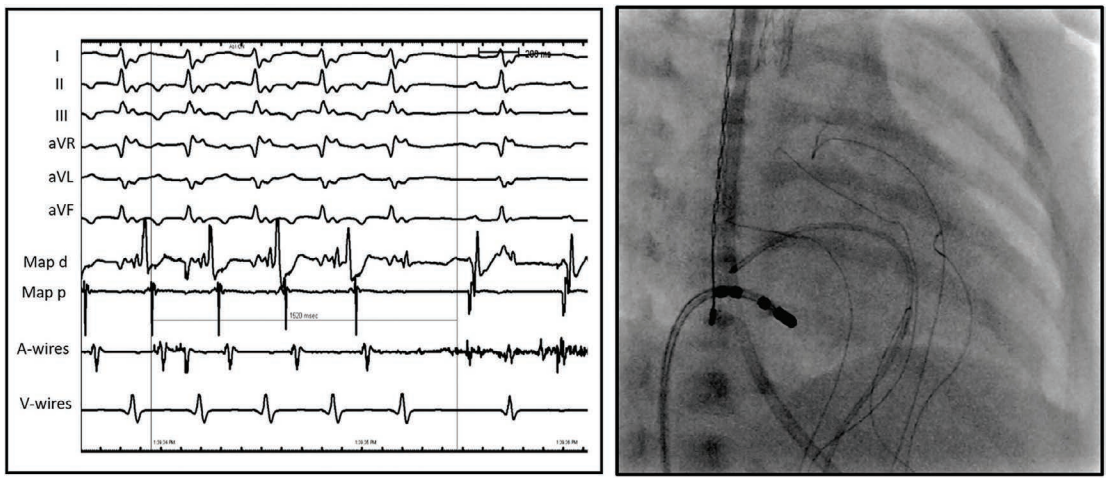

FIGURE 2.1 Six-day-old infant following emergent palliative surgery for severe Ebstein's anomaly, who developed intractable orthodromic tachycardia involving a concealed accessory pathway along the inferior tricuspid valve. After failure of aggressive medical therapy, ablation was performed using a single 5 Fr catheter (4 mm tip) while utilizing postoperative atrial and ventricular pacing wires for additional pacing and recording. The pathway was interrupted less than 2 seconds into the radiofrequency application.

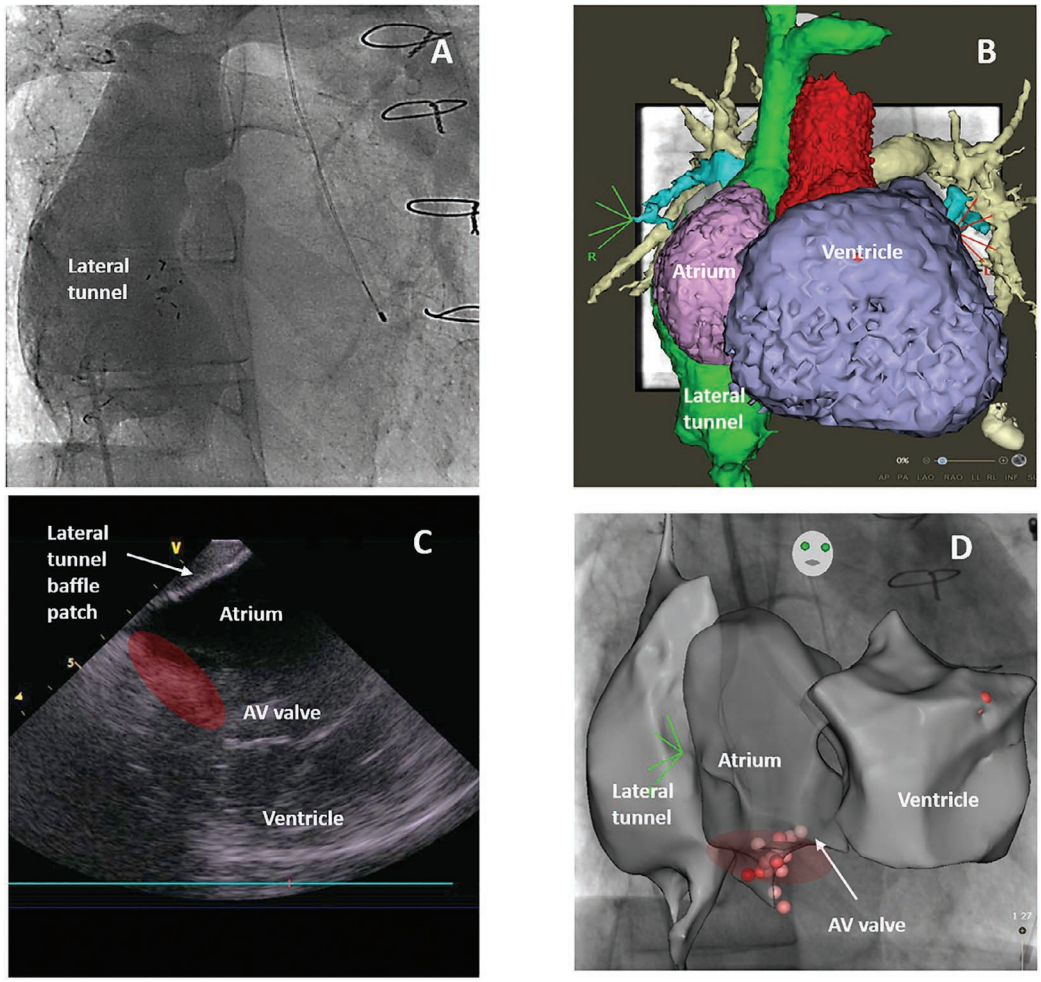

FIGURE 2.2 Multimodality imaging used during ablation of intra-atrial reentrant tachycardia in a patient with double inlet single left ventricle palliated to a lateral tunnel Fontan. (A) Angiography in AP projection showing lateral tunnel Fontan baffle. (B) Segmented cardiac CT showing Fontan baffle (green), atrium (pink), single left ventricle (purple), aorta (red), pulmonary veins (blue), and pulmonary arteries (beige). (C) Intracardiac echocardiogram defining baffle patch, atrium, atrioventricular valve, and ventricle. The red shaded area marks the isthmus between the AV valve and the IVC aspect of the lateral tunnel, which was the critical corridor for this circuit. (D) RAO view showing anatomic reconstruction and the red shaded site of successful ablation, which was reached by transbaffle puncture.

reentry and atrial flutter (AFL), either of which can become incessant in utero and result in cardiac decompensation with fetal hydrops, culminating in some cases with fetal demise. In utero treatment can be difficult, but effective control can be achieved in many instances by transplacental diffusion of antiarrhythmic drugs administered to the mother. If tachycardia cannot be controlled and the fetus remains compromised, early delivery is the best remaining option assuming fetal lungs have matured sufficiently to tolerate extrauterine life. Fetal AFL, once converted, rarely recurs if the infant has a structurally normal heart, but APs can remain problematic throughout the neonatal period and beyond.

Mechanisms for Supraventricular Tachycardia in Pediatric and CHD Patients

Supraventricular tachycardia (SVT) accounts for the vast majority of pediatric ablation procedures. Among patients with structurally normal hearts, the mechanism in roughly half the cases involves an AP, a quarter AVNRT, about 10% EAT, and the remainder an assortment of uncommon disorders. The profile is much different for patients with CHD in whom macroreentrant atrial tachycardias dominate.

Accessory Pathways

Tachycardias involving an AP may begin as early as fetal life but the frequency peaks during infancy and again during adolescence. Multicenter data indicate that Wolff-Parkinson-White (WPW) syndrome involving APs capable of bidirectional conduction is present in more than 50% of pediatric patients undergoing ablation, while APs with unidirectional retrograde conduction (concealed APs) are identified in approximately 40%.[7] Pathways with unidirectional anterograde conduction (conventional atrioventricular connections as well as atriofascicular pathways) can also be seen in pediatric patients, though their incidence is low. Approximately 10% of pediatric patients undergoing ablation will be found to have multiple APs, seen most commonly among those with Ebstein's anomaly or cardiomyopathy.

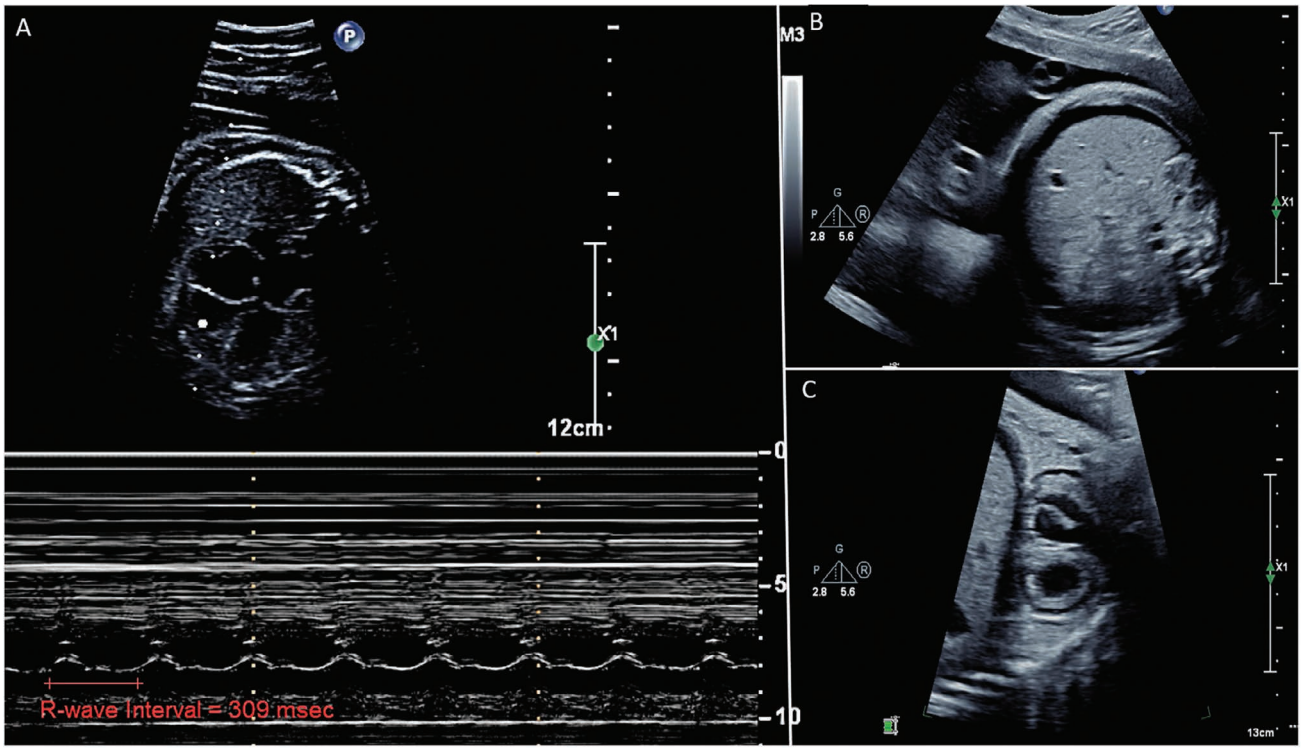

FIGURE 2.3 (A) Fetal echocardiogram with 4-chamber view and corresponding M-mode of the atrium and ventricle during tachycardia with CL 309 ms and 1:1 AV relationship. Fetal hydrops is suggested by ascites (B) and pericardial effusion (C).

The initial presentation for pediatric patients with manifest WPW usually involves sustained orthodromic reciprocating tachycardia. Those old enough to verbalize symptoms will be brought to medical attention promptly, but infants and young children who are preverbal may escape detection and remain in SVT for hours or even days, resulting in congestive heart failure at presentation. Apart from the occasional case involving an atriofascicular pathway, antidromic reciprocating tachycardia is quite rare as a presenting arrhythmia in pediatric patients, but will be induced occasionally during electrophysiologic study. Preexcited atrial fibrillation (AFib) with rapid anterograde conduction over the AP is clearly the most concerning presentation for WPW at any age. Preexcited AFib is rare in infants and toddlers but is well documented beginning in school-aged children.

Management of young patients with symptomatic WPW syndrome varies according to age. The infant age group is managed medically unless there are extenuating circumstances that justify above-average ablation risks.[8] Older children with symptomatic WPW are referred for catheter ablation as soon as the clinician judges the risk of an invasive procedure to be lower than the risks of continued medical therapy or break-through SVT. This calculation is patient-specific and institution-specific, taking into account age/size, severity of symptoms, likely AP location based on ECG pattern, center experience, and the presence of any comorbidities.

Although the risk for sudden cardiac death in all series examining children and adolescents with WPW is numerically low, it can be a sentinel event in the young age group. For this reason, when a WPW pattern is detected incidentally in an asymptomatic child, it is recommended that some attempt be made to evaluate the anterograde conduction potential with either exercise testing, ambulatory monitoring, or electrophysiology study. A consensus document from the Pediatric and Congenital Electrophysiology Society published in 2012 considered persistence of the delta wave at maximum heart rates, short AP refractory periods, induction of SVT, multiple pathways, and short preexcited RR intervals during AFib, all to be indications for elective AP ablation in asymptomatic children with a WPW pattern, whereas asymptomatic patients with intermittent preexcitation and/or abrupt loss of the delta wave in response to sinus tachycardia could be followed conservatively.[9] However, more recent pediatric data have raised concern regarding the predictive accuracy of noninvasive risk-assessment. Poor concordance has now been demonstrated between intermittent preexcitation and data obtained by invasive EP testing in young patients,[10] and a multicenter study of children with WPW who suffered life-threatening events found that nearly 25% failed to meet accepted criteria for high risk.[11] This has resulted in a more aggressive approach to ablation in asymptomatic young patients, although careful consideration must still be given to size and anticipated pathway location.

For pediatric patients with orthodromic SVT due to a concealed AP in whom the risk of preexcited AFib is absent, those with symptoms will still usually undergo elective ablation at some point, but as long as episodes can be managed with vagal maneuvers or relatively benign medications, this can be deferred to allow growth to a size the clinician considers appropriate.

An important subclass of concealed AP is the slowly conducting variety that causes PJRT (Figure 2.4). The age of presentation is variable since rates are slow compared to conventional SVT, and may not cause significant symptoms until tachycardia-induced myopathy develops. Flecainide is one of the few