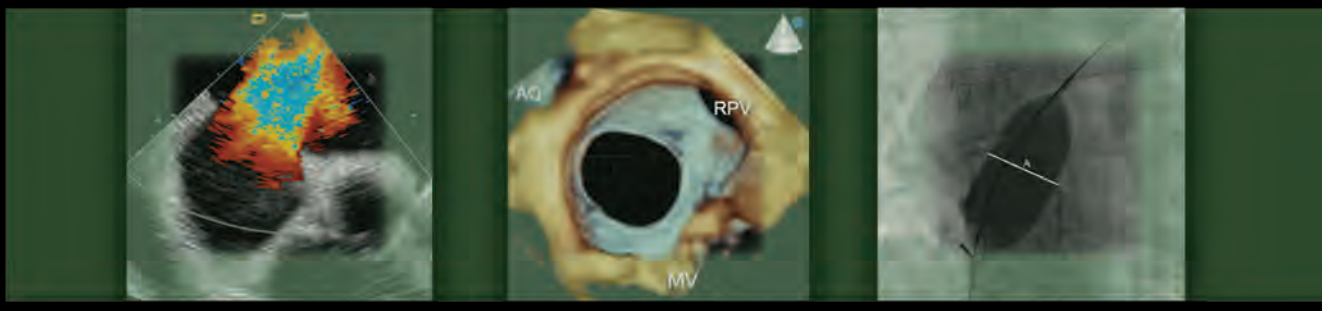
TRANSCATHETER CLOSURE OF

ASDs AND PFOs

A COMPREHENSIVE ASSESSMENT



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Foreword

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Reflecting on my own 49-year career as a pediatric cardiologist, it is hard to comprehend what has been achieved in the repair of atrial septal defects (ASDs) during that period of time. While still in medical school, I had the privilege of witnessing a very new and exciting "open heart" surgical closure of an ASD. This was accomplished using the new technique of hypothermic cardiac arrest (ice in a bathtub). At the time, this intracardiac repair was undoubtedly revolutionary, but the actual procedure seemed barbaric, too. Even as a medical student, I knew there had to be a better way. By the time I began my cardiology residency a few years later, cardiopulmonary bypass had become almost routine. With that, the surgical repair of ASDs already was being considered a simple and low-risk procedure. But, in addition to the risks of the early bypass procedures, it still required opening the chest and the heart, which, at the very least, was quite uncomfortable for the patient, the parents, and the physicians caring for them.

In 1966, Dr. William J. Rashkind published his paper on the improbable procedure of using a catheter with a balloon at its tip for the *creation* of ASDs in very sick infants *in the catheterization laboratory*. This procedure was to replace the high-risk, "closed" surgical procedure that was used for the same palliation. The Rashkind septostomy procedure saved thousands of infants' lives, but of probably equal importance, it stimulated the creative imagination of many pediatric cardiologists. If we could create defects in the septum with a catheter, why couldn't we close cardiac defects with a catheter-delivered device? Early and fairly crude devices for closure of the patent ductus appeared almost immediately. But the dream for a catheter-delivered device for atrial septal defects was not realized, even in its most rudimentary form, for almost another decade. Once demonstrated to be

feasible, the procedures and devices for catheter-delivered device closure of ASDs evolved into the standard of care over the next three decades.

Transcatheter Closure of ASDs and PFOs: A Comprehensive Assessment provides a comprehensive view of the long and arduous course taken in order to progress from the surgical repair of secundum ASDs, to the early devices, and finally to the more sophisticated catheter devices and procedures, which we now take for granted. It also extensively covers the technical aspect of the earlier as well as the very latest devices along with the details of the procedures for implanting them and the particular advantages and problems of each device.

Considering the progress that has occurred in catheter closure of ASDs since the 1970s, it is hard to imagine that, in the ensuing three or four decades, there could possibly be comparable advances in the management of ASDs. But, although we now have effective and safe catheter-delivered devices applicable for almost 80% of atrial defects, the goal of the perfect device/procedure still leaves much to be accomplished in the future. The ultimate catheter-delivered atrial septal occlusion device will have to be simple to implant, delivered through an even smaller catheter system, preferably leave no residual or permanent foreign material in the body, and have no real or potential risks to the patient.

For the practitioner today, this book presents a wealth of practical material that is invaluable for the current management of ASDs and provides a glimpse into the future of treating them.

Preface

Interest in the atrial septal defect (ASD) and patent foramen ovales (PFOs) was sparked in the mid-1970s when Terry D. King, MD, an interventional cardiologist, and Noel Mills, MD, a cardiac surgeon, performed the first transcatheter closure of an ASD on a 17-year-old female. Since that time, interventional congenital cardiologists have been on a mission: to create devices and procedures that enable physicians to close defects in the atrial septum as effectively as our colleagues in surgery do, and of course without the morbidity of open surgery.

When Steven Korn from Cardiotext Publishing approached us to write a book, we were not sure what to write about. We have edited a few books in the past related to different topics in congenital and structural heart disease intervention. But while we were discussing the project, we were surprised to realize that there is no book dedicated to the atrial septum at all. Therefore, the idea of writing such a book was born.

We have assembled the best of the best to contribute to this exciting project, organizing their work in four sections that comprehensively present the most important areas of knowledge for today's practitioners.

Part I discusses anatomy, pathophysiology, and natural history. We believe that every physician treating patients with ASDs and PFOs should have full knowledge of the anatomy, pathophysiology, and natural history of the disease process. Part II addresses imaging of the septum and the assessment of the defects, reviewing all of the imaging modalities, from transthoracic and transesophageal echocardiography to computed tomography and magnetic resonance imaging of the septum. Part III focuses on the technical aspects of closure of ASDs and PFOs. Each chapter discusses in detail specific technical details encountered in clinical practice. And part IV examines the devices available to

interventional cardiologists. We made every attempt to include all available devices. If a device was not mentioned, this was not intentional. Also, we were as careful as possible to be fair when providing details about the most commonly used devices.

We hope that you will enjoy reading this book, and we know that you will glean information that will help you take care of your patients.

We would like to thank all of our patients. It is from them that we collect images for teaching ourselves to be better doctors.

Finally, we would like to give a big thank you to Steven Korn, Mike Crouchet, and Caitlin Crouchet with Cardiotext Publishing and to Zan Ceeley with Trio Bookworks for keeping us on time and providing us with the best support to achieve this project.

—Ziyad M. Hijazi,
Ted Feldman,
Mustafa H. Abdullah al-Qbandi,
and Horst Sievert

Acknowledgments

I want to thank Steve Korn, Mike Crouchet, and Caitlin Crouchet from Cardiotext Publishing for their efforts in pushing hard for this book. I would like to thank and dedicate this book to all my patients all over the world with ASDs and PFOs who I treated over the years—you have taught me what I know today. I want to thank my family for their support during the writing of this book and throughout my professional career, which would have been impossible without their help, dedication, and understanding. Finally, I want to thank Dr. Charles "Chuck" Mullins for agreeing to write the foreword. Dr. Mullins has been a great friend for many years and his contributions to our field are seen every day in our catheterization laboratories.

ZH

Special thanks to our patients, who have formed the basis of our experience. A great cath lab axiom says, "Good judgment comes from experience, and experience comes from bad judgment." One of the best outcomes from this book that we can hope for is the sharing of experience and a contribution to procedure decision making for many of our colleagues that comes without the expense of too many difficult procedures. Shared learning in the interventional community is transmitted in many forms, and we hope this book and the collected knowledge and experience it contains will be among them.

TF

I would like to express my gratitude to the staff at Hospital for Sick Children in Toronto, who taught me the essentials of pediatric cardiology. It was my great fortune to have a chance to work with Dr. Robert M. Freedom and Dr. Jeff Smallhorn, who played a key role in upgrading my academic career as a pediatric cardiologist, from resident to staff position, during the period of 1995–2001. During my career in Kuwait, I came to know Professor Ziyad M. Hijazi, who used to help us in some difficult interventional cases during his many visits to Kuwait. I would like to very much thank Professor Hijazi for his continuous teaching and giving me a chance in being one of the editors of this book. Finally, I would like to thank my wife and children, for their patience and consideration, and to dedicate this book to my mother and father. My family's love and support during this endeavor has been of the utmost importance.

MHAQ

Dr. Ziyad M. Hijazi suggested that we all should write a paragraph of acknowledgment. My initial thought was that it would not be appropriate to thank our families in this kind of book. However, Ziyad replied "of course you can thank your family! I did!"

So I take this opportunity to thank my family, my children Nìko, Inga, Eiko, and Kolja, and especially my lovely wife, Nicola, not only for their help regarding this book but for their patience and continuous support over the years.

HS

PART I

Anatomy, Pathophysiology, and Natural History

1

Anatomy of the Atrial Septum

Akash R. Patel, Lisa C. A. D'Alessandro, and Paul M. Weinberg

Normal Atrial Septal Embryology and Anatomy

The atrial septum is composed largely of the septum primum and septum secundum. The septum primum has its embryological origin from the atrial roof and migrates anteriorly and somewhat inferiorly toward the endocardial cushions. The space between the crescent-like septum primum and the atrioventricular endocardial cushions is the embryonic ostium primum. The most superior aspect of the septum primum forms a half-moon shape with the two ends typically attaching to the left side of the septum secundum. During the growth of the septum, the space between the two septa constitutes the ostium secundum. Once the septum primum attaches to the septum secundum, this space becomes the foramen ovale. The inferior portion of the septum primum is contiguous with the vestibular spine, a structure that originates from the right pulmonary ridge and provides for the joining of the septum primum with the endocardial cushions and the closure of ostium primum. This region becomes muscularized and transitions to the gossamer valve of the fossa ovalis, viz., septum primum.

Septum secundum forms as an infolding of the roof of the atria at the point of indentation by the embryonic truncus, to the right of the septum primum.[1] As will be discussed later, in certain cases the septum secundum may be very shallow or nonexistent and may not be adjacent to the septum primum. The leading edge of the septum secundum becomes the superior limbus of the fossa ovalis and normally allows apposition of the valve of fossa ovalis and therefore

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functional closure of the ostium secundum (foramen ovale). Thus the foramen ovale (or fossa ovalis), between these structures, is not a true deficiency in the atrial septum but rather an interatrial communication, which is vital in prenatal circulation. The atrial septation nears completion by 3 months gestation; although in most cases the septum primum is cellophane-like until the end of gestation or even after birth, with muscularization continuing postnatally (Fig 1.1).

Anatomically, the atrial septum is composed of an interatrial portion, dividing the left and right atrium, and an atrioventricular portion, dividing the right atrium and left ventricle.[1,2] The interatrial portion is composed of septum primum, septum secundum, and part of the atrioventricular canal septum. The interatrial portion measures 4- to 8-mm thick in adolescents and adults except for the valve of the fossa ovalis, which measures 1 mm in thickness.[3] The atrioventricular portion is composed of the atrioventricular canal septum. The muscular portion of the atrioventricular septum measures approximately 10 mm in thickness, and the membranous portion measures 1 mm.[3] With age, the atrial septum thickens and anatomic sealing of the patent foramen ovale occurs in two-thirds of patients[4,5] (Fig 1.2).

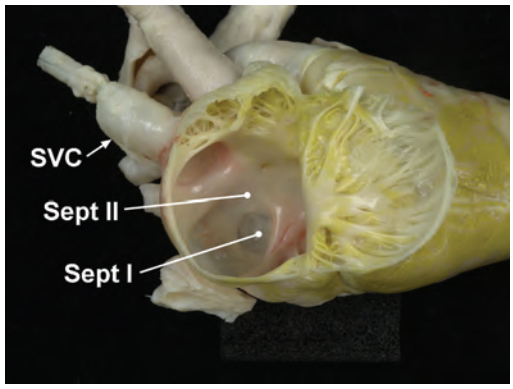

Fig 1.1A—Right atrial view of atrial septum in an infant. Septum primum (Sept I) is the thin flap valve of the foramen ovale, which closes against the thick muscular septum secundum (Sept II). Sept II is medial to the entrance of the superior vena cava (SVC).

Structures adjacent to the septum are important when considering atrial septal anatomy.[1,3,4] Anterosuperiorly, septum secundum abuts the right aortic sinus of Valsalva. The atrioventricular portion of the atrial septum lies anteroinferiorly and adjacent to the septal leaflet of the tricuspid valve and the right coronary–noncoronary aortic commissure. This region contains the atrioventricular node. Consideration should also be given to the systemic venous connections, right pulmonary veins, coronary sinus, and eustachian valve when determining atrial septal interventions.

Patent Foramen Ovale

As mentioned before, the patent foramen ovale is a gap between the septum secundum, which forms the limbus of the fossa ovalis, and septum primum, which forms the flap valve that covers the fossa ovalis.[1,6,7] Based on autopsy studies, the patent foramen ovale is circular to elliptical in shape and located in the anterosuperior portion of the atrial septum. The patent foramen ovale diameter ranges from 1 to 19 mm with a mean of 4.9 mm.[8] The patent foramen ovale length, also referred to as the tunnel length, ranges from 3 to 18 mm with a mean of 8 mm.[7] Both the diameter and length increase with age but not

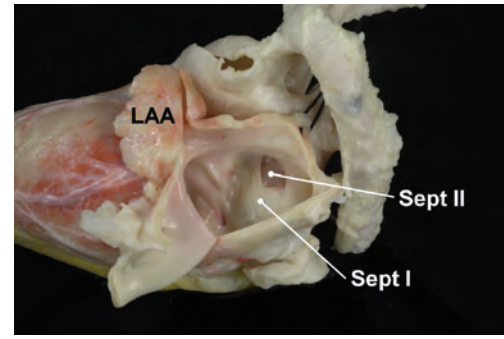

Fig 1.1B—Left atrial view of atrial septum in an infant. Note the half-moon shape of the superior margin of Sept I as it attaches to Sept II. This is the location of the foramen ovale. Abbreviation: LAA, left atrial appendage.

body surface area. The mean diameter is 3.4 mm in the first decade of life and 5.8 mm in the 10th decade of life.[8] It is important to note that there are limited evaluations on size correlation between those based on pathologic specimens and those obtained by echocardiography and balloon sizing.

The effective size of the foramen ovale is not only dependent on the size of the space between the two septal components but also the degree of valvar competency.[9] Valvar competency occurs when there is appropriate apposition of the valve of the fossa ovalis and septum secundum to completely cover the foramen ovale. There can be valvar incompetency in three scenarios. First, stretching of the superior limbus of the fossa ovalis seen in atrial dilation leads to a lack of apposition with the valve of fossa ovalis. Second, aneurysmal formation of the septum primum prevents complete closure of the interatrial communication. Third, the patent foramen ovale can be associated with deficiencies of septum primum, resulting in a true secundum ASD.

When choosing the correct closure device, consider the mechanism of the interatrial communication and the relationship of the patent foramen ovale to its surrounding structures. The patent foramen is located in the superior portion of the atrial septum.[8] The crescentic superior boundary of the foramen is the superior limbus of the fossa ovalis—the muscular septum secundum.[6] There is no true inferior boundary as mentioned because this defect is a flap-valve communication that creates a tunneled interatrial communication.[10] However, the superior margin of the septum primum has a rather consistent half-moon shape that forms the lower boundary of the foramen ovale. Based on an autopsy study, the average distance from the patent foramen ovale to the superior vena cava is 12.2 mm and 8.1 mm to the aortic annulus.[7] These measurements did not increase with age but rather with increasing body surface area.[7]

Ostium Secundum ASD

Ostium secundum atrial septal defects (ASDs) are the most common ASDs. The defects are due to deficiency in septum primum or, rarely, an "unguarded" foramen ovale from deficiency in septum secundum.

The vast majority of these defects are a complete absence (Fig 1.3), deficiency (Figs 1.4 and 1.5), or multiple fenestrations of septum primum (Figs 1.6 and 1.7).[11–13] When the fossa ovalis valve is absent, the defect is typically circular. The superior limbus forms the superior and posterosuperior boundaries of the defect. The absence of the fossa ovalis valve may result

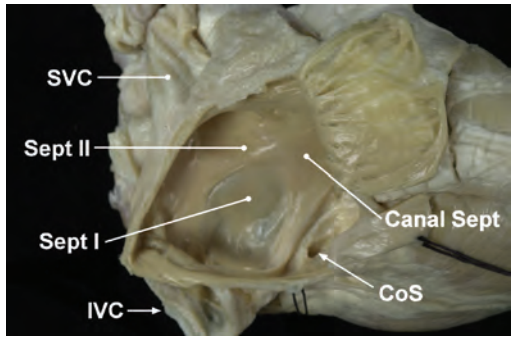

Fig 1.2A—Right atrial view of mature atrial septum. Sept I is thick and muscularized. The superior margin as seen from the right atrial side is the fossa ovalis. Sept II covers Sept I. Between Sept I and the atrioventricular valve is the canal septum (Canal Sept). Abbreviations: CoS, coronary sinus ostium; IVC, inferior vena cava.

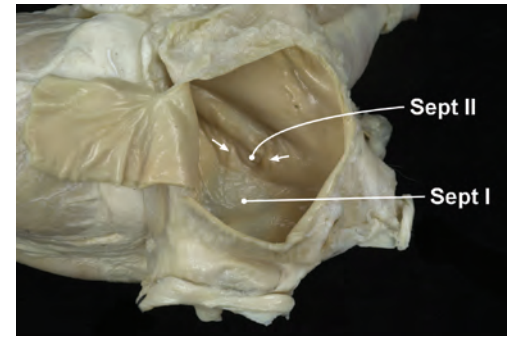

Fig 1.2B—Left atrial view of mature atrial septum. Even though the foramen ovale is sealed, the two attachments of Sept I to Sept II (arrows) with the intervening half-moon shape of the superior margin of Sept I are easily visible.

in shallow posteroinferior and inferior rims. The atrial floor between the superior limbus and the atrioventricular septum does however form an anterior ridge. With deficiency of the valve of the fossa ovalis, the ASD is typically elliptical in shape and centrally located but can assume almost any shape or location within septum primum. The rims include the remaining septum primum plus septum secundum superiorly and posteriorly, the canal septum anteriorly, and septum primum plus left venous valve of the inferior vena cava inferiorly. Similarly, fenestrations can be variable and located anywhere in the contiguous septum primum, which can result in variable amounts of rim. In situations in which either atrium is dilated, septum primum may become stretched, while the two main attachments on either side of the half-moon shaped superior edge remain fixed. This stretching of septum primum results in incompetence of the fossa ovalis valve, and may be considered the "foramen ovale" type of ostium secundum ASD without there being frank deficiency of septum primum.

A rare cause of an ostium secundum ASD is complete absence or incomplete development of the superior limbus of septum secundum, typically in association with left-sided juxtaposition of the atrial appendages.[11–13] The superior limbus from posterosuperior to anterosuperior is underdeveloped or absent because of the marked rightward position of the great arteries (which normally indent the roof of the atria and initiate the infolding, which results in septum secundum). Not only does the absence or shallow nature of septum secundum result in the inability to form the flap-valve mechanism of the fossa ovalis, but in many cases, septum primum is deviated markedly to the left with its superior portion positioned horizontally with attachment to the left lateral atrial wall between the two juxtaposed appendages. This results in an ASD located in the half-moon–shaped septum primum between the right atrium, superiorly, and the left atrium, inferiorly. What would have been the superior rim is insufficient and formed by the lateral atrial wall. The posteroinferior, inferior, and anteroinferior rims are sufficient and formed by the valve of the fossa ovalis.

The secundum ASD type, size, and shape can vary greatly. It is important to note that all these defects involve the fossa ovalis and do not include the vena cava, right pulmonary veins, coronary sinus, or atrioventricular valves. However, relationships to these structures remain important when considering device closure.[3,5] Identification of the enface anatomic rims viewed from the right atrial surface are defined as follows[14]: the posterosuperior rim is the distance to the superior vena cava, the anterosuperior rim is the distance to the aorta, the posteroinferior rim is the distance to the inferior vena cava, the anteroinferior rim is the distance to the tricuspid valve. Other

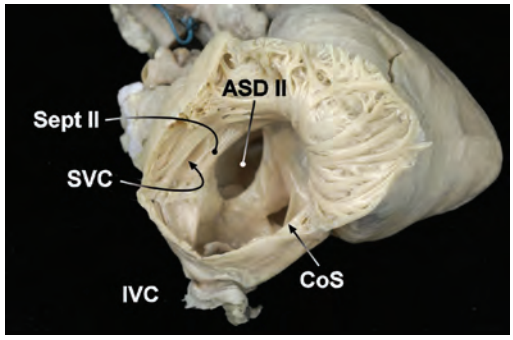

Fig 1.3A—Right atrial view of large ostium secundum atrial septal defect (ASD II). Sept II forms the superior margin of the defect and the canal septum the anterior margin. Variable amounts of inferior and posterior rims are present.

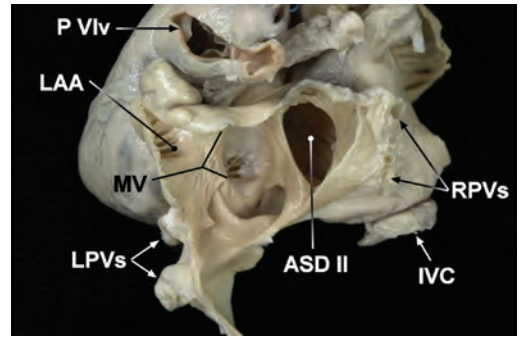

Fig 1.3B—Left atrial view of same defect. Note the relationship of the defect to the right (RPVs) and left pulmonary veins (LPVs) and to the mitral valve (MV).
Abbreviation: P Vlv, pulmonary valve.

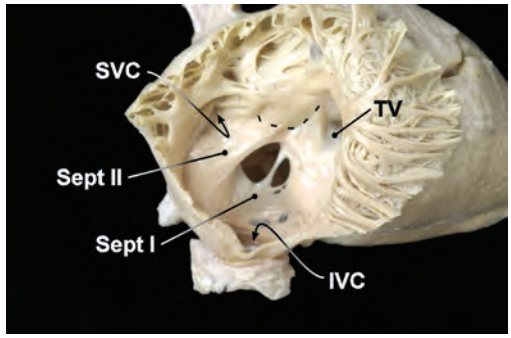

Fig 1.4A—Right atrial view of ASD II with persistent remnants of Sept I. Note the location of the right sinus of Valsalva (dotted line) within the anterosuperior rim of the ASD. Abbreviation: TV, tricuspid valve.

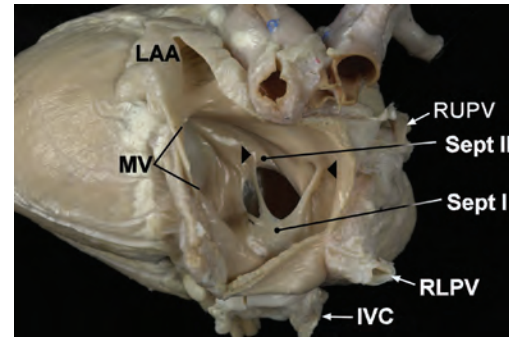

Fig 1.4B—Left atrial view of same defect. Note the persistent attachments of Sept I to Sept II (black arrows). Abbreviations: RLPV, right lower pulmonary vein; RUPV, right upper pulmonary vein.

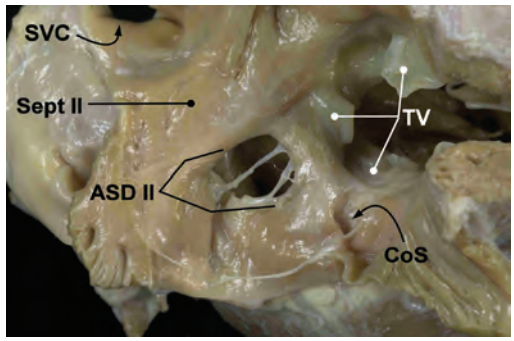

Fig 1.5A—Right atrial view of ASD II with strands of persistent Sept I. Note relationship to tricuspid valve (TV) and coronary sinus ostium (CoS).

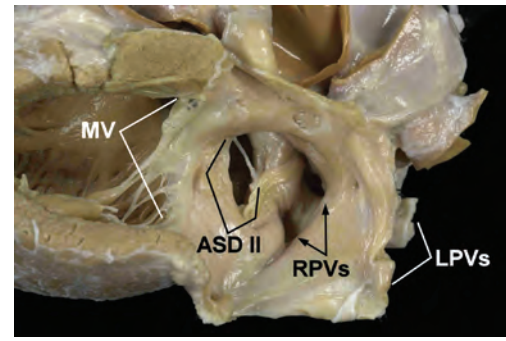

Fig 1.5B—Left atrial view of same defect. Note proximity to mitral valve (MV).

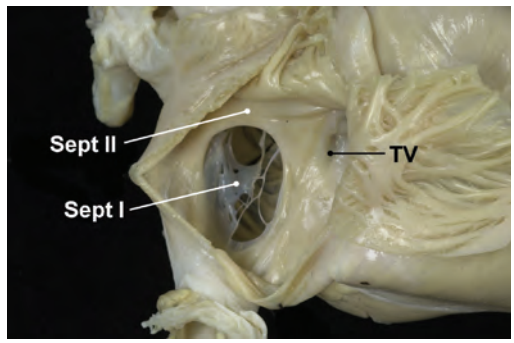

Fig 1.6A—Right atrial view of fenestrated Sept I.

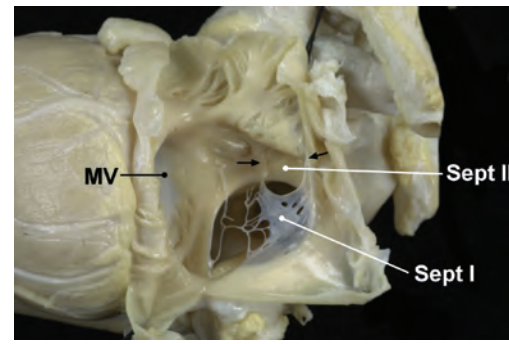

Fig 1.6B—Left atrial view of same defect. Note the normal attachments of Sept I to Sept II (black arrows).

nearby structures to avoid with device closure include the coronary sinus and the right pulmonary veins. Also the left venous valve of the inferior vena cava, which is normally adherent to the atrial septum, may be separated from it by several millimeters. In that situation it can be confused with the posteroinferior rim, but is not capable of anchoring a device. Furthermore, the eustachian valve can also be mistaken for the inferior rim of an ASD.

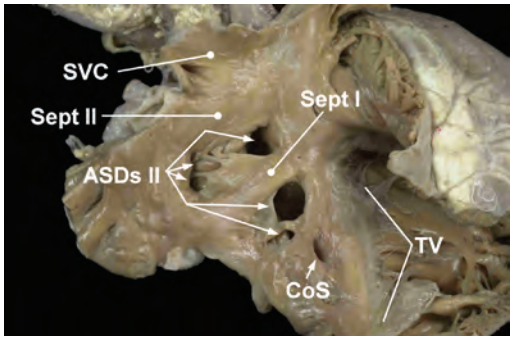

Fig 1.7A—Right atrial view of multiple ASDs II within muscular Sept I.

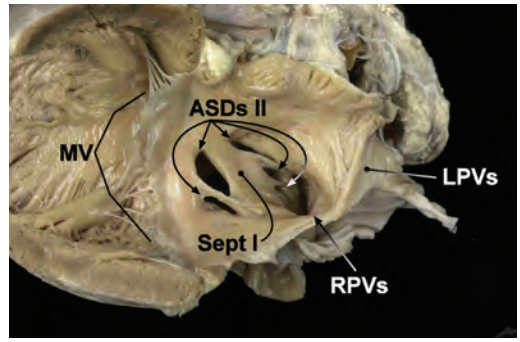

Fig 1.7B—Left atrial view of same defects.

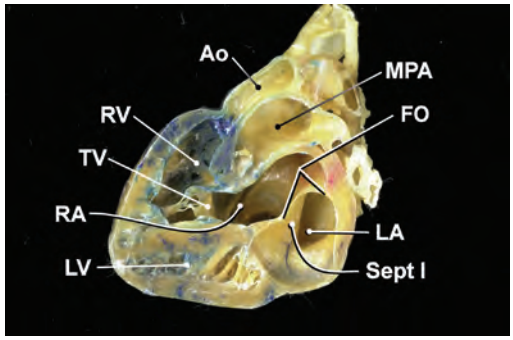

Fig 1.8A—Left-sided juxtaposition of atrial appendages, sagittal section, right side. Note horizontal Sept I with unguarded foramen ovale (FO) permitting blood flow between superiorly located right atrium (RA) and inferiorly located left atrium (LA). Abbreviations: Ao, aorta; LV, left ventricle; RV, right ventricle.

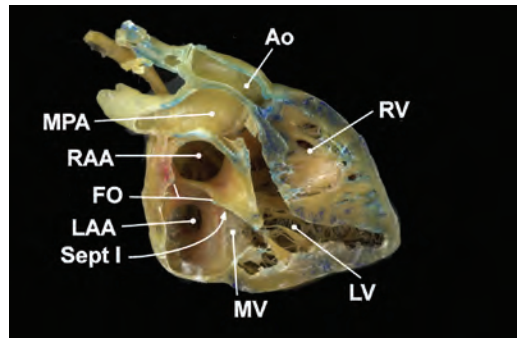

Fig 1.8B—Left side of same specimen demonstrates the horizontal Sept I extending to the lateral atrial wall between left atrial appendage (LAA) and right atrial appendage (RAA).

Deviation of Septum Primum

Leftward and/or posterior deviation of the atrial septum is another mechanism of interatrial communication. There are four different types of deviation of septum primum: (1) that seen with left-sided juxtaposition of the atrial septum (described earlier); (2) deviation of the anterosuperior portion of septum primum relative to septum secundum associated with hypoplasia or atresia of the left-sided atrioventricular valve, usually as part of hypoplastic left heart syndrome; (3) deviation of the anterior portion of septum primum in the setting of unbalanced atrioventricular canal at atrial level, also known as double outlet right atrium; and (4) deviation of the posterior aspect of the atrial septum to the left of some or all pulmonary vein orifices.

In juxtaposition of the atrial appendages, the atrial septum may have a horizontal orientation at its superior aspect when there is little or no septum secundum (Fig 1.8). The half-moon–shaped opening at the upper end of septum primum, being "unguarded" by septum secundum, is effectively an ostium secundum ASD. The margins of the defect are septum primum anteriorly, rightward, and posteriorly, and atrial wall leftward.

Leftward and posterior deviation of the anterosuperior portion of septum primum is the second most common atrial septal configuration in hypoplastic left heart syndrome. Most

of these cases have mitral and aortic atresia. In one series of 129 patients with left atrioventricular valve hypoplasia (129 patients with normally aligned great arteries and two ventricles, 29 with double outlet right ventricle [DORV], and 8 with single ventricle), 62 patients had deviation of the atrial septum primum.[15] Although casual inspection appears to show a large ostium secundum ASD from apparent absence of septum primum at its expected location immediately to the left of septum secundum; in fact, septum primum is present but, being deviated to the left, leaves a gap between the two septa (Fig 1.9). Furthermore, the superior aspect of septum primum is attached to the roof of the left atrium near the mouth of the atrial appendage rather than to the left side of septum secundum. Once again there is an "unguarded" foramen ovale far to the left of septum secundum making it more difficult to pass a catheter across the foramen ovale. In addition, the left atrium is usually quite small making balloon septostomy challenging if one can enter the left atrium. Unlike the normally attached septum primum where increased pulmonary venous return after birth stretches the foramen ovale, some cases of this form of displaced septum primum can actually lead to postnatal obstruction of the foramen ovale as septum primum is forced against the roof of the atrium.

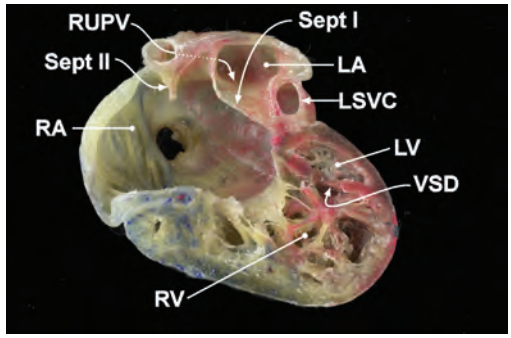

Fig 1.9A—Lower section of four-chamber view of hypoplastic left heart with leftward displacement of Sept I relative to Sept II. Note how Sept I forms a hood over right upper pulmonary vein (RUPV). These patients typically have mitral atresia (ie, no connection between left atrium [LA] and left ventricle [LV]). This case has a small LV with a ventricular septal defect (VSD). There is also a persistent left superior vena cava (LSVC).

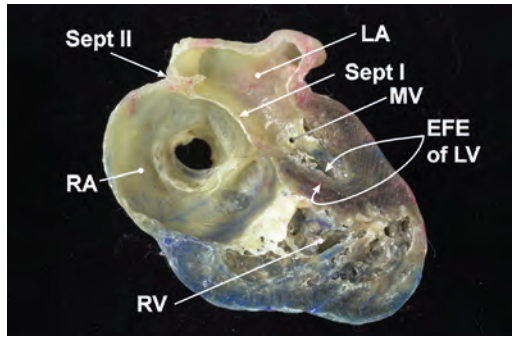

Fig 1.9C—Comparison view of specimen with hypoplastic left heart but normal atrial septum, that is, Sept I attached to Sept II. These patients typically have a patent MV and often have endocardial fibroelastosis (EFE) of the left ventricle (LV).

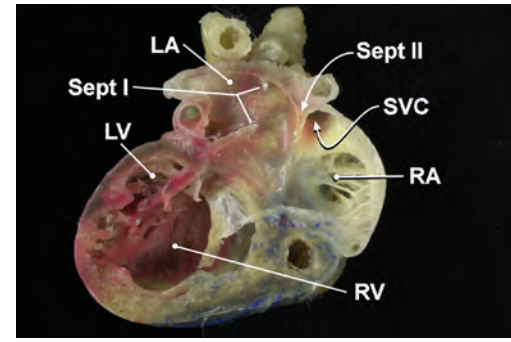

Fig 1.9B—Upper section of same specimen. Note the large gap between the two attachments of Sept I to the roof of left atrium (LA) and Sept II, in its normal location, medial to superior vena cava (SVC).

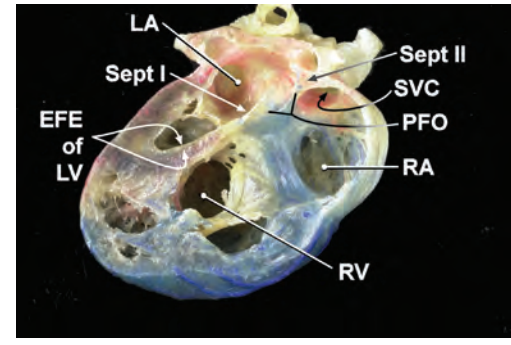

Fig 1.9D—Upper section of same specimen as in part C. Note that there is no gap between attachments of Sept I and Sept II.

Fig 1.9 continues on following page

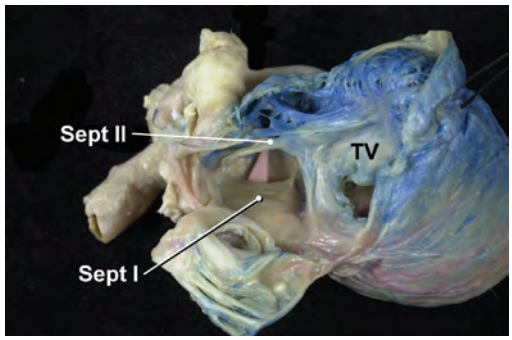

Fig 1.9E—Right atrial view of case similar to parts A and B with marked displacement of Sept I away from Sept II. Arrow-shaped probe in foramen ovale.

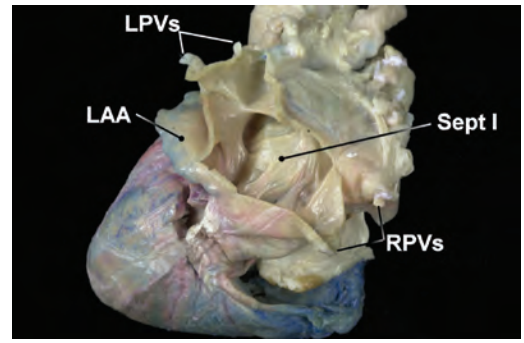

Fig 1.9F—Left atrial view of same specimen as in part E. Note small volume of left atrium with Sept I attached closer to pulmonary vein entrances than normal. However, pulmonary veins are still to the left of Sept I.

Deviation of the anterior portion of septum primum in cases of common atrioventricular canal is a rare form of unbalanced canal at the atrial rather than ventricular level.[16] Similar to the previous type, the surgeon's view from the right atrium can be mistaken for a common atrium with absence of the atrial septum, when, in fact, the atrial septum is deviated far to the left of its expected location. As such, the deviated septum can be mistaken for the left atrial free wall with associated common atrium. Thus if the apparent ASD is closed with a patch, significant pulmonary venous obstruction can result from the persistent deviated atrial septum. In this form the left atrium "sees" only a small fraction of the left side of the common AV valve, while the right atrium "sees" both sides of the valve—so-called double outlet right atrium.

Leftward deviation of the posterior aspect of septum primum is a rare but important etiology of intracardiac partial or total anomalous pulmonary venous return but with normal pulmonary venous connection.[17] In other words, the pulmonary veins enter the left atrium normally, but the septum primum is attached to the left of some or all of the pulmonary veins. In this situation, there is a large left-to-right shunt at the atrial level (anomalous pulmonary venous *return*) despite normal pulmonary venous *connection*. The degree of displacement can be described relative to the entrance of the pulmonary veins: between the right and left pulmonary veins, or lateral to the entrance of the left pulmonary veins. When the septum is to the left of all pulmonary veins, systemic output is from that portion of pulmonary venous return that passes through the foramen ovale. Unlike total anomalous pulmonary venous connection, the streaming of pulmonary venous blood through the foramen ovale yields normal systemic saturation; whereas in total anomalous pulmonary venous connection the systemic flow is mildly desaturated because of total mixing at right atrial level.

Interatrial Communications Not Amenable to Device Closure

Coronary sinus defects, sinus venosus defects, and ostium primum ASDs are interatrial communications that are not amenable to catheter-based device closure because of the anatomic nature of the lesions.

Coronary sinus defects are quite rare, occurring in < 1%, and are not true defects in the atrial septum.[18] Rather there is an interatrial communication that exists due to a defect in the wall between the coronary sinus and the left atrium—the sinus septum (Fig 1.10). The defect

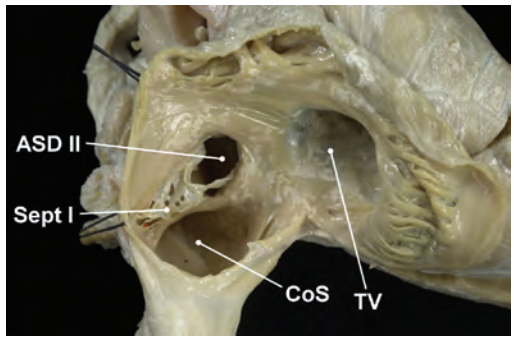

Fig 1.10A—Right atrial view of enlarged coronary sinus ostium (CoS) and ASD II in a patient with a partially unroofed coronary sinus (shown in part B). Note the fenestrations in Sept I. Although there appears to be a lower rim to the ASD II, the sinus septum (shown in part B) would, most likely, preclude proper seating of a device. The CoS is effectively an ASD because of the ability for left atrial blood to pass from left atrium (LA) through the sinus septal defect to the CoS to the right atrium (RA).

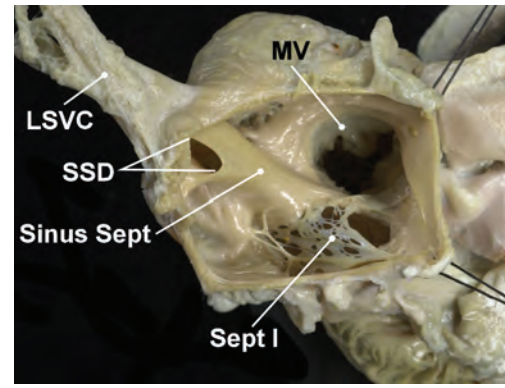

Fig 1.10B—Left atrial view of same specimen as in part A. Note left superior vena cava (LSVC) to coronary sinus ostium (CoS) with the sinus septum (Sinus Sept) indicated. There is a sinus septal defect (SSD) in this wall between the dilated CoS and the left atrium (LA). There are two sites of left-to-right shunt: through the fenestrated Sept I and through the SSD to CoS.

is often located at the site of the coronary sinus ostium with a dilated coronary sinus. It is inferior and anterior to the fossa ovalis and superior and anterior to the inferior vena cava-right atrial junction. The coronary sinus is either partially or completely unroofed.[18] In the partially unroofed coronary sinus, the boundaries of the defect are the remnants of the coronary sinus septum.[19–22] In the completely and incompletely unroofed coronary sinus, the perceived defect viewed from the right atrium is actually the coronary sinus ostium.[18,23] The coronary sinus defect is usually associated with a persistent left superior vena cava and in the completely unroofed defect, the left superior vena cava attaches to the roof of the left atrium.[23,24] Surgery is required to close the sinus septal defect or reroute the left superior vena cava, so that device closure of the coronary sinus ostium defect is not advisable. These defects are often associated with a variety of other congenital cardiac malformations.

Sinus venosus defects account for 4% to 11% of atrial level communications and are also not true defects in the atrial septum.[18] Rather there is an interatrial communication created by an abnormal connection of the right pulmonary vein or veins, the superior vena cava, or the inferior vena cava to both atria such that the mouth of the vein(s) or cava straddle the atrial septum.[25–28] The most common variant is the sinus venosus defect of the superior vena cava type. [25,29,30] In this instance, the right upper and/or middle pulmonary vein insertions straddle the atrial septum at the superior vena cava-to-right atrial junction (Fig 1.11). This results in the creation of an interatrial communication from the left atrium to the right atrium. The anterior and inferior boundary of the defect is the posterosuperior portion of the septum secundum. The remaining boundaries are the ostia of the pulmonary veins and superior vena cava. Rarely one can see a superior vena cava alone straddling the septum—so-called right superior vena cava to left atrium[31]—with essentially normal pulmonary venous connection (Fig 1.12). This too is a form of sinus venosus defect of the superior vena caval type. The other major sinus venosus defect is that of the inferior vena cava type.[25,30] In this instance, the inferior vena cava straddles the atrial septum, usually without pulmonary venous abnormality (Fig 1.13), but occasionally with involvement of the right lower pulmonary vein. This creates an interatrial communication

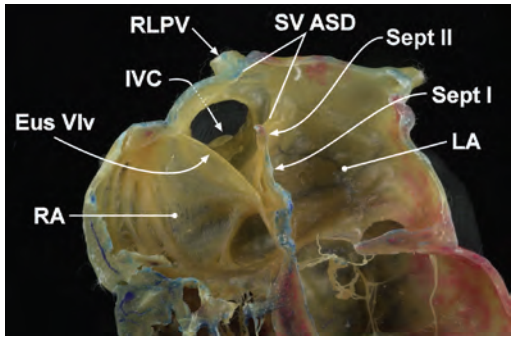

Fig 1.11A—Four-chamber view, inferior half showing a sinus venosus atrial septal defect (SV ASD). Note the entrance of the right lower pulmonary vein (RLPV) behind the atrial septum—both Sept II and Sept I. Even though this part of the defect is close to the inferior vena cava (IVC), the IVC is entirely to the right of the septum indicating that it is the mouth of the RLPV that *is* the SV ASD. Abbreviation: Eus VIV, Eustachian valve.

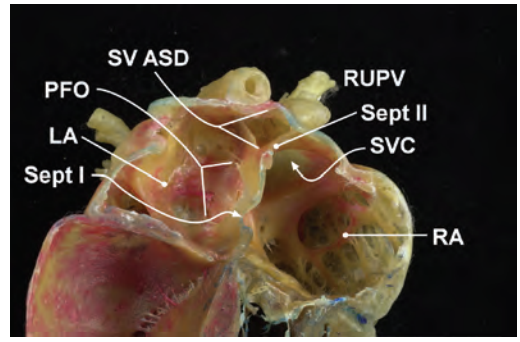

Fig 1.11B—Superior half of specimen shown in part A. Right upper pulmonary vein (RUPV) straddles the atrial septum behind Sept II and Sept I, both of which are well formed (ie, not defective). Note that the SV ASD is relatively remote from the patent foramen ovale (PFO) and from the entrance of the superior vena cava (SVC).

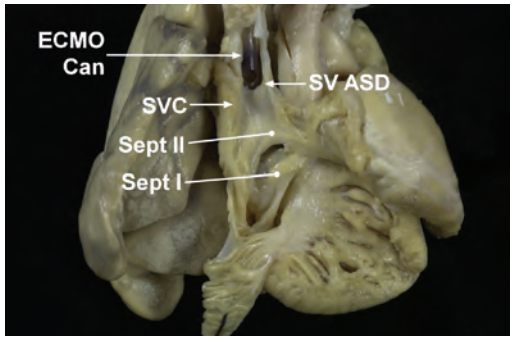

Fig 1.12—Right atrial and opened superior vena cava (SVC) view of SV ASD demonstrating an ECMO cannula (ECMO Can) passing through the defect to the left atrium. The atrial septum itself—Sept I and Sept II—looks normal.

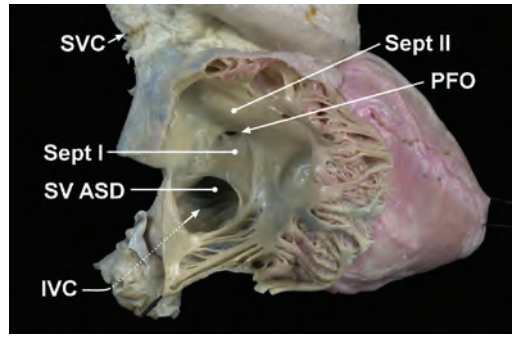

Fig 1.13A—Right atrial view of SV ASD of the inferior vena cava (IVC) type. Note the entrance of the IVC below Sept I so that the mouth of the IVC *is* the SV ASD. Note the normal superior aspect of Sept I with a patent foramen ovale (PFO).

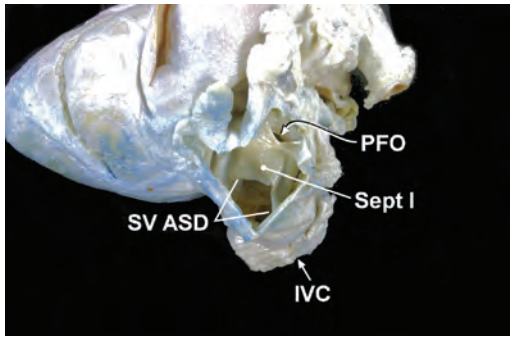

Fig 1.13B—Left atrial view of same specimen as in part A. Normal Sept I and patent foramen ovale (PFO) are noted.

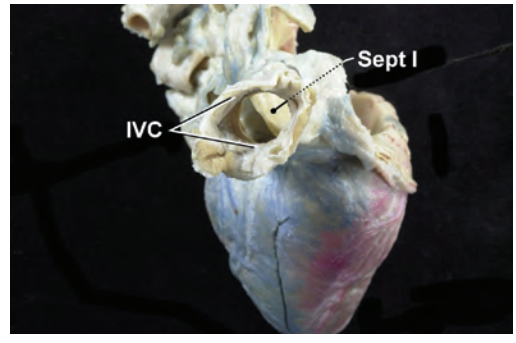

Fig 1.13C—Inferior view through the inferior vena cava (IVC) shows that it straddles Sept I thus entering both right atrium (RA) and left atrium (LA).

with the superior and anterior boundary of the defect being the inferior portion of septum primum. The remaining boundaries are the ostia of the inferior vena cava and possibly a pulmonary vein. The atrial septum has no defect in either condition but rather a "defect" that allows for blood to cross from the left atrium to the right atrium through the mouth of one or more venous structures as they straddle the atrial septum. Because a large portion of the boundary of these defects is straddling vein, device closure is not feasible.

Ostium primum ASDs are defects in the canal septum.[32–35] The defect is due to failure of division of the embryonic atrioventricular canal and specifically to failure of fusion of septum primum with the endocardial cushions. The defect is in the portion of the septum located between the septum primum and the common atrioventricular valve (Fig 1.14). The boundaries of the defect include septum primum posteriorly and superiorly and the atrioventricular valves anterior and inferiorly. Because the anterior and inferior border is the atrioventricular valve, device closure is not feasible.

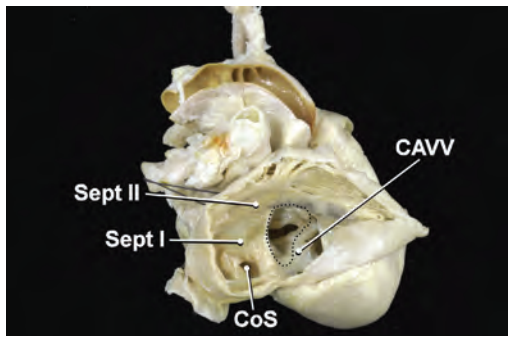

Fig 1.14A—Right atrial view of ostium primum atrial septal defect (dotted line) seen in common atrioventricular canal. The posterior border of the defect is the normal appearing Sept I, the superior border is Sept II, but the anterior and inferior border is the common atrioventricular valve (CAVV). In this case of so-called incomplete or partial atrioventricular canal, there is a strip of valve tissue that divides the valve into one with two orifices (seen on either side of the dotted line).

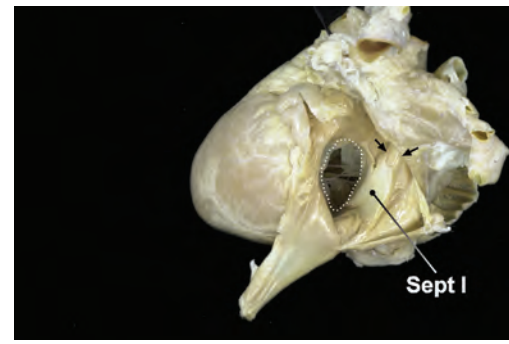

Fig 1.14B—Left atrial view of same specimen as in part A showing the ostium primum atrial septal defect (dotted line). Note the normal Sept I posterior to the defect with the two normal attachments (black arrows) of Sept I to Sept II on either side of the half-moon shaped edge of the foramen ovale.

References

1. Anderson RH, Brown NA, Webb S. Development and structure of the atrial septum. *Heart*. 2002:88(1);104–110,
2. Sweeney LJ, Rosenquist GC. The normal anatomy of the atrial septum in the human heart. *Am Heart J*. 1979;98:51–54.
3. Edwards W. Cardiac anatomy and examination of cardiac specimens. Atrial Septum. In: Allen HD, Driscoll DJ, Shaddy RE, Feltes TF, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young Adult*. 7th ed. Philadelphia: Wolters Kluwer, 2007;(vol 1):10–11.
4. Hutchins GM, Moore GW, Jones JF, et al. Postnatal endocardial fibroelastosis of the valve of the foramen ovale. *Am J Cardiol*. 1981;47:90–94.
5. Porter CJ, Edwards W. Atrial septal defects. Anatomy, embryology, and pathology. In: Allen HD, Driscoll DJ, Shaddy RE, Feltes TF, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young*

Adult. 7th ed. Philadelphia: Wolters Kluwer, 2007;(vol 1): 632–645.

6. McKenzie JA, Edwards WD, Hagler DJ. Anatomy of the patent foramen ovale for the interventionalist. *Cathet Cardiovasc Intervent.* 2009; 73(6):821–826.
7. Hagen P, Scholz D, Edwards W. Incidence and size of patent foramen ovale during the first 10 decades of life: An autopsy study of 965 normal hearts. *Mayo Clin Proc.* 1984;59:17–20.
8. Ho SY, McCarthy KP, Rigby ML. Morphological features pertinent to interventional closure of patent oval foramen. *J Interv Cardiol.* 2003;16:33–38.
9. Marshall AC, Lock JE. Structural and compliant anatomy of the patent foramen ovale in patients undergoing transcatheter closure. *Am Heart J*. 2000;140:303–307.
10. Spence MS, Khan AA, Mullen MJ. Balloon assessment of patent foramen ovale morphology and the modification of tunnels using a balloon detunnelisation technique. *Cathet Cardiovasc Intervent*. 2008;71:222–228.
11. Blom NA, Ottenkamp J, Jongeneel TH, DeRuiter MC, Gittenberger-de Groot AC. Morphogenetic differences of secundum atrial septal defects. *Pediatr Cardiol*. 2005;25(4):338–343.
12. Chan KC, Godman MJ. Morphological variations of fossa ovalis atrial septal defects (secundum): feasibility for transcutaneous closure with the clam-shell device. *Br Heart J.* 1993; 69(1):52–55.
13. Ferreira SM, Ho SY, Anderson RH. Morphological study of defects of the atrial septum within the oval fossa: implications for transcatheter closure of left-to-right shunt. *Br Heart J.* 1992;67(4):316–320.
14. Marx GR, Sherwood MG, Fleishman C, Van Praagh R. Three-dimensional echocardiography of the atrial septum. *Echocardiography.* 2001;18(5):433–443.
15 Chin AJ, Weinberg PM, Barber G. Subcostal two-dimensional echocardiographic identification of anomalous attachment of septum primum in patients with left atrioventricular valve underdevelopment. *J Am Coll Cardiol.* 1990;15:678–681.
16. Cohen MS, Weinberg PM, Coon PD, Gaynor JW, Rychik J. Deviation of atrial septum primum in association with normal left atrioventricular valve size. *J Am Soc Echocardiogr.* 2001;14:732–737.
17. Van Praagh S, Carrera ME, Sanders S, Mayer JE Jr, Van Praagh R. Partial or total direct pulmonary venous drainage to right atrium due to malposition of septum primum. *Chest.* 1995;107(6):1488–1498.
18. Geva T. Anomalies of the atrial septum. In: Lai W, Mertens K, Cohen M, Geva T, eds. *Echocardiography in Pediatric and Congenital Heart Disease: From Fetus to Adult*. Hoboken: NJ: Wiley-Blackwell, 2009;15.
19. Rose AG, Beckman CB, Edwards JE. Communication between coronary sinus and left atrium. *Br Heart J.* 1974;36:182–185.
20. Freedom RM, Culham JA, Rowe RD. Left atrial to coronary sinus fenestration (partially unroofed coronary sinus): morphological and angiocardiographic observations. *Br Heart J.* 1981;46:63–68.
21. Knauth A, McCarthy KP, Webb S, et al. Interatrial communication through the mouth of the coronary sinus. *Cardiol Young*. 2002;12: 364–372.
22. Adatia I, Gittenberger-De Groot AC. Unroofed coronary sinus and coronary sinus orifice atresia: Implications for management of complex congenital heart disease. *JACC.* 1995; 25(4):948–953.
23. Raghib G, Ruttenberg HD, Anderson RC, Amplatz K, Adams Jr P, Edwards JE. Termination of left superior vena cava in left atrium, atrial septal defect, and absence of coronary sinus: a developmental complex. *Circulation.* 1965;31:906–918.
24. Ootaki Y, Yamaguchi M, Yoshimura N, Oka S, Yoshida M, Hasegawa T. Unroofed coronary sinus syndrome: diagnosis, classification, and surgical treatment. *J Thorac Cardiovasc Surg.* 2003;126:1655–1656.
25. Van Praagh S, Carrera ME, Sanders SP, et al. Sinus venosus defects: unroofing of the right pulmonary veins-anatomic and echocardiographic findings and surgical treatment. *Am Heart J.* 1994;128:365–379.

26. Anderson RH, Ettedgui JA, Devine WA. Sinus venous defect. *Am Heart J.* 1995;129:1229–1230.
27. Van Praagh S, Carrera ME, Sanders SP, et al. Sinus venosus defect [reply]. *Am Heart J.* 1995;129:1231–1232.
28. Blom NA, Gittenberger-de Groot AC, Jongeneel TH, et al. Normal development of the pulmonary veins in human embryos and formulation of a morphogenetic concept for sinus venosus defects. *Am J Cardiol.* 2001;87:305–309.
29. Li J, Al Zaghal AM, Anderson RH. The nature of the superior sinus venosus defect. *Clin Anat.* 1998;11:349–352.
30. Al Zaghal AM, Ahmed M, Li J, et al. Anatomical criteria for diagnosis of sinus venosus syndrome. *Heart.* 1997;78:298–304.
31. Van Praagh S, Geva T, Lock JE, Nido PJ, Vance MS, Van Praagh R. Biatrial or left atrial drainage of the right superior vena cava: anatomic, morphogenetic, and surgical considerations—report of three new cases and literature review. *Pediatr Cardiol.* 2003;24(4):350–363,
32. Cohen MS. Common atrioventricular canal defects anomalies of the atrial septum. In: Lai W, Mertens K, Cohen M, Geva T, eds. *Echocardiography in Pediatric and Congenital Heart Disease: From Fetus to Adult*. Hoboken: NJ: Wiley-Blackwell, 2009;230–248.
33. Pillai R, Ho SY, Anderson RH, Lincoln C. Ostium primum atrioventricular septal defect: an anatomical and surgical review. *Ann Thorac Surg.* 1986;41(4):458–461.
34. Penkoske PA, Neches WH, Anderson RH, Zuberuhler JR. Further observations on the morphology of atrioventricular septal defects. *J Thorac Cardiovasc Surg.* 1985;90:611–622.
35. Piero GP, Leon MG, Wilkinson JG, Lozsadi K, Macartney FJ, Anderson RH. Morphology and classification of atrioventricular defects. *Am Heart J.* 1979;42:621–632.

2

Natural and Unnatural History of a Secundum ASD

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Introduction

Secundum atrial septal defect (ASD) is one of the most common forms of congenital heart defect, with an estimated incidence of 0.2 to 0.5 per 1000 live births.[1–3] ASD accounts for 6% to 10% of all defects at birth, and excluding bicuspid aortic valves, is the most common congenital heart defect presenting in adults.[1,2,4] It affects approximately twice as many females as males.[5] Although the majority of defects are sporadic, they can be associated with other complex cardiac defects and genetic syndromes, such as Holt-Oram Syndrome and Ellis van Creveld syndrome.[6]

An ASD creates a source for intracardiac shunting at the atrial level. The direction of shunting across the ASD is determined by the diastolic properties of the right and left ventricles. In a small ASD, the left atrial pressure is typically slightly higher than the right atrial pressure and left to right shunting occurs mainly in diastole. With large defects, the right and left atrial pressures are equal and left to right shunting occurs due to the increased distensibility and compliance of the right ventricle compared to the left ventricle. The degree of shunting is determined by the size of the defect and the compliance of the two ventricles.[7] Chronic volume overload to the right-sided structures leads to dilation of the right atrium and right ventricle and dilation of the entire pulmonary bed. Over time, microscopic changes can occur in the lungs with medial hypertrophy of the muscular pulmonary arteries and veins and muscularization of the pulmonary arterioles, ultimately leading to pulmonary vascular disease and pulmonary hypertension.[8]

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The natural history of children and adults with an isolated ASD as well as the natural history following surgical or percutaneous closure of an ASD in children and adults are reviewed in this chapter. Currently, most hemodynamically significant ASDs are diagnosed and closed at an early age, making the natural history somewhat difficult to assess. Several observational studies describing the natural history of ASDs were published before the age of enhanced diagnosis by echocardiography.[9–11] Selection bias is a common error in these early observational studies because many of them focused on patients who were brought to medical attention after the onset of symptoms. It is clear from these studies that an unrepaired, hemodynamically significant ASD leads to significant morbidity in adulthood and reduces life expectancy.[9,10,12]

Natural History of an Atrial Septal Defect Diagnosed in Childhood

The right ventricle is relatively stiff in early infancy, and there is little left to right shunting. As the pulmonary vascular resistance drops in the first month of life, the diastolic properties of the right ventricle change allowing more left to right shunt.[13] Infants with an ASD are usually asymptomatic, however, there are rare reports of infants who develop heart failure, and it is not clear what the etiology is, as their hemodynamic features are no different from infants who remain asymptomatic.[14]

When a family is presented with the diagnosis of a secundum ASD in their child, the discussion often turns to the question of what will happen to the ASD over time. A number of studies have addressed this issue.[5,15–18] Results of studies have varied depending on a number of variables such as method of diagnosis, exclusion criteria, age of patients at diagnosis, and length of follow-up. In 1973, Mody published a series of 40 patients with clinical evidence of cardiac enlargement and pulmonary overcirculation who were diagnosed with an ASD at cardiac catheterization.[18] In this study, 11 of 20 patients diagnosed prior to 1 year of age had spontaneous closure of their ASD during follow-up, whereas spontaneous closure did not occur in any patients diagnosed after 1 year of age.[18] Although this study could not quantify the anatomic size of each ASD, it did suggest that the age at diagnosis could help determine the likelihood of spontaneous closure of an ASD over time.

The development of two-dimensional (2D) echocardiography provided the ability to detect atrial septal defects of all sizes, as well as the ability to follow their size over time. Radzik et al[17] followed 101 consecutive infants who were referred at < 3 months of age for a murmur and subsequently diagnosed with an interatrial communication. The study did not exclude infants felt to have a patent foramen ovale. Infants were divided into groups based on the size of their ASD. In this study, all defects < 3 mm in diameter and 87% of defects < 5 mm in diameter closed spontaneously, whereas spontaneous closure did not occur in any infant with defects > 8mm in diameter.[17] Similar findings were noted by Helgason and Jonsdottir,[5] who followed all children in Iceland diagnosed with a secundum ASD of at least 4 mm in diameter by echocardiogram during a 10-year period. In their study, the age of patients at diagnosis ranged from 1 week to 10 years of age. They found that 62% of defects 4 mm in diameter closed spontaneously, whereas 16 of 17 patients with defects 5 to 6 mm in diameter had either a reduction in size (5 patients) or complete closure (11 patients). Only one of eight patients with a defect 7 to 8 mm in diameter had spontaneous closure with four other defects becoming smaller over time. Similar to the report by Radzik,[17] there was no spontaneous closure in defects > 8 mm in diameter with 24 of 26 such defects requiring surgical closure. Interestingly, the median age at diagnosis of patients with defects > 8 mm was 14 months compared to 1 month for those with 4 mm defects. Of note, one patient in the 4-mm group and one in the 5- to 6-mm group actually

had significant increase in the size of the defect during follow-up.[5]

In 2002, Texas Children's Hospital published their experience with isolated ASDs > 3 mm in diameter between the years 1991 and 1998 and found a significant increase in size over time with all ASD sizes. In 34 patients with an ASD between 3 and 6 mm in diameter, they surprisingly found that 17 defects increased in size during follow-up, with 7 defects enlarging to between 8 and 12 mm in diameter, and 3 defects increasing in size to > 12 mm in diameter. Similarly, 8 of 40 moderate-sized defects increased to > 12 mm in diameter. Overall, 66% of their patients had an increase in defect size during follow-up. The mean age at diagnosis in this group of patients was older than other studies at 4.5 years, and this may account for the large percentage of defects that enlarged overtime.[16]

In a study from Austria published in 2006, 200 consecutive patients with ASDs ≥ 4 mm in diameter were followed for > 6 months. Similar to the study by Helgason and Jonsdottir, they found smaller defects in the younger children and larger defects in those diagnosed at a later age. They hypothesized that this finding was either because many ASDs may be an incidental finding on echocardiograms in younger children or that there may be growth of an ASD over time. In their series, 77% of defects decreased in size over time whereas only 18% increased in size. In addition, there was a strong association between defect size at diagnosis and spontaneous closure. Of the defects measuring 4 to 5 mm in diameter, 56% closed spontaneously during follow-up, whereas none of the defects > 10 mm in diameter closed spontaneously. Surgical or device closure was required in 77% of patients with defects > 10 mm. They also found a strong correlation between age at diagnosis and the incidence of spontaneous closure with spontaneous closure occurring in 39% of patients diagnosed at < 1 year of age compared to only 19% of patients diagnosed at > 1 year of age. Using a multivariate analysis, smaller ASD diameter and younger age at diagnosis were both independent predictors of spontaneous closure or regression in ASD size to < 3 mm in diameter.[15]

In summary, the two most important predictors of spontaneous closure of a secundum ASD appear to be the age at diagnosis and the size of the defect. Defects that measure < 3 mm in diameter diagnosed in the first few months of life will most likely close spontaneously. Children diagnosed at < 1 year of age with defects < 6 mm in diameter are likely to undergo complete spontaneous closure or regression of their ASD to < 3 mm. Defects > 8 mm are much less likely to become smaller over time and have a significant chance of requiring surgical or percutaneous closure in the future, regardless of age at diagnosis. Defects > 3 mm in diameter have the potential to increase in size over time, however this seems more likely in children diagnosed after 1 year of age and in those with larger defects at the time of diagnosis.

Natural History of an Unrepaired ASD

An ASD usually has a benign clinical course in children.[19] Complications of an unrepaired ASD occur in adulthood and can include right ventricular failure, atrial arrhythmias, paradoxical embolization, pulmonary hypertension, and cyanosis secondary to reversal of shunt from pulmonary vascular disease (Eisenmenger syndrome).[10,20–22]

Chronic volume overload to the lungs from an ASD may lead to progressive dyspnea and recurrent respiratory infections. As pulmonary vascular disease develops, symptoms of right ventricular heart failure develop. Symptoms are rare in childhood but are progressive with age.[19] Commonly cited early observational studies reported a very low prevalence of symptoms before the age of 30 with about half of the patients becoming symptomatic by 45 years of age and the most common symptoms being exertional dyspnea and fatigue.[9,10] Konstantinides et al reported the presence of exertional

dyspnea in 75% and peripheral edema in 24% of patients with an ASD evaluated at a mean age of 56 years, and 29% of these patients were classified as New York Heart Association (NYHA) class III or IV.[23] Craig and Selzer found that congestive heart failure developed after the age of 40 in their study of patients who were > 18 years of age at diagnosis.[10] Adults with an unrepaired ASD were found to have moderately reduced ventilatory function and markedly reduced exercise capacity by pulmonary function and cardiopulmonary exercise testing.[24,25] Cyanosis is also a late symptom seen in patients with an ASD and is usually secondary to pulmonary vascular disease causing right to left shunt at the atrial level.[20] Although rare before 20 years of age, the incidence of cyanosis increases with age, and in Dexter's early hemodynamic studies of patients with an ASD, 37% had a measurable decrease in oxygen saturation at cardiac catheterization.[7] Konstantinides et al reported cyanosis in 27% of patients studied at a mean age of 56 years and Attie et al reported a mean oxygen saturation of 89% in patients studied at a mean age of 50.8 years.[23,26]

Atrial arrhythmias, primarily atrial flutter and atrial fibrillation, are well-documented complications of an unrepaired ASD and, like other complications, are rare during childhood.[22] Although, the risk of atrial arrhythmias is extremely low in patients before the age of 40, the risk increases with older age and higher mean pulmonary artery pressure.[22,27] The prevalence of atrial arrhythmias in the fifth decade has been reported at 19% to 22%, and patients with atrial arrhythmias are more likely to be classified as NYHA classes III or IV.[27,28]

Pulmonary hypertension and pulmonary vascular disease is one of the most important complications of an ASD. Determining the true incidence of pulmonary hypertension in patients with an unrepaired ASD is complicated because studies have used differing criteria to define significant pulmonary hypertension. Pulmonary hypertension rarely develops before 18 years of age in an uncomplicated, unrepaired ASD.[10,11,29] The incidence of pulmonary hypertension between 20 and 40 years of age in early natural history studies ranged from 14% to 18%.[9,10] Pulmonary hypertension has been shown to be more common in females, and the prevalence increases with age.[10,11,29] Once pulmonary vascular disease develops, it may be progressive and may significantly alter the clinical course and prognosis of a patient with an ASD, including their outcome after surgical repair.[29]

The presence of an ASD allows for systemic embolism of thrombus or air in the presence of transient increases in right atrial pressure that create a right to left shunt. Paradoxical embolism can lead to significant complications including cryptogenic stroke as well as ischemic damage to other major organs.[21,30] Pregnancy is associated with an increased risk of stroke from various etiologies, and the risk of paradoxical embolism due to the presence of a patent foramen ovale or ASD may be increased during pregnancy.[31,32] Transcatheter closure of atrial septal defects has been performed during pregnancy in these situations.[33] Additionally, the presence of an unrepaired ASD during pregnancy is associated with increased risk of maternal pre-eclampsia and fetal mortality.[34]

Early natural history studies of patients with an ASD indicate reduced survival, with an average age at death of 37 to 49 years.[9–11,35] Causes of death in earlier reports were most frequently due to congestive heart failure, pulmonary arterial thrombosis, and bronchopulmonary infections.[10] As mentioned earlier, the selection bias present in these early studies likely overestimates the mortality figures. More recent studies suggest a better prognosis, and survival to 90 years of age has been reported in patients with an unrepaired ASD.[28,35,36] Campbell calculated survival rates for each decade in patients with an ASD based on both necropsy reports and longitudinal studies, and his calculations show < 1% per year mortality rate in the first two decades; increasing in successive decades to 7.5% per year in the sixth decade.[12]

In summary, an ASD is well tolerated during childhood with symptoms developing during early adulthood. Although early natural history studies may have overestimated the

true mortality and morbidity of patients with an ASD, it is clear that patients with an ASD are prone to developing significant complications such as heart failure, atrial arrhythmias, and pulmonary vascular disease during early adulthood, ultimately leading to reduced life expectancy.

Unnatural history of an ASD: *surgical closure*

It is generally accepted that children and young adults with evidence of a hemodynamically significant ASD resulting in right atrial and/or right ventricular volume overload should have their ASD closed either surgically or percutaneously. Guidelines from the American Heart Association (AHA) recommend closure of a secundum ASD in the presence of symptoms or evidence of a large shunt; defined as the presence of a diastolic flow rumble, electrocardiographic evidence of right ventricular hypertrophy, chest radiographic evidence of cardiomegaly or increased pulmonary vascular markings, echocardiographic evidence of right ventricular enlargement or paradoxical septal motion, or a pulmonary to systemic flow ratio (Qp:Qs) ≥ 1.5.[37] Surgical closure of a secundum ASD is both safe and effective. The long-term survival of patients who have surgical closure of an ASD during childhood is similar to age and sex matched controls with no heart disease.[38,39] Roos-Hesslink et al demonstrated this point in a longitudinal study of 135 patients who underwent surgical ASD closure during childhood, reporting no cardiovascular mortality and no evidence of stroke, heart failure, or pulmonary hypertension in any patients at 15- and 26-year follow-up evaluations.[38] In addition, the prevalence of atrial arrhythmias was only 6% at 15-year follow-up with an additional 2% at 26-year follow-up, which is much lower than that seen after surgical ASD closure in adults as well as in adults with an unrepaired ASD.[27,38,39] Despite excellent clinical outcomes following surgical ASD repair, right ventricular enlargement and abnormal ventricular septal wall motion may persist.[40] In long-term follow-up of 104 patients repaired prior to the age of 15 years, Meijboon et al found persistent right ventricular enlargement in 26%.[41]

Younger patients appear to have better long-term prognosis than older patients following surgical ASD closure. A comparison between patients with surgical closure of an ASD during childhood to patients with surgical closure as adults demonstrated more frequent development of late heart failure, stroke, and atrial arrhythmias in the older group, and age at operation was an independent predictor of long-term survival.[39] There has been some controversy as to whether older adults truly benefit from surgical closure of an ASD. A historical, prospective, nonrandomized study published in 1994 evaluated patients over the age of 45 who had previously been diagnosed with an ASD, and compared patients who underwent surgical closure to those who had medical management. The study reported no significant difference in survival, symptoms, or other morbidities between the two groups.[28] However, several studies show that patients older than the age of 40 do well after surgical ASD closure, with improvement in symptoms and overall mortality compared to medical treatment alone.[23,26,42] In 2001, Attie et al reported the results of their prospective, randomized controlled trial, in which patients more than 40 years old with an ASD were assigned to either surgical or medical management. Their study showed surgery improved both the composite of major cardiovascular events as well as overall mortality compared to medical management.[26] In addition, exercise capacity as measured by cardiopulmonary exercise testing, significantly improves following either surgical or transcatheter closure of an ASD in older patients, even in those who reported no symptoms prior to closure.[24,25] Unfortunately, the risk of late atrial arrhythmias does not seem to change significantly following surgical repair at an older age compared to patients with an unrepaired ASD.[27] Older age at the time of surgery (> 40 years), the presence of preoperative atrial fibrillation or flutter, and the presence of

early postoperative atrial fibrillation or flutter were all found to be independent predictors of late atrial arrhythmias.[27] The fact that little improvement is seen in atrial arrhythmias following closure in adults is likely due to structural changes having already occurred in the atrial tissue. The addition of the Cox maze procedure at the time of surgical ASD closure has been associated with a decreased incidence of atrial arrhythmias postoperatively at short and intermediate follow-up.[43,44]

Pulmonary vascular disease and fixed pulmonary hypertension in patients with an unrepaired ASD is associated with high mortality postoperatively, and maintaining an atrial septal communication may be necessary in these patients to allow for right to left shunting at the atrial level to maintain an adequate cardiac output at the expense of cyanosis. Steel et al reported low postoperative mortality and regression of symptoms in patients with total pulmonary resistance < 15 Wood units/M^2, however total pulmonary resistance > 15 Wood units/M^2 was associated with poor long-term survival. In addition, preoperative oxygen saturation was predictive of outcome in patients with borderline total pulmonary resistance.[29]

Unnatural history of an ASD: transcatheter closure

Transcatheter closure of a secundum ASD was first performed by King and Mills in 1976 using a double umbrella device, and the procedure has evolved significantly since that time with the development of several different devices.[45,46] Transcatheter closure of a secundum ASD has been shown to be safe and efficacious in both children and adults, having similar short-term success rate and mortality as surgery.[47–50] In addition, Du et al reported decreased morbidity and length of hospital stay with transcatheter closure compared to surgery.[47]

The CardioSEAL/STARFlex and AMPLATZER Septal Occluder (ASO) devices account for the majority of follow-up data regarding transcatheter closure of atrial septal defects. Histologic analysis of piglets who underwent ASD closure with an ASO device demonstrate complete neoendocardium coverage of both the right and left atrial discs by 1–3 months after device placement.[51] The success rate of closure with the ASO device has been very high in multiple studies, and residual shunting is rarely more than trivial to mild following device placement.[47,48,52–54] An early study published by Chan et al in 1999 reported complete closure in 85% of patients at 24 hours from closure with an ASO device, and complete closure in 99% at 3 months after the procedure.[54] In 2002, Du et al reported results on 423 patients who had defects closed with an ASO device, demonstrating complete closure of the defect in 73% of patients at 24 hours and in 98% of patients at 6-months follow-up.[47] Although residual shunting more than a month after closure is rare with the ASO device, it has been shown to be more frequent following closure with the CardioSEAL or STARFlex device. In a study published in 2004, Butera et al compared 153 patients who had defects closed with an ASO device to 121 patients with defects that were closed with either the CardioSEAL or STARFlex device. Their study showed residual shunting at discharge in only 3% of patients closed with an ASO device compared to 21% of patients whose defect was closed with either the CardioSEAL or STARFlex device, and there was no significant difference in closure rates between the CardioSEAL and STARFlex devices.[55]

Periprocedural complications with transcatheter closure are uncommon, the most common and significant short-term complication being device embolization or malposition that requires percutaneous or surgical removal of the device.[56] A review of the Manufacturer and User Facility Device Experience (MAUDE) database for ASO devices reported an overall mortality of < 0.1%, with 0.83% of cases requiring a rescue operation for adverse events related to device placement.[57] Cardiac perforation due to erosion of the device through cardiac structures has been a rare but serious and life-threatening complication following ASD closure with the

ASO device, resulting in a change in the device sizing guidelines.[58,59] Cardiac perforations typically occur within 3 days of the procedure, however, they have been reported as long as 3 years after the procedure.[58]

Transcatheter closure of a secundum ASD has only recently gained wide acceptance, and therefore surveillance and collection of data for long-term results and complications is ongoing. Masura et al reported no residual shunt, no significant complications, and no death at a median follow up of 78 months in 151 patients who underwent closure of a secundum ASD with an ASO device.[49] This and other studies show that midterm outcomes following transcatheter closure of a secundum ASD are very good in both children and adults, and late complications related to the device are uncommon.[49,50,56]

Following device closure of an ASD, there is evidence of regression of the right atrial and right ventricular enlargement.[60,61] In a study of 38 patients undergoing transcatheter ASD closure, Kort et al demonstrated normalization of right ventricular size 24 months after transcatheter ASD closure. Although there was also significant reduction in right atrial size, the right atrial size remained large compared to controls at 24 months. The authors also noted greater reduction in right atrial size in patients closed at a younger age, suggesting that younger patients may have a greater potential for remodeling. In contrast, no relationship between the age at closure and the change in the right ventricular volume was evident.[60]

In summary, a secundum ASD is a common congenital heart defect with good prognosis during childhood and the development of significant morbidity and mortality during early adulthood. Surgical and transcatheter closure of an ASD are both safe and effective, decreasing the morbidity and mortality associated with an unrepaired ASD. Although long-term results regarding transcatheter closure are still being evaluated; with appropriate patient selection, it is associated with similar safety and efficacy as surgical closure.

References

1. Carlgren LE. The incidence of congenital heart disease in children born in Gothenburg 1941–1950. *Br Heart J.* 1959;21(1):40–50.
2. Dickinson DF, Arnold R, Wilkinson JL. Congenital heart disease among 160 480 liveborn children in Liverpool 1960 to 1969. Implications for surgical treatment. *Br Heart J.* 1981;46(1):55–62.
3. Ferencz C, Rubin JD, McCarter RJ, et al. Congenital heart disease: prevalence at livebirth. The Baltimore-Washington Infant Study. *Am J Epidemiol.* 1985;121(1):31–36.
4. Fuster V, Brandenburg RO, McGoon DC, Giuliani ER. Clinical approach and management of congenital heart disease in the adolescent and adult. *Cardiovasc Clin.* 1980;10(3): 161–197.
5. Helgason H, Jonsdottir G. Spontaneous closure of atrial septal defects. *Pediatr Cardiol.* 1999;20(3):195–199.
6. Vaughan CJ, Basson CT. Molecular determinants of atrial and ventricular septal defects and patent ductus arteriosus. *Am J Med Genet.* 2000;97(4):304–309.
7. Dexter L. Atrial septal defect. *Br Heart J.* 1956;18(2):209–225.
8. Haworth SG, Hislop AA. Pulmonary vascular development: normal values of peripheral vascular structure. *Am J Cardiol.* 1983;52(5): 578–583.
9. Campbell M, Neill C, Suzman S. The prognosis of atrial septal defect. *Br Med J.* 1957;1 (5032):1375–1383.
10. Craig RJ, Selzer A. Natural history and prognosis of atrial septal defect. *Circulation.* 1968; 37(5):805–815.
11. Markman P, Howitt G, Wade EG. Atrial septal defect in the middle-aged and elderly. *Q J Med.* 1965;34(136):409–426.
12. Campbell M. Natural history of atrial septal defect. *Br Heart J.* 1970;32(6):820–826.
13. Mathew R, Thilenius OG, Arcilla RA. Comparative response of right and left ventricles to volume overload. *Am J Cardiol.* 1976;38(2):209–217.
14. Mainwaring RD, Mirali-Akbar H, Lamberti JJ, Moore JW. Secundum-type atrial septal defects

with failure to thrive in the first year of life. *J Cardiol Surg.* 1996;11(2):116–120.
15. Hanslik A, Pospisil U, Salzer-Muhar U, Greber-Platzer S, Male C. Predictors of spontaneous closure of isolated secundum atrial septal defect in children: a longitudinal study. *Pediatrics.* 2006;118(4):1560–1565.
16. McMahon CJ, Feltes TF, Fraley JK, et al. Natural history of growth of secundum atrial septal defects and implications for transcatheter closure. *Heart.* 2002;87(3):256–259.
17. Radzik D, Davignon A, van Doesburg N, Fournier A, Marchand T, Ducharme G. Predictive factors for spontaneous closure of atrial septal defects diagnosed in the first 3 months of life. *J Am Coll Cardiol.* 1993;22(3):851–853.
18. Mody MR. Serial hemodynamic observations in secundum atrial septal defect with special reference to spontaneous closure. *Am J Cardiol.* 1973;32(7):978–981.
19. Rostad H, Sorland S. Atrial septal defect of secundum type in patients under 40 years of age. A review of 481 operated cases. Symptoms, signs, treatment and early results. *Scand J Thorac Cardiovasc Surg.* 1979;13(2):123–127.
20. Beghetti M, Galie N. Eisenmenger syndrome a clinical perspective in a new therapeutic era of pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;53(9):733–740.
21. Bartz PJ, Cetta F, Cabalka AK, et al. Paradoxical emboli in children and young adults: role of atrial septal defect and patent foramen ovale device closure. *Mayo Clin Proc.* 2006;81(5):615–618.
22. Berger F, Vogel M, Kramer A, et al. Incidence of atrial flutter/fibrillation in adults with atrial septal defect before and after surgery. *Ann Thorac Surg.* 1999;68(1):75–78.
23. Konstantinides S, Geibel A, Olschewski M, et al. A comparison of surgical and medical therapy for atrial septal defect in adults. *N Engl J Med.* 1995;333(8):469–473.
24. Helber U, Baumann R, Seboldt H, Reinhard U, Hoffmeister HM. Atrial septal defect in adults: cardiopulmonary exercise capacity before and 4 months and 10 years after defect closure. *J Am Coll Cardiol.* 1997;29(6):1345–1350.
25. Brochu MC, Baril JF, Dore A, Juneau M, De Guise P, Mercier LA. Improvement in exercise capacity in asymptomatic and mildly symptomatic adults after atrial septal defect percutaneous closure. *Circulation.* 2002;106(14):1821–1826.
26. Attie F, Rosas M, Granados N, Zabal C, Buendia A, Calderon J. Surgical treatment for secundum atrial septal defects in patients >40 years old. A randomized clinical trial. *J Am Coll Cardiol.* 2001;38(7):2035–2042.
27. Gatzoulis MA, Freeman MA, Siu SC, Webb GD, Harris L. Atrial arrhythmia after surgical closure of atrial septal defects in adults. *N Engl J Med.* 1999;340(11):839–846.
28. Shah D, Azhar M, Oakley CM, Cleland JG, Nihoyannopoulos P. Natural history of secundum atrial septal defect in adults after medical or surgical treatment: a historical prospective study. *Br Heart J.* 1994;71(3):224–227; discussion 228.
29. Steele PM, Fuster V, Cohen M, Ritter DG, McGoon DC. Isolated atrial septal defect with pulmonary vascular obstructive disease–long-term follow-up and prediction of outcome after surgical correction. *Circulation.* 1987;76(5):1037–1042.
30. Loscalzo J. Paradoxical embolism: clinical presentation, diagnostic strategies, and therapeutic options. *Am Heart J.* 1986;112(1):141–145.
31. Treadwell SD, Thanvi B, Robinson TG. Stroke in pregnancy and the puerperium. *Postgrad Med J.* 2008;84(991):238–245.
32. Kozelj M, Novak-Antolic Z, Grad A, Peternel P. Patent foramen ovale as a potential cause of paradoxical embolism in the postpartum period. *Eur J Obstet Gynecol Reprod Biol.* 1999;84(1):55–57.
33. Schrale RG, Ormerod J, Ormerod OJ. Percutaneous device closure of the patent foramen ovale during pregnancy. *Cathet Cardiovasc Interv.* 2007;69(4):579–583.
34. Yap SC, Drenthen W, Meijboom FJ, et al. Comparison of pregnancy outcomes in women with repaired versus unrepaired atrial septal defect. *BJOG.* 2009;116(12):1593-601.
35. Perloff JK. Ostium secundum atrial septal defect–survival for 87 and 94 years. *Am J Cardiol.* 1984;53(2):388–389.
36. Nomura M, Nakaya Y, Kishi F, et al. A 90-year old patient with atrial septal defect and sinus rhythm. *Acta Cardiol.* 1996;51(4):377–380.

37. Driscoll D, Allen HD, Atkins DL, et al. Guidelines for evaluation and management of common congenital cardiac problems in infants, children, and adolescents. A statement for healthcare professionals from the Committee on Congenital Cardiac Defects of the Council on Cardiovascular Disease in the Young, American Heart Association. *Circulation.* 1994;90(4):2180–2188.
38. Roos-Hesselink JW, Meijboom FJ, Spitaels SE, et al. Excellent survival and low incidence of arrhythmias, stroke and heart failure long-term after surgical ASD closure at young age. A prospective follow-up study of 21–33 years. *Eur Heart J.* 2003;24(2):190–197.
39. Murphy JG, Gersh BJ, McGoon MD, et al. Long-term outcome after surgical repair of isolated atrial septal defect. Follow-up at 27 to 32 years. *N Engl J Med.* 1990;323(24):1645–1650.
40. Pearlman AS, Borer JS, Clark CE, et al. Abnormal right ventricular size and ventricular septal motion after atrial septal defect closure: etiology and functional significance. *Am J Cardiol.* 1978;41(2):295–301.
41. Meijboom F, Hess J, Szatmari A, et al. Long-term follow-up (9 to 20 years) after surgical closure of atrial septal defect at a young age. *Am J Cardiol.* 1993;72(18):1431–1434.
42. John Sutton MG, Tajik AJ, McGoon DC. Atrial septal defect in patients ages 60 years or older: operative results and long-term postoperative follow-up. *Circulation.* 1981;64(2):402–409.
43. Sandoval N, Velasco VM, Orjuela H, et al. Concomitant mitral valve or atrial septal defect surgery and the modified Cox-maze procedure. *Am J Cardiol.* 1996;77(8):591–596.
44. Bonchek LI, Burlingame MW, Worley SJ, Vazales BE, Lundy EF. Cox/maze procedure for atrial septal defect with atrial fibrillation: management strategies. *Ann Thorac Surg.* 1993;55(3):607–610.
45. King TD, Thompson SL, Steiner C, Mills NL. Secundum atrial septal defect. Nonoperative closure during cardiac catheterization. *JAMA.* 1976;235(23):2506–2509.
46. Majunke N, Sievert H. ASD/PFO devices: what is in the pipeline? *J Interv Cardiol.* 2007;20(6):517–523.
47. Du ZD, Hijazi ZM, Kleinman CS, Silverman NH, Larntz K. Comparison between transcatheter and surgical closure of secundum atrial septal defect in children and adults: results of a multicenter nonrandomized trial. *J Am Coll Cardiol.* 2002;39(11):1836–1844.
48. Masura J, Gavora P, Formanek A, Hijazi ZM. Transcatheter closure of secundum atrial septal defects using the new self-centering AMPLATZER septal occluder: initial human experience. *Cathet Cardiovasc Diagn.* 1997;42(4):388–393.
49. Masura J, Gavora P, Podnar T. Long-term outcome of transcatheter secundum-type atrial septal defect closure using AMPLATZER septal occluders. *J Am Coll Cardiol.* 2005;45(4):505–507.
50. Butera G, De Rosa G, Chessa M, et al. Transcatheter closure of atrial septal defect in young children: results and follow-up. *J Am Coll Cardiol.* 2003;42(2):241–245.
51. Sharafuddin MJ, Gu X, Titus JL, Urness M, Cervera-Ceballos JJ, Amplatz K. Transvenous closure of secundum atrial septal defects: preliminary results with a new self-expanding nitinol prosthesis in a swine model. *Circulation.* 1997;95(8):2162–2168.
52. Thanopoulos BD, Laskari CV, Tsaousis GS, Zarayelyan A, Vekiou A, Papadopoulos GS. Closure of atrial septal defects with the AMPLATZER occlusion device: preliminary results. *J Am Coll Cardiol.* 1998;31(5):1110–1116.
53. Hijazi ZM, Cao Q-L, Patel HT, Rhodes J, Hanlon KM. Transesophageal echocardiographic results of catheter closure of atrial septal defect in children and adults using the AMPLATZER device. *Am J Cardiol.* 2000;85(11):1387–1390.
54. Chan KC, Godman MJ, Walsh K, Wilson N, Redington A, Gibbs JL. Transcatheter closure of atrial septal defect and interatrial communications with a new self expanding nitinol double disc device (AMPLATZER septal occluder): multicentre UK experience. *Heart.* 1999;82(3):300–306.
55. Butera G, Carminati M, Chessa M, et al. CardioSEAL/STARFlex versus AMPLATZER devices for percutaneous closure of small to moderate (up to 18 mm) atrial septal defects. *Am Heart J.* 2004;148(3):507–510.

56. Chessa M, Carminati M, Butera G, et al. Early and late complications associated with transcatheter occlusion of secundum atrial septal defect. *J Am Coll Cardiol.* 2002;39(6):1061–1065.
57. DiBardino DJ, McElhinney DB, Kaza AK, Mayer JE, Jr. Analysis of the US Food and Drug Administration Manufacturer and User Facility Device Experience database for adverse events involving AMPLATZER septal occluder devices and comparison with the Society of Thoracic Surgery congenital cardiac surgery database. *J Thorac Cardiovasc Surg.* 2009;137(6):1334–1341.
58. Divekar A, Gaamangwe T, Shaikh N, Raabe M, Ducas J. Cardiac perforation after device closure of atrial septal defects with the AMPLATZER septal occluder. *J Am Coll Cardiol.* 2005;45(8):1213–1218.
59. Amin Z, Hijazi ZM, Bass JL, Cheatham JP, Hellenbrand WE, Kleinman CS. Erosion of AMPLATZER septal occluder device after closure of secundum atrial septal defects: review of registry of complications and recommendations to minimize future risk. *Cathet Cardiovasc Interv.* 2004;63(4):496–502.
60. Kort HW, Balzer DT, Johnson MC. Resolution of right heart enlargement after closure of secundum atrial septal defect with transcatheter technique. *J Am Coll Cardiol.* 2001;38(5):1528–1532.
61. Teo KS, Carbone A, Piantadosi C, et al. Cardiac MRI assessment of left and right ventricular parameters in healthy Australian normal volunteers. *Heart Lung Circ.* 2008;17(4):313–317.

3

ASDs: Clinical Perspectives

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Atrial Septal Defect

Definition

Atrial septal defects (ASDs) are congenital cardiac defects that allow communication between the left and right atria and account for 10% of all congenital heart disease (CHD). There are several different types of ASDs. The most common is secundum, present in the region of the fossa ovalis and accounting for 75% of all ASDs. Secundum ASD is the most common CHD in adult patients after bicuspid aortic valve. It is more common in females with a female to male ratio of 2:1.

The primum ASD (15%–20% of ASD cases) is positioned in the inferior part of the atrial septum, near the crux of the heart. This defect is associated with atrioventricular septal defects. The sinus venosus type (5%–10% of ASD cases) is located in the superior or inferior part of the septum, near the superior or inferior vena cava entry to the right atrium. The superior type is usually associated with partial anomalous pulmonary venous drainage.

The uncommon coronary sinus septal defect (< 1%), allows shunting through the ostium of the coronary sinus.

Patent foramen ovale (PFO) is a flaplike communication in which the septum primum covering the fossa ovalis overlaps with the superior limbic band of the septum secundum. In some patients, the septum primum or secundum is aneurysmal and may have multiple small fenestrations.

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