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# Common Congenital Heart Disorders in Adults

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**C**ongenital heart disease (CHD) is one of the most common inborn defects, occurring in 0.5-1.2% of newborns.<sup>1</sup> Increasing numbers of affected infants now survive into adulthood, which is a testament to the major advances in surgical technique, post-operative care, and medical treatment. The number of adults with CHD in the U.S. has reached ~800,000, and this number will undoubtedly continue to grow with time.<sup>2</sup> Therefore, adult cardiologists should have some understanding of the medical management of this burgeoning population. Currently, most adults with CHD are followed by an adult cardiologist who has virtually no dedicated training in the diagnosis or management of CHD, or by a pediatric cardiologist who has had little experience in comprehensive adult care.<sup>3</sup> Because of this discrepancy in quality care delivery, the American College of Cardiology convened the 32nd Bethesda Conference and made the following recommendations:<sup>4</sup>

- Over the next 10 years, more cardiologists should be trained in the subspecialty of adult congenital heart disease (ACHD).
- One regional ACHD center should be created to serve a population of 5 to 10 million people so that 30 to 50 such centers should be developed or strengthened across the entire U.S.
- Every adult cardiology and cardiothoracic surgery program should have a referral basis with a regional ACHD center.
- A structured plan should exist to help CHD patients transition smoothly from pediatric to adult care.
- All adults with moderate and complex CHD should be referred to an ACHD cardiologist.
- Cardiac catheterization, electrophysiological testing, and surgical procedures in adults with moderate and complex CHD should be performed in regional ACHD centers.
- A multidisciplinary approach should be established for pregnancy care and delivery in ACHD patients.

**TABLE 1.** Incidence per million live births

Lesion	Number of studies	Mean	SD	Lower quartile	Median	Upper quartile	NERICP 1975-1977
VSD	43	3570	2878	1757	2829	4482	345
PDA	40	799	1399	324	567	782	135
ASD	43	941	1043	372	564	1059	65
AVSD	40	348	165	242	340	396	110
PS	39	729	731	355	532	836	73
AS	37	401	543	161	256	388	41
Coarc	39	409	246	289	356	492	165
Tetralogy	41	421	188	291	356	577	196
d-TGA	41	315	115	231	303	388	218
HRH	32	222	199	105	160	224	—
Tricuspid atresia	11	79	52	24	92	118	56
Ebstein's anomaly	5	114	138	38	40	161	12
Pul atresia	11	132	123	76	83	147	69
HLH	36	266	216	154	226	279	163
Truncus	30	107	71	61	94	136	30
DORV	16	157	103	82	127	245	32
SV	23	106	70	54	85	136	54
TAPVC	25	94	46	60	91	120	58
All cyanotic	37	1391	590	1078	1270	1533	888
All CHD*	43	9596	7484	6020	7669	10,567	2033
BAV	10	13,556	13,049	5336	9244	13,817	—

\*Excluding bicuspid nonstenotic aortic valves, isolated partial anomalous pulmonary venous connection, and silent ductus arteriosus.

BAV, bicuspid aortic valve; CHD, congenital heart disease; Coarc, coarctation of the aorta; NERICP, New England Regional Infant Cardiac Program. Other abbreviations as in legend to Figure 5.

[From Hoffman JI, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol* 2002;39:1890-900. Reprinted with permission.]

## Classification of CHD

The incidences of individual major forms of CHD were recently compiled from 44 studies (see Table 1).<sup>1</sup> Since several common lesions, such as bicuspid aortic valve (BAV), mitral valve prolapse (MVP), and partial anomalous pulmonary venous connection (PAPVC), may not be recognized clinically, the actual number of CHD cases is likely to be underestimated. Traditionally, CHD can be categorized into either acyanotic or cyanotic lesions. *Acyanotic* defects include those with (1) simple left-to-right shunt physiology or (2) obstructive outflow or regurgitant valvular lesions. *Cyanotic* lesions are caused by the presence of desaturated blood in the systemic circulation, which may be due to (1) diminished pulmonary blood flow with obligatory right-to-left shunt or (2) increased pulmonary blood flow ultimately resulting in increased pulmonary resistance with late onset right-to-left shunt, ie, Eisenmenger

**TABLE 2.** Classification of congenital heart disease

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Left-to-right shunt

- Atrial septal defect
- Ventricular septal defect
- Patent ductus arteriosus
- Partial anomalous pulmonary venous connection
- Endocardial cushion defect
- Sinus of Valsalva aneurysm
- Coronary artery fistula

Outflow obstruction lesions

- Bicuspid aortic valve
- Coarctation of aorta
- Pulmonary stenosis

Cyanosis and decreased pulmonary blood flow

- Tetralogy of Fallot
- Tricuspid atresia
- Pulmonary atresia
- Hypoplasia of right ventricle
- Ebstein's anomaly

Cyanosis and increased pulmonary blood flow

- Transposition of great arteries
- Double-outlet ventricle
- Double-inlet ventricle
- Truncus arteriosus
- Total anomalous pulmonary venous connection

Cyanosis and increased pulmonary vascular resistance

- VSD with Eisenmenger syndrome
- PDA with Eisenmenger syndrome
- ASD with Eisenmenger syndrome

Anomalies of major blood vessels

- Congenitally corrected transposition of great arteries
  - Coronary artery anomalies
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syndrome. Another approach classifies CHD according to simple or complex lesions. *Simple* lesions include atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA), aortic stenosis (AS), pulmonic stenosis (PS), and coarctation of the aorta (CoA). *Complex* lesions include Ebstein's anomaly, transposition of the great arteries, congenitally corrected transposition of the great arteries (CCTGA), tetralogy of Fallot (TOF), and Eisenmenger's syndrome. The third approach combines both the physiologic (acyanotic versus cyanotic) and the anatomic (simple versus complex) classification and is listed in Table 2.

## Evaluation and Management

The evaluation of CHD patients encompasses a detailed knowledge of (1) the original anatomy and physiology; (2) the dynamic changes that

occur with time; (3) the effects of “adult” disease (eg, systemic arterial hypertension, coronary artery disease) or conditions (eg, pregnancy) superimposed on the native physiology; (4) the types of operative repair (both past and present) for each lesion; (5) the presence and extent of possible postoperative residua, sequelae, and complications; and (6) the proper selection, performance, and interpretation of modalities required for anatomic imaging and hemodynamic assessment.<sup>5</sup>

In general, patients with simple CHD require a modest level of clinical care aimed at prevention of complications (eg, endocarditis). Those with medium or high-risk CHD may require extensive evaluation and management of cardiac function, arrhythmias, surgical revisions, genetic counseling, and pregnancy issues. The incidence of CHD in offspring of women with CHD is significantly higher at 5 to 6%, and the cardiac lesions are often different than the mother.<sup>6</sup> Contraindications to pregnancy include severe pulmonary hypertension ( $>3/4$  systemic), functional class III or IV heart failure (due to ventricular dysfunction), Marfan’s syndrome with an aortic root  $> 40$  mm (unpredictable risk of aortic dissection and rupture), severe cyanosis (because of adverse fetal outcome), and severe obstructive lesions.<sup>7</sup> Patients with severe fixed obstructive lesions (eg, aortic stenosis, pulmonary stenosis, and hypertrophic obstructive cardiomyopathy) can poorly tolerate the hemodynamic changes that occur during pregnancy (40 to 50% increase in plasma volume) because of their inability to increase cardiac output.<sup>8</sup> Management of pregnant CHD patients should be undertaken in tertiary care center with expertise in ACHD.<sup>9</sup> Prevention or treatment of infective endocarditis (IE) is a constant theme.<sup>10</sup>

Careful physical examination consists of gathering information from five main sources: physical appearance, arterial pulse, jugular venous pulse, precordial palpation, and auscultation.<sup>11</sup> In many lesions, physical examination alone can be diagnostic. Routine electrocardiogram (ECG) can be helpful in determining the QRS and QT duration, which can portend risks for future ventricular tachycardia. Patients at particular risks for arrhythmias include those with Mustard or Senning procedure for D-transposition of great arteries, post-Fontan procedure, and repaired TOF.<sup>12</sup> Noninvasive imaging studies are helpful in determining the anatomic and functional features of the disease and associated defects, including routine chest X-ray (CXR), echocardiography, computed tomography (CT), and magnetic resonance imaging (MRI). Comprehensive 2-D echocardiography with spectral Doppler, color-flow imaging, and echocontrast is considered the mainstay in the diagnosis and follow-up assessment of most CHD patients.<sup>5,13</sup> Finally, familiarity with different

**TABLE 3.** Palliative procedures for congenital heart disease

Name of procedure	Description	Complications
Pulmonary artery banding	Constriction of main pulmonary artery	Inadequate band with consequent pulmonary vascular disease. Branch pulmonary artery stenosis. Pulmonic valve dysfunction.
Waterston shunt	Ascending aorta to right pulmonary artery	Pulmonary hypertension due to too large a shunt or kinked right pulmonary artery.
Potts shunt	Descending aorta to left pulmonary artery	Kinking of left pulmonary artery or excess shunt and pulmonary hypertension.
Blalock–Taussig shunt	Subclavian artery to branch pulmonary artery	Inadequate shunt to maintain pulmonary blood flow or stenosis of pulmonary branch to which connected or excess pulmonary blood flow with pulmonary hypertension.
Modified Blalock–Taussig shunt	Gore-Tex graft from subclavian artery to pulmonary artery	Excessive shunt resulting in pulmonary hypertension.
Glenn shunt	Superior vena cava to right pulmonary artery with division of main pulmonary artery	Postoperative cyanosis due to increased collaterals from superior to inferior vena cava or pulmonary arteriovenous fistulas.
Bidirectional Glenn shunt	Superior vena cava to both (undivided) pulmonary arteries	Postoperative cyanosis due to increased collaterals from superior to inferior vena cava or pulmonary arteriovenous fistulas.

types of “palliative” and “corrective” surgery as well as their potential long-term complications is essential (see Tables 3-5).

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**Dr. Gary Webb:** Other patients who commonly have an associated arrhythmia are older patients with ASD's and Ebstein's anomaly.

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## Case Presentations

In the next section, we present 12 representative cases of CHD seen in our Ahmanson-UCLA Adult Congenital Heart Disease Center over the last 20 years. To provide a point of departure for discussion, the case format begins with a patient history and then delves into a broader

**TABLE 4.** Corrective procedures for “simple” congenital heart lesions

<b>Lesion</b>	<b>Corrective procedure</b>	<b>Complications and residual abnormalities</b>
Atrial septal defect	Suture repair, patch closure, or transcatheter closure	Residual shunting. Associated mitral valve abnormalities. Persistent pulmonary hypertension. Right heart chamber enlargement.
Ventricular septal defect	Surgical repair (via right transatrial approach)	Residual patch leak. Arrhythmias if ventricular incision needed.
Patent ductus arteriosus	Surgical ligation or catheter device closure	Residual shunting (more likely if calcified).
Bicuspid aortic valve	Surgical or balloon valvuloplasty Pulmonic autograft Valve replacement	Associated lesions (ventricular septal defect, coarctation). Restenosis. Prosthetic valve dysfunction.
Subaortic stenosis	Excision of membrane or fibromuscular ridge; septal myotomy	Aortic regurgitation. Iatrogenic ventricular septal defect. Conduction defects. Mitral valve injury. Recurrent stenosis.
Coarctation of aorta	Multiple repair procedures	Residual or recurrent coarctation. Left ventricular hypertrophy. Associated lesions (eg, bicuspid aortic valve, parachute mitral valve, supramitral ring).
Ebstein's anomaly	Surgical repair or tricuspid valve with annuloplasty or valve replacement	Residual tricuspid regurgitation. Atrial arrhythmias and atrioventricular conduction defects. Associated lesions (patent foramen ovale, atrial septal defects, pulmonic stenosis, ventricular septal defects).
Pulmonic stenosis	Balloon dilation Surgical repair	Residual stenosis. Pulmonic regurgitation. Dynamic right ventricular outflow obstruction (early postoperative).
Coronary artery anomalies	Various repair procedures	Left ventricular dysfunction. Mitral regurgitation. Myocardial ischemia and infarction.

**TABLE 5.** Corrective procedures for “complex” malformations

<b>Lesion</b>	<b>Corrective Procedure</b>	<b>Complications and Residual Abnormalities</b>
Transposition of the great arteries (TGA)	Atrial switch surgery (Senning or Mustard procedure)	Rhythm and conduction disturbances Baffle leaks and obstruction Vena caval and pulmonary venous obstruction Tricuspid regurgitation Right ventricular dysfunction
TGA	Arterial switch procedure	Supravalvular pulmonic stenosis Supravalvular aortic stenosis (less common) Regional wall motion abnormalities of the left ventricle
Tricuspid atresia or double-inlet single ventricle	Fontan repair (right atrium to pulmonary artery or right ventricle)	Cavoatrial shunting, atrial septal shunting, thrombus, right atrial to pulmonary artery obstruction
Atrioventricular canal defects	Patching of atrial and/or ventricular septal defects combined with valve repair	Residual mitral regurgitation Iatrogenic mitral stenosis Subaortic stenosis Patch leaks
Tetralogy of Fallot	VSD patch and relief of infundibular pulmonic stenosis	Pulmonic regurgitation Right ventricular aneurysms (with older repairs) Residual right ventricular outflow obstruction Ventricular septal patch leaks
TGA with ventricular septal defect (VSD) and pulmonic stenosis	Rastelli repair (conduit from right ventricle to pulmonary artery with VSD patch directing subaortic flow)	VSD patch leak, subaortic obstruction Prosthetic valve dysfunction
TGA with VSD and subaortic stenosis	Damus–Kaye–Stansel procedure	VSD patch leak Pulmonic regurgitation
Congenitally corrected TGA	Various repairs, depending on associated defects	Left-sided atrioventricular valve regurgitation Heart block Systemic (anatomic right) ventricular systolic dysfunction
Double-outlet right ventricle	Rastelli repair	Obstruction of left ventricular to aortic baffle Residual VSDs Obstruction in right-sided conduit

discussion of the pathophysiology of disease, physical examination, diagnostic imaging, and management options. Cases 1 to 7 are considered simple CHDs and cases 8 to 12 are complex CHDs.

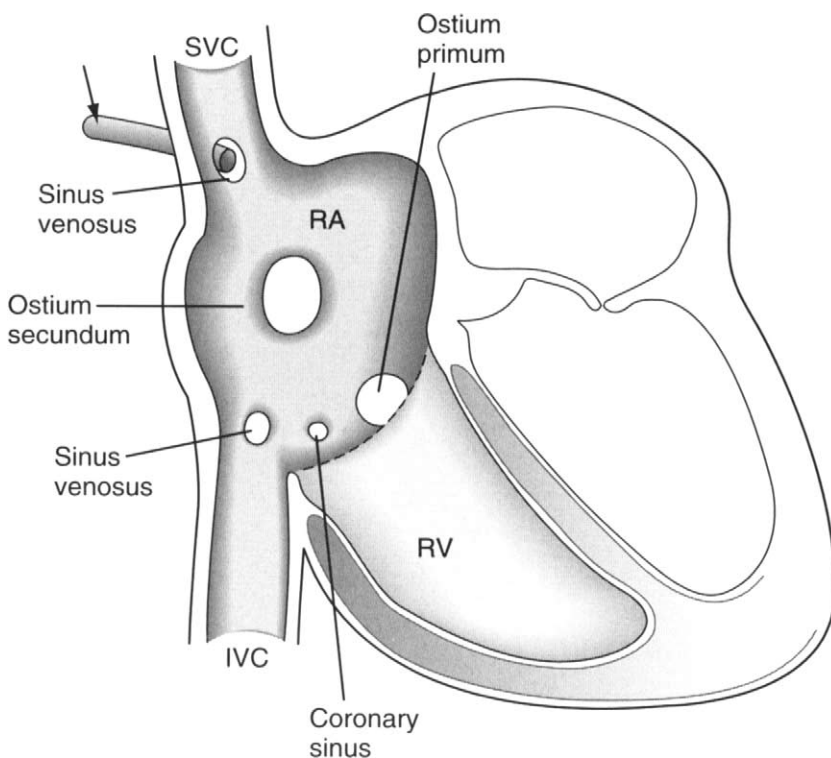
### *Case 1: Atrial Septal Defect*

A 35-year-old man presented to his primary care doctor for evaluation. An avid runner, he had noted a gradual decrease in exercise tolerance over the past 2 years. A systolic murmur was noted and the patient was referred to the cardiology clinic for definitive diagnosis. Examination revealed a mild right ventricular parasternal impulse, a fixed split S<sub>2</sub>, and a 2/6 mid-systolic crescendo-decrescendo murmur best heard at the left upper sternal border (LUSB). ECG showed normal sinus rhythm, rSR' in lead V<sub>1</sub>, and right-axis deviation. Transthoracic echocardiography (TTE) confirmed the presence of a secundum atrial septal defect with predominantly left-to-right shunt. Cardiac catheterization showed oxygen saturation step-up at the right atrium (RA) and right ventricle (RV) compared to the superior vena cava (SVC) and the inferior vena cava (IVC). The calculated pulmonary-to-systemic blood flow ratio ( $Qp/Qs$ ) was 1.7.

ASD accounts for about 7 to 11% of all CHD and 30% of adult CHD. It occurs twice as frequently in women than men.<sup>14</sup> The various subtypes are classified according to the location of defect. Ostium secundum is due to absence of tissue in the fossa ovalis and is the most common defect (75%). Ostium primum (15%) is due to a deficiency in the lowest or inlet portion of the septum, a form of partial endocardial cushion defect (or "atrioventricular septal defect"), often associated with a cleft mitral valve and mitral regurgitation. Sinus venosus defect (5 to 10%) is located directly between the left atrium and superior vena cava at the entrance of superior vena cava into the high right atrium. It is often associated with PAPVC. Blood from the right pulmonary veins flows preferentially through the atrial defect into the RA and RV, whereas blood from the left pulmonary veins flows predominately into the left atrium (LA) and left ventricle (LV).<sup>15</sup> Coronary sinus defect (1%) is rare and is associated with "unroofing" or absence of the coronary sinus with a direct connection of the left SVC to the LA (Fig 1).

ASDs are usually large, often 2 to 4 cm in diameter. The degree of left-to-right shunt depends on the defect size, the compliance of RV and LV, and the pulmonary vascular resistance (PVR) versus the systemic vascular resistance (SVR). In most adults, the RV is more compliant than the LV. Therefore, when all four cardiac chambers are in free communication during diastole, blood from the LA is shunted to the RA, causing increased blood flow and gradual dilatation of the RA, RV, and pulmo-





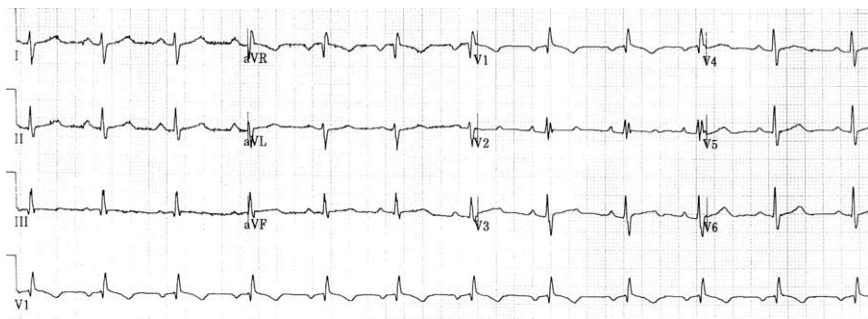
**FIG 1.** Schema of the various types of atrial septal defects. Unmarked arrow at upper left points to the right superior pulmonary vein. RA, right atrium; RV, right ventricle; IVC, inferior vena cava. (Adapted from Perloff JK. *Clinical Recognition of Congenital Heart Disease*, Philadelphia, PA: Saunders, 2003.)

nary arteries. Over time, the augmented pulmonary blood flow may result in medial hypertrophy of the pulmonary arteries, which can cause increased PVR and increased pulmonary arterial pressure (PAP). In rare instances, these changes can cause PVR to be greater than SVR, leading to right-to-left shunting as seen in the Eisenmenger's syndrome.<sup>16</sup> In most instances, however, systemic levels of PAP with a secundum ASD is due to co-existence of two diseases, namely ASD and primary pulmonary hypertension.

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**Dr. Gary Webb:** As a general rule, the mean pulmonary artery pressure in patients with ASD could be expected to be half the patient's chronologic age. When more substantial pulmonary hypertension is present, another diagnosis should be sought.

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**FIG 2.** ECG of a 28-year-old woman with an atrial secundum defect. Note the classic rSR' at lead V1 and right-axis deviation.

Diagnosis of ASD may be made by physical findings alone, which include a mid-systolic murmur over the left sternal edge, wide and fixed split S2, palpable and sustained RV impulse, and, occasionally, a diastolic rumble at the left lower sternal border (LLSB). Due to the enlarged RV, the ECG typically shows an “incomplete right bundle branch” pattern along with either a right-axis deviation in ostium secundum or a left-axis deviation in ostium primum; a left or low atrial rhythm suggests a sinus venosus ASD (Fig 2). A patient with an ASD usually has normal sinus rhythm for the first three decades of life, after which atrial fibrillation and supraventricular tachycardia may appear.<sup>17</sup> On CXR, a small aortic arch with moderate cardiomegaly due to dilatation of right-sided chambers, a small aortic arch, enlarged pulmonary arteries, and increased pulmonary vasculature may exist (Fig 3). Echocardiographic features include RV enlargement and paradoxical ventricular septal motion. Ostium primum and secundum defects can usually be visualized by TTE while sinus venosus defect and PAPVC are best detected using transesophageal echocardiography (TEE). Cardiac catheterization is rarely needed to confirm the diagnosis, unless defining the degree of left-to-right shunting, PAP, or coronary anatomy is crucial.

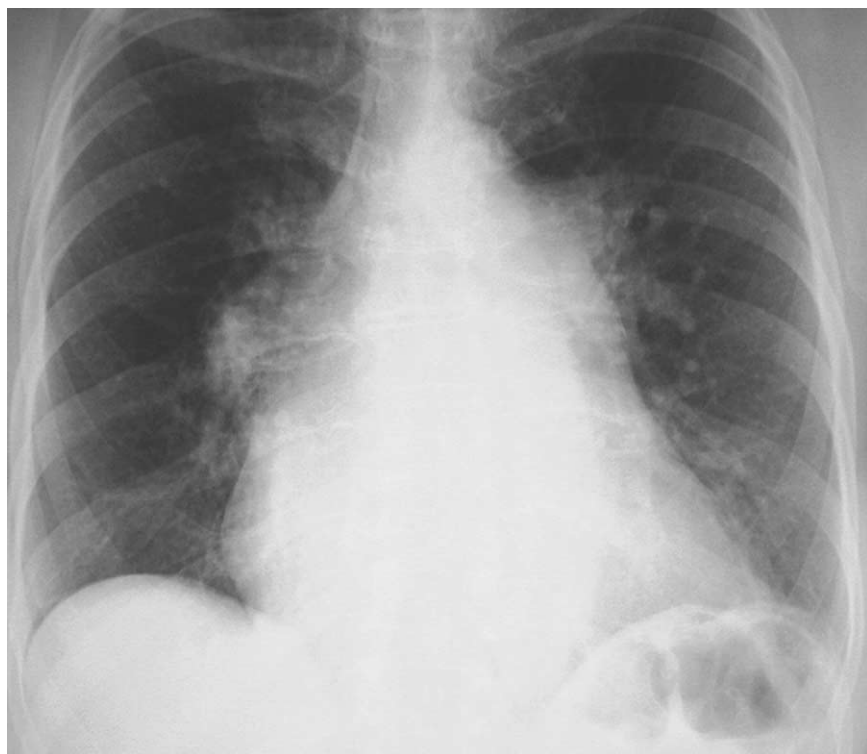
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**Dr. Gary Webb:** The most common arrhythmia in the ASD patient is atrial flutter. In the patient who has had surgical repair of an ASD, the patient may have an atypical form of atrial flutter known as intra-atrial reentrant tachycardia. As a rule, atrial fibrillation is a reflection of aging and is seen in the older patient.

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**Dr. Gary Webb:** MRI is also useful for the detection of sinus venosus defect and PAPVC.

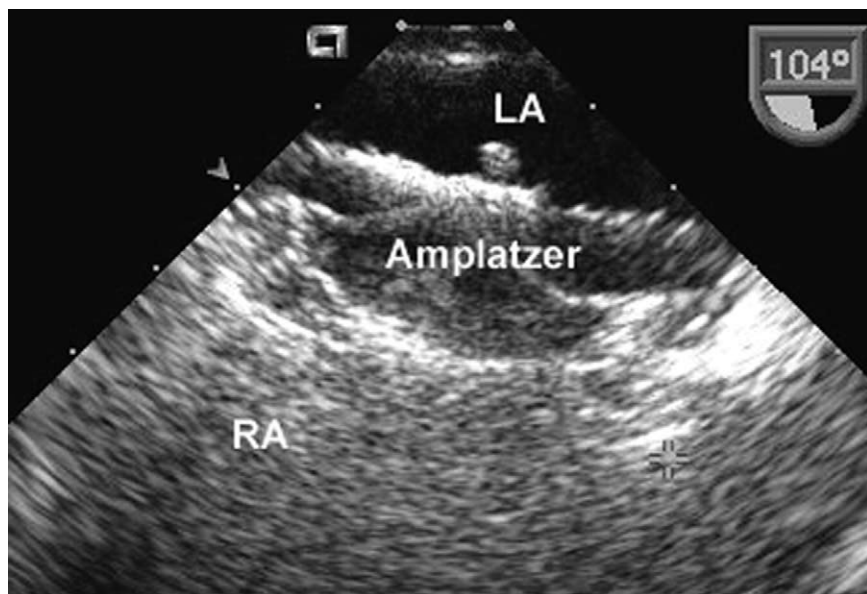
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**FIG 3.** CXR of a 51-year-old woman with a large atrial secundum defect and moderately elevated pulmonary arterial pressure. Note the cardiomegaly due to right atrial and ventricular enlargement along with prominent main pulmonary artery and vasculature.

## Management

Indications for ASD closure include large left-to-right shunt ( $Q_p/Q_s > 1.5/1$ ), significant RV dilatation, progressive pulmonary hypertension, and an episode of paradoxical embolism. In general, a small ASD ( $<0.5$  cm in diameter) is associated with no hemodynamic sequelae and patients can be followed. A large ASD often leads to palpitations, exertional dyspnea, and/or fatigue, the most common presenting symptoms in adult ASD patients.<sup>14</sup> Large defects should be repaired even if the patient is asymptomatic. In separate studies, the survival at 10 years after surgery surpassed medical therapy (95% vs. 84%)<sup>18</sup> and surgery prevented further clinical deterioration in most patients.<sup>19</sup> Surgical closure is performed by suturing a pericardial or Dacron patch over the defect. Operative mortality is less than 1% and most complications are related to perioperative arrhythmias such as atrial flutter, atrial fibrillation, or junctional rhythm.<sup>20</sup>



**FIG 4.** TEE of an Amplatzer device properly deployed between the left atrium (LA) and right atrium (RA).

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**Dr. Gary Webb:** “The Canadian Guidelines” (Therrien J et al. *Can J Cardiol* 2002;17:940-59, 1029-50, and 1135-58) suggest any significant ASD should be closed. The mere presence of right heart overload in the presence of a 10-mm or larger ASD would be sufficient reason to intervene. The presence of symptoms would be an additional stimulus to recommend closure. Only occasionally would the occurrence of paradoxical emboli be an indication.

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Recently, device closures have been shown to be safe and effective in the majority with secundum ASD.<sup>21</sup> The Amplatzer Septal Occluder (AGA Medical Corp., Golden Valley, MN) is approved by the FDA for closure of atrial secundum defects. It is a self-expandable, double disc device made from a Nitinol wire mesh. The two discs are linked together by a short connecting waist corresponding to the size of the ASD. To increase their closing ability, the discs and the waist are filled with polyester fabric. The polyester fabric is securely sewn to each disc by a polyester thread. The devices can be deployed under fluoroscopic guidance usually with TEE or intracardiac echocardiography guidance (Fig 4). Although no consensus exists, patients are typically treated with antiplatelet agents (eg, aspirin or clopidogrel) for 6 to 9 months to prevent

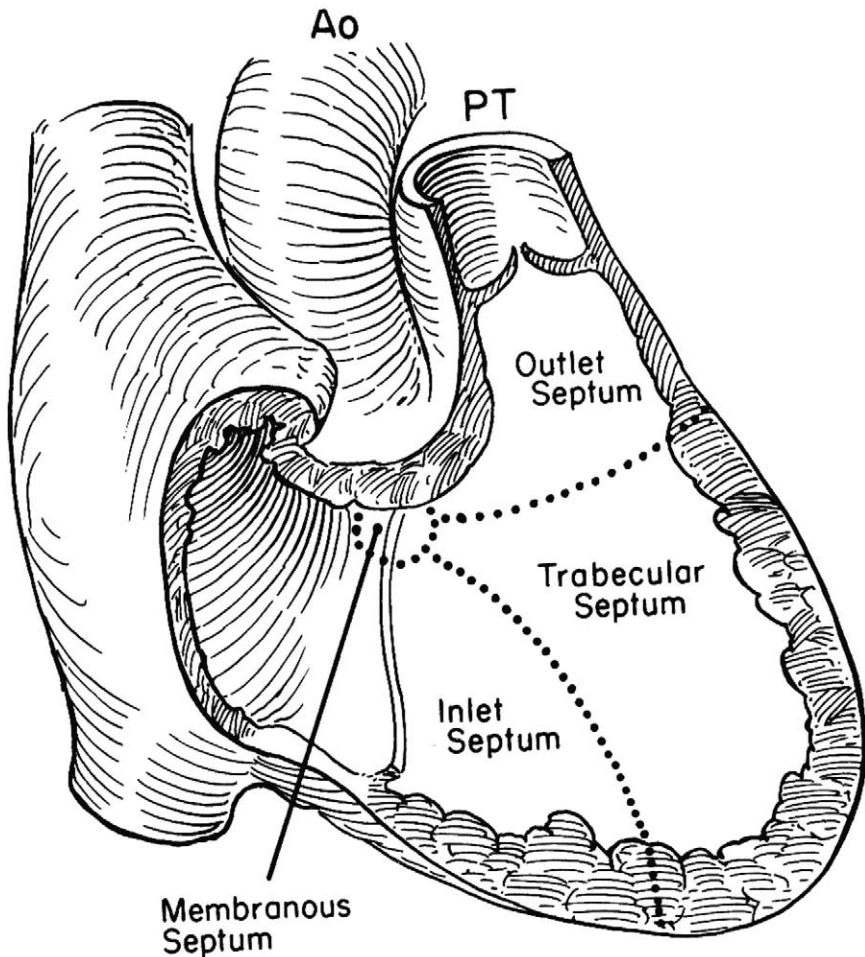
thrombus formation on the device.<sup>22</sup> This non-surgical approach has generated considerable excitement among those with an appropriately sized secundum ASD, including our patient who chose percutaneous device closure over surgical closure and has been doing well since. Device closure is not currently applicable to other anatomic types of ASD. Patients with ostium primum defects and mitral regurgitation should receive prophylaxis against IE.<sup>23,24</sup>

## *Case 2: Ventricular Septal Defect*

An 18-year-old woman noted progressive perioral cyanosis and clubbing of her digits. She was born in the Philippines and was told of a cardiac murmur at birth. She presented after being lost to follow-up. Examination revealed blood pressure of 130/75 and oxygen saturation of 92% on room air. At the LLSB, a 1/6 holosystolic murmur was heard along with a palpable impulse. A loud P2 followed by a mid-diastolic murmur was heard at the LUSB. TTE with Doppler imaging revealed bi-directional flow across the VSD. The peak velocity of left-to-right shunt was 3.5 m/s, representing a pressure difference between the LV and RV of 49 mmHg. Since the aortic systolic blood pressure was 130 mmHg, the right ventricular systolic pressure (RVSP) was estimated at 81 mmHg. Right heart catheterization (RHC) showed the RVSP was 85/12 mmHg; PAP was 90/24 mmHg, and pulmonary capillary wedge pressure (PCWP) was 20 mmHg. Systemic arterial oxygen saturation = 91%.

VSD is the most common congenital cardiac malformation in infants and children, accounting for 20% of all cases. It occurs with similar frequency in males and females. In 5% of patients, VSDs coexist with other major cardiac anomalies, particularly coarctation of the aorta and patent ductus arteriosus. In another 25%, the VSD is a component of tetralogy of Fallot, persistent truncus arteriosus, single ventricle, tricuspid atresia, double-outlet right ventricle, and interruption of the aortic arch.<sup>25</sup> Anatomically, 70% are located in the membranous portion of the interventricular septum, 20% in the muscular portion of the trabecular septum, 5% beneath the pulmonary valve in the outlet septum, and 5% near the tricuspid valve in the inlet septum (Fig 5). For muscular VSD, spontaneous closure occurs 90% by the time the infant is 10 months.<sup>26</sup> The mechanisms of spontaneous closure include adherence of the septal leaflet of tricuspid valve to the perimembranous defect, prolapse of an aortic cusp into the outlet defect, hypertrophy of muscle bundles sealing off the muscular VSD, and fibrotic changes at the margins of defects.<sup>25</sup>

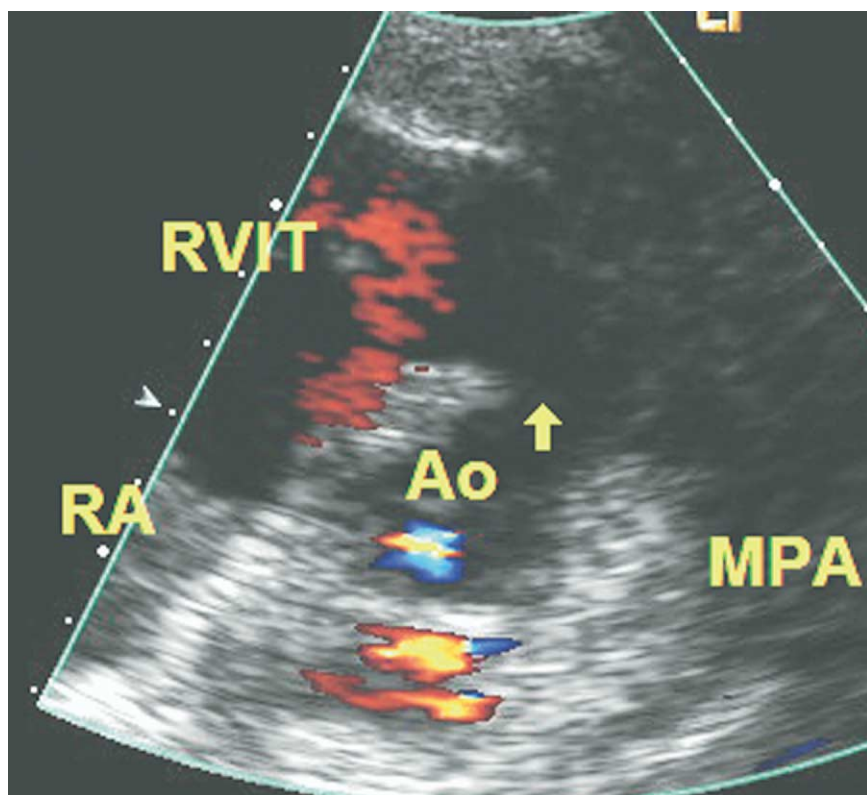
Similar to ASDs, the hemodynamic consequences of VSDs depend on



**FIG 5.** Schema of four common locations of ventricular septal defects. (Adapted from Perloff JK. *Clinical Recognition of Congenital Heart Disease*, Philadelphia, PA: Saunders, 2003.)

the size of the defect (varies from 1 mm to 2.5 cm in diameter) and the relative resistance of the PVR and SVR. Note that during systole, blood flows directly from the LV to the right ventricular outflow tract (RVOT) via the VSD. Therefore, the RV is *not* subjected to increased volume. In general, a small defect (“restrictive VSD”) causes no major effect since the pulmonary blood flow is increased minimally. In contrast, a large defect (“nonrestrictive VSD”) greater than 1 cm<sup>2</sup>/m<sup>2</sup> or 75% of the diameter of the aorta cause significant left-to-right shunt in the presence of a low PVR (Fig 6). Over time, PVR increases, compensatory RV

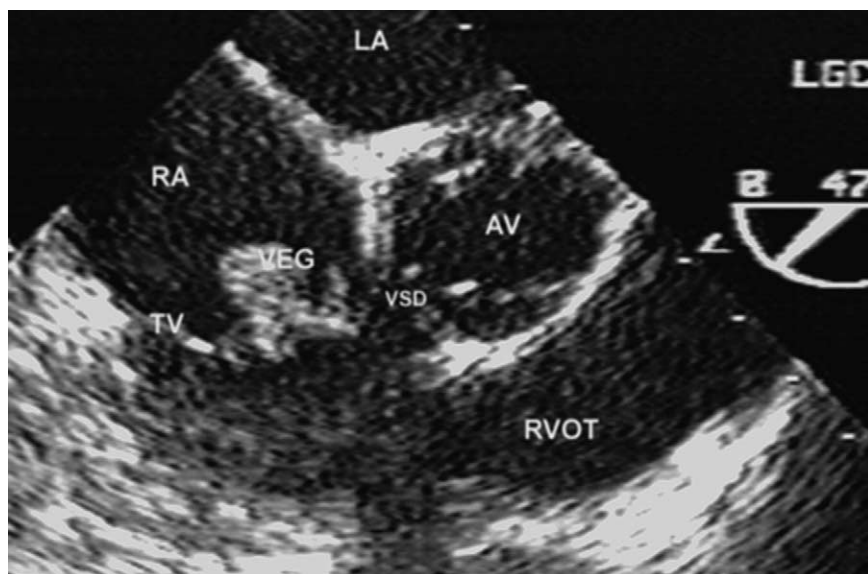




**FIG 6.** Transthoracic echocardiogram shows short-axis diastolic frame of a non-restrictive ventricular septal defect at the subpulmonic region (arrow). There is a small jet of aortic regurgitation. Ao, aorta; RA, right atrium; RVIT; right ventricular inflow tract; MPA, main pulmonary artery.

hypertrophy develops, and the magnitude of the shunting decreases and may even reverse in severe pulmonary hypertension.

On examination, a holosystolic murmur is best heard along the LLSB in the third and fourth intercostal spaces. The loudness of the murmur varies and does *not* necessarily correlate with the size of the defect. Smaller defects usually have larger interventricular gradients and create high-velocity turbulent flow.<sup>27</sup> Large defects often lead to pulmonary hypertension, resulting in minimal left-to-right shunt and no VSD murmur. The ECG may be normal with a small defect and a small left-to-right shunt or show findings consistent with LA enlargement and LV hypertrophy, indicating a moderate-sized defect with a >2:1 left-to-right shunt. ECG evidence of RV hypertrophy is seen in adults with Eisenmenger's



**FIG 7.** TEE shows vegetation attached to the tricuspid valve. Due to high-velocity jet flowing across the ventricular defect and hitting the tricuspid septal leaflet, this is the most common site of infective endocarditis. VEG, vegetation; TV, tricuspid valve; VSD, ventricular septal defect; RVOT, right ventricular outflow tract.

syndrome. Depending on the degree of shunt and PVR, the CXR may range from normal findings to increased pulmonary vascular markings (significant left-to-right shunt) to peripheral pruning of the pulmonary vasculature (pulmonary hypertension).

## Management

Most adults with VSD will fall into one of four categories: (1) those with previous surgical or spontaneous closure and no shunt; (2) those with a small restrictive defect ( $Qp/Qs < 2:1$ ) and normal RV pressure; (3) those with a moderate defect and mild elevation of RVSP; and (4) those with a large nonrestrictive defect and Eisenmenger's syndrome with bidirectional shunt.<sup>28</sup> Endocarditis prophylaxis is required for all patients with a VSD. Asymptomatic patients with a small VSD can be followed conservatively with extra vigilance toward IE prophylaxis. Once endocarditis occurs, it may be prudent to advocate surgical closure to prevent future recurrences (Fig 7). In patients with a large VSD and an elevated PVR to SVR ratio  $\geq 0.7$ , surgery is not recommended due to excessive operative mortality and morbidity. Small VSDs (ie, those with normal to mildly elevated RVSP and  $Qp/Qs \leq 1.5/1$ ) are usually not closed.



Simple perimembranous, high muscular, or subarterial VSDs can be closed via a right transatrial approach to avoid ventricular incisions and their electrical and mechanical consequences. Multiple muscular defects may require left ventriculotomy for adequate visualization, with the attendant risks of missed or incompletely closed defects, ventricular arrhythmia, and left ventricular dysfunction.<sup>29</sup> Intraoperative TEE with color-flow imaging is imperative to detect and size these leaks in the operating room at the time of closure.<sup>5,13</sup>

With advances in transcatheter technology, device closures have also been helpful for multiple muscular VSDs, for persistent postoperative VSD in complex conotruncal malformations, and even for acquired postinfarction VSD.<sup>30</sup> The CardioSEAL device (NMT Medical, Boston, MA) is a modified clamshell, self-expanding, double-umbrella device designed to close secundum ASD or patent foramen ovale (PFO), and some VSDs. The StarFLEX is a newer generation of the CardioSEAL designed to self-center once deployed. Its framework is able to close most holes and adapt to a variety of septal anatomy.<sup>31</sup> Future studies are needed to determine short-term and long-term risks and benefits of transcatheter versus surgical VSD closure. Because our patient already has pulmonary hypertension and peripheral cyanosis, she is not a candidate for either surgical or interventional closure.

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**Dr. Gary Webb:** The devices that are mentioned are not routinely used for VSD closure. Other devices have been developed for this use, the safety and efficacy of which are being evaluated.

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**Dr. Gary Webb:** The term peripheral cyanosis is commonly used by clinicians, although its significance is seldom clear. In patients with congenital heart disease, cyanosis is almost always central or “warm.” In other words, the arterial blood is desaturated centrally. To me, the term “peripheral cyanosis” is synonymous with “cold cyanosis,” reflecting critically low tissue perfusion reflecting a serious circulatory problem.

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**Dr. Gary Webb:** A Flolan infusion may well benefit patients with Eisenmenger physiology as well as those with other causes of pulmonary vascular disease. Unfortunately, such seems not to be the situation with this patient.

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### *Case 3: Patent Ductus Arteriosus*

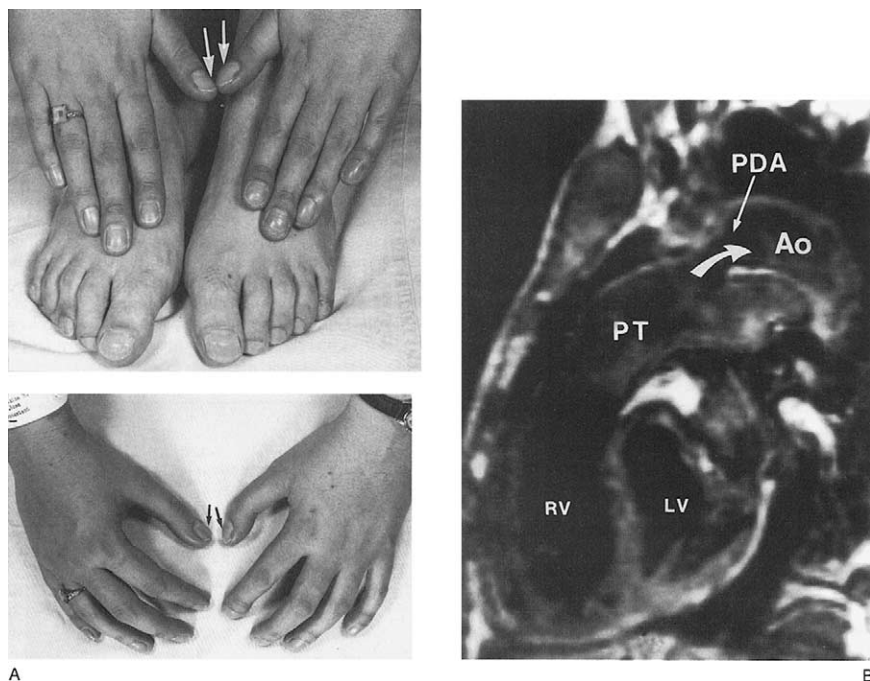
A 45-year-old lawyer was told of a cardiac murmur since childhood for which she had been taking antibiotic prophylaxis. The patient did

relatively well until age 40 when she developed exercise intolerance. A RHC revealed PAP of 100/57 mmHg, PCWP of 12 mmHg, and cardiac index of 3.8 L/min. She was treated with constant Flolan infusion for 3 years for presumed “primary” pulmonary hypertension but noted no improvement. As a result, she consulted many physicians for expert opinions. On one particular visit, a cardiologist noted *differential* cyanosis and clubbing of her extremities; the fingers were relatively acyanotic and not clubbed, while the toes were cyanotic and clubbed. The patient underwent a cardiac MRI which confirmed a large PDA. Left heart catheterization (LHC) showed a step-down in oxygen saturation from aortic arch to upper ascending aorta due to the right-to-left shunt from the pulmonary artery to the descending aorta.

In the fetus, the ductus arteriosus connects the proximal portion of the left pulmonary artery with the proximal descending aorta immediately below the entrance of the left subclavian artery. It allows pulmonary arterial blood to bypass the unexpanded lungs and enter the descending aorta for oxygenation in the placenta. It normally closes by 4 to 7 days after birth.<sup>32</sup> In some infants, particularly those born prematurely or with maternal rubella, the ductus may remain open and cause a continuous left-to-right shunt from the high-pressure aorta to the low-pressure pulmonary artery. From a clinical perspective, persistent PDA during adulthood can be classified as follows:<sup>33</sup>

- Silent: Tiny PDA detected only by non-clinical means (usually echocardiography), no audible heart murmur.
- Small: Audible left infraclavicular continuous murmur, often radiating to the left upper back, left-to-right shunt, negligible hemodynamic changes.
- Moderate: Audible continuous murmur, enlargement of the LA and LV, some degree of pulmonary hypertension.
- Large: Usually adult patients have Eisenmenger physiology, absent continuous murmur, right-to-left shunt, differential cyanosis and toe clubbing, auscultatory features of pulmonary hypertension (ejection sound, loud single S2, and Graham Steele pulmonary regurgitation murmur). See Fig 8.

Patients with a nonrestrictive PDA and low PVR typically have bounding peripheral arterial pulses, a widened pulse pressure, and a hyperdynamic LV impulse. When the aortic pressure is greater than pulmonary pressure during systole and diastole, there is a continuous “machinery-like” murmur that peaks near S2 and is heard best in the second left anterior intercostal space. However, as the PVR rises, the PAP



**FIG 8.** (A) Photographs of a 28-year old woman with patent ductus arteriosus (PDA), suprasystemic pulmonary vascular resistance, and reversed shunt. The patient is sitting with her hands placed on the dorsum of her feet. Cyanosis and clubbing are seen only in the left hand and feet. (B) Magnetic resonance image shows a nonrestrictive PDA and reversed shunt (curved arrow) from the pulmonary trunk (PT) into the aorta (Ao). (Adapted from Perloff JK. *Clinical Recognition of Congenital Heart Disease*. Philadelphia, PA: Saunders, 2003.)

can equalize with the aortic diastolic pressure, causing the *diastolic* ductal flow to diminish. As the PVR rises further, the PAP equalizes with the aortic systolic pressure, causing the *systolic* ductal murmur to diminish, and ultimately leaving the ductus murmur-free.<sup>11</sup> As PVR rises, the bounding pulses resolve. The ECG, CXR, and echocardiographic features vary according to the hemodynamic consequences. The ECG may be normal (a small PDA) or show isolated left ventricular hypertrophy (moderate-sized PDA), or biventricular hypertrophy (large PDA with elevated PAP). The CXR findings range from normal to increased pulmonary flow pattern, proximal pulmonary artery dilatation, a prominent aortic arch, and to “pruned” peripheral pulmonary arteries due to pulmonary vascular disease. With TTE, the shunt flow can usually be visualized at the LUSB or suprasternal notch using color-flow imaging. Cardiac catheterization is not typically needed for diagnosis, but can be used to obtain the hemodynamic and oximetry data.

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**Dr. Gary Webb:** Oximetry data are unreliable in patients with PDAs as a means of assessing the amount of left-to-right shunting. One cannot find an adequately mixed PA sample upon which to base shunt calculations. The amount of shunt flow can be inferred from a variety of other non-invasive measures including the size of the PDA, the dimensions of the left heart chambers, left ventricular hypercontractility, a wide arterial pulse pressure, and other factors.

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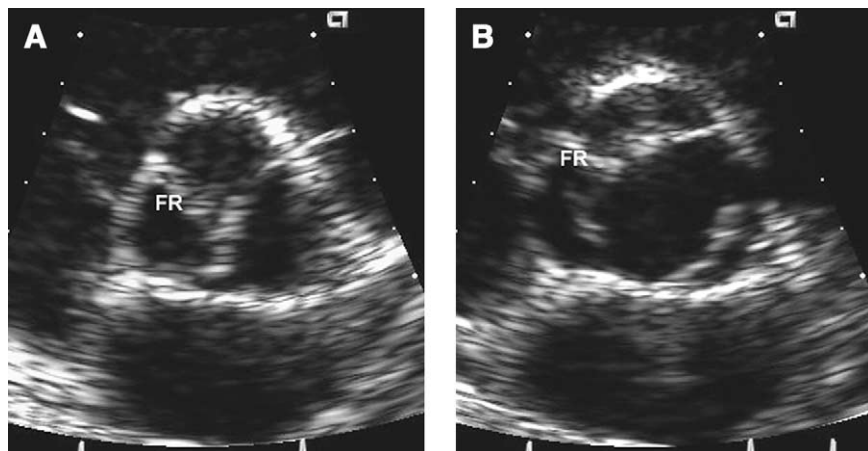
## Management

PDA is ordinarily detected in childhood, but a couple of undiagnosed patients are still seen in our ACHD center each year. In one report, 117 patients with PDA were diagnosed at the mean age of 36 years old between 1951 and 1984.<sup>34</sup> In general, closure of PDA is recommended to prevent left heart failure, to eliminate the risk of endarteritis, and to reduce the risk of pulmonary vascular disease in adults.<sup>35</sup> Operative closure of simple PDA in younger patients leaves few residua. In older patients, calcification is common and the ductus can tear during ligation. Other postoperative complications may include laryngeal nerve, phrenic nerve, or thoracic duct damage. Therefore, catheter device closure (provided the size is <10 mm) may be preferred in adults, with one study showing 95% closure rate and no events of delayed device migration, endocarditis, thromboembolism, or device disruption.<sup>36</sup> Endocarditis prophylaxis is recommended for 6 months after PDA device or surgical closure, or for life if any residual defect persists. This patient was referred to us at a late stage with elevated PVR, right-to-left shunt reversal across the ductus with Eisenmenger's physiology and should only be managed medically (see Case 12).

## Case 4: Bicuspid Aortic Valve

A 52-year-old woman previously healthy was admitted to hospital for a 2-week history of fever and chills. Blood cultures were positive for *Streptococcus viridans*. Cardiac auscultation revealed a loud 3/6 systolic crescendo-decrescendo murmur over the RUSB plus a high frequency early diastolic murmur. TTE showed a vegetation attached to a bicuspid valve. The ascending aorta was enlarged to 50 mm. She underwent combined aortic valve replacement and aortic root repair. Incidentally, she reported teeth cleaning by her dentist 6 weeks previously but was unaware of the BAV and thus did not take antibiotics for prophylaxis.

Left ventricular outflow tract (LVOT) obstruction may occur below the valve (due to subvalvular fibrous membrane), above the valve (supra-val-



**FIG 9.** TEE shows a bicuspid aortic valve during both diastole (A) and systole (B). The false raphe (FR) can often masquerade as a trileaflet aortic cusp during diastole but the classic oval “fish mouth” appearance during systole is pathognomonic.

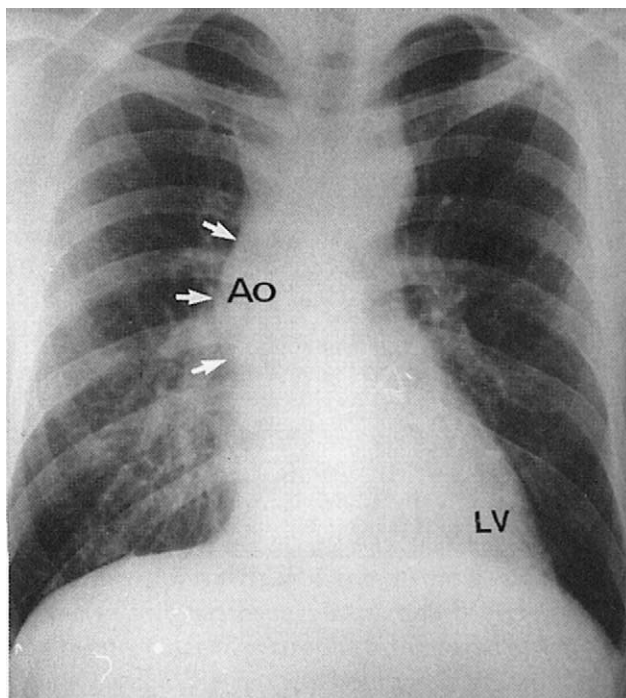
vular stenosis as seen in Williams syndrome), or at the level of the aortic valve. Stenotic aortic valves may be unicuspid, bicuspid, tricuspid, or quadricuspid, but approximately 70 to 85% involves a BAV. In the United States, estimated occurrence rate of BAV is 0.5 to 2% of the general population.<sup>37</sup> It is more common in males (ratio ranges from 3:1 to 5:1). Offspring of BAV patients have a higher incidence of BAV (~3.6%).<sup>38</sup> In 20% of patients, BAV is associated with other cardiac defects, including coarctation of aorta (most common), PDA, and VSD.

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**Dr. Gary Webb:** Most patients with BAV do not develop clinically important aortic valve disease.

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BAV is a classic example of a cardiac anomaly that is usually asymptomatic in childhood but becomes symptomatic in adulthood. The condition is often diagnosed because a murmur or click is noted during a routine physical. Dizziness, chest pain, or congestive heart failure do not appear until the area of the aortic orifice is less than 0.7 to 1.0 cm<sup>2</sup>. Anatomically, the BAV consists of two cusps, often of unequal sizes. The larger one usually contains the false raphe (Fig 9). The deformed valves are subjected to hemodynamic stress and over time lead to accelerated thickening of the aortic valve and calcification of the leaflets by age 50 to 60 years, in contrast to acquired calcific aortic stenosis, where symptoms develop at age 70 to 80 years.



**FIG 10.** CXR from a 28-year-old man with mild bicuspid aortic stenosis. Except for conspicuous ascending aortic dilatation (Ao) due to aortic medial tissue abnormalities, the CXR is normal. (Adapted from Perloff JK. *Clinical Recognition of Congenital Heart Disease*. Philadelphia, PA: Saunders, 2003.)

On physical examination, an ejection click is heard at both the apex and the RUSB. This is followed by a systolic ejection murmur that at times can radiate to the neck. The ECG exhibits normal sinus rhythm, a normal or vertical QRS axis, and varying degrees of LV hypertrophy. The CXR may show a prominent ascending aorta which is due to intrinsic medial weakness even in the presence of minor hemodynamic abnormality of the BAV<sup>39</sup> (Fig 10). Echocardiography is instrumental in identifying the level, morphologic type, and severity of stenosis.<sup>40</sup> On TTE, the parasternal long-axis view identifies the doming of aortic valve during systole while the parasternal short-axis view identifies a single closure line during diastole as well as the anatomy of the aortic root. Doppler interrogation establishes the gradient and permits calculation of the orifice size.

## Management

Those with BAVs are at much higher risk for bacterial endocarditis, accounting for 13.3% of all cases in one study.<sup>10,41</sup> Most common



organisms are *S. viridans* and *Staphylococci*. Patients must be instructed about the importance of good oral hygiene, routine dental care, proper skin care, and the appropriate use of antibiotics for IE prophylaxis.<sup>42,43</sup> Options of surgical or balloon valvotomy depend on the age of presentation, severity of obstruction, frequency of symptoms, and co-existing lesions. Intervention is recommended in those with symptoms, severe stenosis (peak gradient > 50 mmHg or aortic valve area < 0.5 cm<sup>2</sup>/m<sup>2</sup>), or with an abnormal ECG response to exercise (ST-segment depression > 2 mm).<sup>44</sup> Pre-operative coronary angiography is indicated in those at risk for coronary artery disease.<sup>45</sup> Due to intrinsic medial abnormality, aortic root disease may result in progressive aortic dilatation regardless of the severity of aortic stenosis or aortic regurgitation.<sup>39</sup> Aortic dissection can occur. As such, monitoring of aortic root size is important. If enlarged, beta-blockers may be necessary unless the dimension progressively changes or exceeds 50 mm, for which surgery should be considered.

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**Dr. Gary Webb:** I would take issue with reference to the ST segment depression on exercise testing as an indication for “intervention.” This is used in pediatric practice as an indication for aortic valvectomy—either surgical or balloon. This is not an accepted indication for aortic valve replacement in an adult patient with aortic stenosis.

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**Dr. Gary Webb:** The use of beta-blockers may be quite reasonable in such patients, although data supporting the use of these agents are best in patients with Marfan syndrome or those who have had an aortic dissection.

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Surgical or balloon valvuloplasty is often palliative in young adults but can induce significant aortic regurgitation. Most patients ultimately require valve replacement. Options include a mechanical valve, a bioprosthetic valve (homograft or heterograft), or a Ross procedure. In the Ross procedure, the patient’s pulmonic valve is used as an autograft to replace the dysfunctional BAV; a homograft usually is then used to replace the pulmonary valve. This procedure allows for growth of the “neo-aortic” valve, does not require anticoagulation, and is favored in the pediatric population. Bioprosthetic degeneration at the pulmonary valve position in a low-pressure RV should be tolerated well, though repeat operation is sometimes necessary. A recent study of 348 Ross procedures noted low surgical morbidity and mortality (96% at 1 year).<sup>46</sup> Because of her age and preferences, our patient underwent a mechanical aortic valve replacement, though homograft or Ross valve replacement is felt to be generally more infection resistant.

## Case 5: Pulmonary Stenosis

A 54-year-old businessman was noted to have a murmur as a teenager during a military service induction examination. He had been physically active with no complaints of angina, palpitation, or peripheral edema. At a recent routine visit, his primary care doctor ordered a TTE which noted "right ventricular enlargement." A follow-up chest CT scan noted a "pulmonary artery aneurysm." The patient was referred to our ACHD center for consultation. On examination, there was an ejection click at the LUSB that decreased with inspiration followed by 1/6 midsystolic murmur. Repeat TTE showed mild RV enlargement, trace tricuspid regurgitation, and mild valvular pulmonary stenosis with a domed-shape valve.

PS is the most common form of right-sided obstruction. Usually an isolated congenital anomaly, it occurs in 7 to 10% of CHD patients. Valve morphology can be one of three types: mobile dome-shaped, dysplastic, and bicuspid.<sup>47</sup> A mobile thin dome-shaped valve is most common and is associated with pulmonary trunk dilation because of an inherent medial abnormality.<sup>39</sup> A dysplastic valve is much less common and is caused by myxomatous thickening of all three leaflets. A bicuspid valve is often a feature of tetralogy of Fallot. PS may also be associated with various genetic disorders, including Noonan, Williams, and Alagille syndromes.<sup>11</sup> Noonan's syndrome is characterized by short stature, webbed neck, hypertelorism, low-set ears, pectus excavatum or carinatum, and micrognathia. Williams syndrome is characterized by mental retardation, wide-set eyes, a broad forehead, patulous lips, a small chin, and supraaortic stenosis. Alagille syndrome, also referred to as arteriohepatic dysplasia, is an autosomal dominant disorder with abnormalities of the heart, liver, eyes, kidneys, and skeleton. Facial appearance is characterized by prominent overhanging forehead, deep-set eyes, and a small pointed chin (Fig 11).

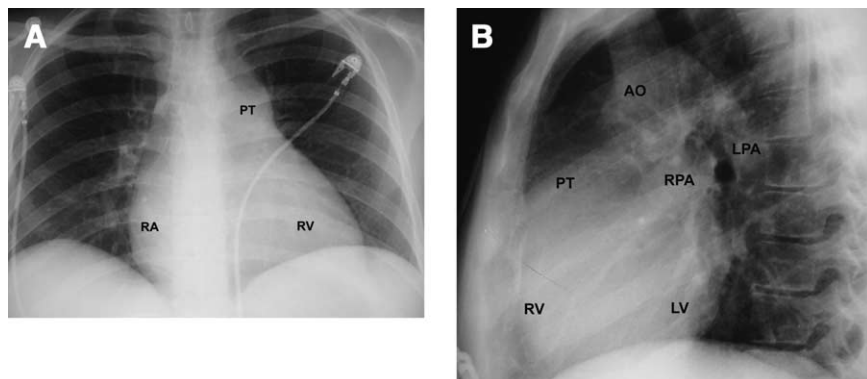
On physical examination, there may be a prominent jugular "a" wave (due to forceful RA contraction to fill a noncompliant RV), a palpable parasternal RV impulse (due to RV hypertrophy), an ejection click at the LUSB (due to abrupt opening of the leaflets or a dilated main pulmonary artery), and a parasternal crescendo-decrescendo midsystolic murmur (due to flow turbulence across a stenotic valve). ECG may be normal in mild PS or may show right-axis deviation and RV hypertrophy in severe PS. The characteristic CXR feature is a prominent pulmonary artery caused by dilatation of the main and left pulmonary arteries (Fig 12). The right pulmonary artery branches at acute right angle from main pulmo-





**FIG 11.** (A) The chubby round bloated face of an infant with typical mobile dome-shaped pulmonary valve stenosis. (B) Facial appearance of arteriohepatic dysplasia (Alagille syndrome) characterized by deeply set eyes, prominent overhanging forehead, and small pointed chin. (C) Noonan syndrome in an 18-year-old phenotypic male with webbing of the neck, low-set ears, abnormal auricles, hypertelorism, and a small chin. (D) Low posterior hair line of a neonate with Noon syndrome. (Adapted from Perloff JK. *Clinical Recognition of Congenital Heart Disease*. Philadelphia, PA: Saunders, 2003.)

nary artery and therefore is not dilated. Echocardiography is the diagnostic method of choice to show the conical or dome-shaped stenotic valve leaflets as well as identifying paradoxical motion of the interventricular septum when RV overload is present. Continuous-wave Doppler imaging allows estimation of the transvalvular gradient. The modified Bernoulli equation  $[(\text{pressure gradient} = 4 \times (\text{peak velocity}^2))]$  can be applied to the peak velocity across the pulmonic valve to derive the peak and mean pulmonary valve pressure gradient as well as the tricuspid regurgitant



**FIG 12.** CXR features of a patient with pulmonary stenosis in PA (A) and lateral (B) views. Note the enlarged right ventricle (RV) adjacent to the sternum. The pulmonary trunk (PT) and left pulmonary artery (LPA) are dilated, but not the right pulmonary artery (RPA).

velocity to derive the RVSP.<sup>48</sup> MRI can also be used to assess the level of obstruction and other associated lesions such as peripheral pulmonary artery stenosis.

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**Dr. Gary Webb:** The duration of ejection systolic murmurs in patients with pulmonary stenosis varies directly with the severity of the obstruction. As the gradients get greater, one expects the murmur to fill most of systole and even perhaps to extend beyond the aortic closure sound in a very severe case. Clinicians should describe the length of the murmur in cases like this, or draw a picture of what they hear in the medical record.

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## Management

Management requires elucidation of the degree of obstruction, the level of stenosis (infundibular, valvular, supraventricular), and any associated abnormalities. The degree of obstruction is classified as the following:<sup>49</sup>

- *Trivial* (<25 mmHg transvalvular gradient and <50 mmHg RVSP)
- *Mild* (25-49 mmHg transvalvular gradient and 50-74 mmHg RVSP)
- *Moderate* (50-75 mmHg transvalvular gradient and 75-100 mmHg RVSP)
- *Severe* (>80 mmHg transvalvular gradient and >100 mmHg RVSP)

Trivial and mild PS can be followed medically and patients can engage in unrestricted physical activity. Moderate to severe PS should have relief of the obstruction, even if asymptomatic. For isolated simple PS,

transcatheter balloon valvuloplasty is the procedure of choice in patients of all ages. In 488 patients followed for a mean of 31 months, only 89 (21%) patients required repeat dilatation or open surgery.<sup>50</sup> Thus, this technique provides satisfactory results, albeit sometimes at the expense of increased pulmonic regurgitation and right ventricular enlargement.<sup>51</sup> Occasionally, we encounter adults with previous surgical valvuloplasty. Careful follow-up for residual pulmonary stenosis and/or pulmonic regurgitation in both balloon and surgical valvuloplasty patients is required. Patients with severe pulmonary regurgitation, progressive RV dilatation, and reduced exercise capacity should have pulmonary valve replacement. Because our patient reports no complaints and the TTE showed only mild PS, we recommend biannual evaluation. Patients with PS should have IE prophylaxis.

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**Dr. Gary Webb:** Careful follow-up is not indicated for all patients with residual pulmonary stenosis and/or pulmonary regurgitation. Patients with mild residual stenosis or mild regurgitation do not need expert follow-up and may in fact be followed by their family physicians. Note that the requirement for cardiology follow-up is considered by some insurance companies as an indication that the patient is not eligible for insurance at standard rates. We cardiologists should keep the implications of our recommendations in mind.

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**Dr. Gary Webb:** The incidence of IE in these patients is so low that the recommendation for IE prophylaxis should be seen as controversial.

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### *Case 6: Coarctation of Aorta*

A 34-year-old firefighter was diagnosed with hypertension for the past 6 months. Despite multiple medications, his blood pressure was never well controlled. His ECG showed LV hypertrophy and he was referred to a cardiologist for management. Examination showed a brachial-femoral pulse delay. Blood pressure in the right arm was 173/95 mmHg, left arm 170/92 mmHg, right leg 130/90 mmHg, and left leg 130/88 mmHg. Diagnosis of CoA was confirmed with a chest MRI. He underwent balloon angioplasty and endovascular stent implantation. On a subsequent clinic visit, his blood pressure in the right arm was 130/78 and the right leg was 125/75. He remained on a beta-blocker for blood pressure control and vascular protection of his ascending aorta.

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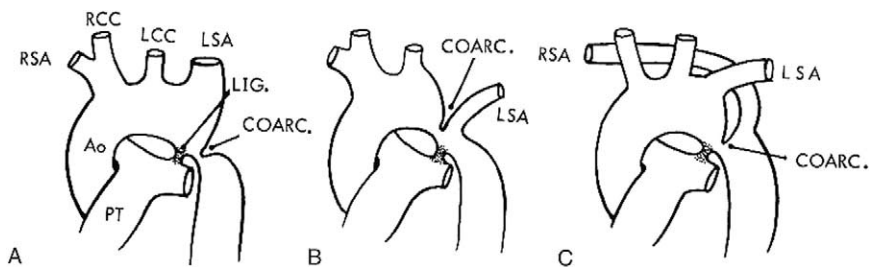
**Dr. Gary Webb:** It is not clear that this patient requires antihypertensive therapy since he has had successful interventional therapy. A trial of antihypertensive medication should be considered.

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CoA, the most common abnormality of the aortic arch, accounts for approximately 8% of all cases of CHD, although 20% of the cases are newly diagnosed during adolescence or adulthood. The male-to-female ratio ranges from 1.4:1 to 3:1.<sup>11</sup> Etiology is unknown and morphology varies with age. In neonates, the reduction in luminal size appears to be related to constriction of ductal tissue. In adults, fixed obstruction almost always includes the junction of the distal aortic arch and descending aorta just below the origin of the left subclavian artery.<sup>52</sup> Associated defects may include BAV, PDA, VSD, and MVP. The major physiologic consequence is an increase in the afterload of the LV. The blood pressure is dramatically increased in the aorta and arterial branches proximal to the coarctation site and is decreased distal to it. The lower body blood flow is maintained by the development of collaterals in the subclavian, internal mammary, intercostals, and spinal arteries. The systemic hypertension has been attributed to either a mechanical obstruction or a renal hypoperfusion phenomenon.<sup>11</sup>

Detailed evaluation is needed for proper diagnosis. On ophthalmologic examination, findings of hypertensive retinopathy may be present depending on the severity of the upper limb hypertension. Simultaneous palpation of brachial and femoral arteries can detect a delay in the femoral pulse. The blood pressure in all four extremities should be measured. An arm blood pressure  $\geq 20$  mmHg systolic over leg blood pressure confirms the clinical suspicion. If the blood pressure in the left arm is lower than the right arm, the left subclavian artery may be at the site of coarctation. If the blood pressure in the right arm is lower than the left arm, the right subclavian artery may have arisen anomalously distal to the coarctation (Fig 13). Auscultation reveals a loud aortic closure sound, and in patients with associated BAV, auscultation reveals an aortic ejection click followed by a midsystolic murmur radiating to the base (see Case 4). A soft systolic murmur may be heard over the back, particularly between the scapulae. Presence of large collateral vessels may give rise to continuous murmurs in the back or abdomen.

ECG may show varying degrees of LV hypertrophy as a function of the duration and severity of coarctation or systemic hypertension. Characteristic CXR features may include a prominent ascending aorta (suggests associated BAV), reversed figure-of-3 sign (formed by aortic arch and



**FIG 13.** (A) Typical coarctation of the aorta showing the localized obstruction is just *distal* to the left subclavian artery (LSA). (B) Coarctation is immediately *proximal* to the LSA. (C) The right subclavian artery (RSA) arises anomalously *distal* to the coarctation. Ao, ascending aorta; LCC, left common carotid artery; LIG, ligamentum arteriosum; PT, pulmonary trunk; RCC, right common carotid artery; RSA, right subclavian artery. (Adapted from Perloff JK. *Clinical Recognition of Congenital Heart Disease*. Philadelphia, PA: Saunders, 2003.)

poststenotic segment), and bilateral rib notching (from enlargement of intercostal collateral arteries).<sup>53</sup> Echocardiography is useful for identifying associated cardiac abnormalities.<sup>13</sup> From the suprasternal notch, details of the ascending, transverse, and descending aorta can be demonstrated on TTE. The Doppler peak systolic velocity in the descending aorta correlates better with narrowing of the aortic arch than does the systolic blood pressure gradient between the upper and lower limbs; peak velocities  $> 2.5$  m/s effectively detect  $> 25\%$  narrowing.<sup>54</sup> More important, perhaps, is detection of continuous diastolic antegrade flow at the site of obstruction.<sup>5,13</sup> More recently, MRI has become the preferred imaging modality because it allows precise evaluation of the thoracic aorta, the degree and length of luminal narrowing, and other associated anomalies<sup>55</sup> (Fig 14). Cardiac catheterization is indicated to determine the pressure gradient across the coarctation (significant if  $> 20$  mmHg) and to assess coronary anatomy in patients over the age of 40 years prior to anticipated surgery.

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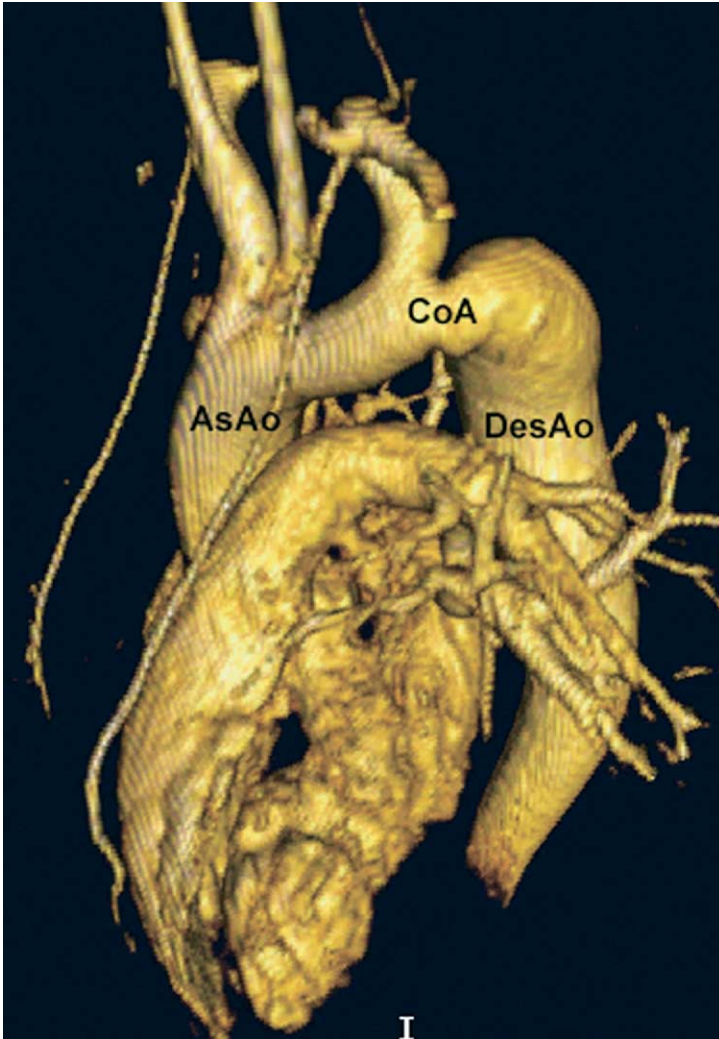
**Dr. Gary Webb:** I would accept a Doppler peak systolic velocity in the descending aorta up to 20 mmHg as within normal limits. Doppler estimation of possible aortic coarctation can be quite inaccurate, especially in the presence of a fairly long narrowing.

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**Dr. Gary Webb:** Cardiac catheterization is seldom indicated to get a pressure gradient in a patient with aortic coarctation.

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**Dr. Gary Webb:** Coronary angiography may indeed be wise to exclude coronary disease in coarctation patients facing surgical correction. Nonethe-



**FIG 14.** Magnetic resonance three-dimensional (reconstruction) image of a patient with moderate aortic coarctation (CoA). AsAo, ascending aorta; DesAo, descending aorta.

less, the management options here should include the possibility of an interventional procedure, as was used in this case, prior to which coronary angiography would not be required.

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## Management

Most adults with CoA are asymptomatic. Minor symptoms include recurrent epistaxis, headache, claudication, dizziness, and palpitation.

Major symptoms are related to five eventualities: (1) uncontrolled hypertension; (2) congestive heart failure; (3) rupture or dissection of the aorta; (4) infectious endarteritis or endocarditis; and (5) cerebral hemorrhage.<sup>56</sup> Due to the markedly increased risk of early cardiovascular and cerebrovascular events, CoA should be aggressively treated. If the condition is symptomatic, repair is best done in infancy; otherwise, timing is “elective” in the recognition that, the later in life the repair is performed, the more likely there will be persistent hypertension and accelerated coronary artery disease.<sup>57</sup> In general, intervention is recommended in the following groups of patients: (1) all *symptomatic* patients with a gradient  $> 30$  mmHg across the coarctation; (2) *asymptomatic* patients with a gradient  $> 30$  mmHg *and* upper limb hypertension, pathological blood pressure response during exercise, or significant LV hypertrophy; (3) significant aortic valve stenosis or regurgitation; (4) aneurysm of the ascending aorta; (5) aneurysm at the site of previous treatment; and (6) symptomatic aneurysms of the circle of Willis.<sup>58,59</sup>

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**Dr. Gary Webb:** Of all commonly performed congenital interventional procedures, dilation of aortic coarctation is the most dangerous. In my opinion, this procedure should be done by people with real expertise in this procedure, and not by the practitioners who may “do an occasional coarctation.”

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Surgical repair of coarctation may be technically difficult. Morbidity with recoarctation, aneurysm formation, stroke, paraplegia from spinal cord ischemia, paradoxical rebound hypertension, and recurrent laryngeal nerve injury is of concern. Patch aortoplasty has largely been abandoned because of the risk of subsequent aneurysm formation. Resection with end-to-end anastomosis can be a more successful operation, resulting in less aneurysm formation and rebound hypertension.<sup>60</sup> More recently, angioplasty along with expandable endovascular stents has been shown to be an effective and safe strategy in adults. This procedure avoids the risks of thoracotomy and is associated with good outcomes. In one study, stents were successfully implanted in 32/33 patients: at follow-up (mean  $29 \pm 17$  months), there was no evidence of re-coarctation, aneurysm formation, stent displacement, or fracture. Pressure gradient decreased from  $39 \pm 18$  to  $4 \pm 6$  mmHg, and peak Doppler gradient decreased from  $51 \pm 26$  to  $13 \pm 11$  mmHg.<sup>61</sup> All patients who undergo surgical or interventional treatment should have annual visits to assess for evidence of restenosis and monitor both resting and exercise blood pressures. Lifelong prophylaxis against endocarditis is also recommended.<sup>42</sup>



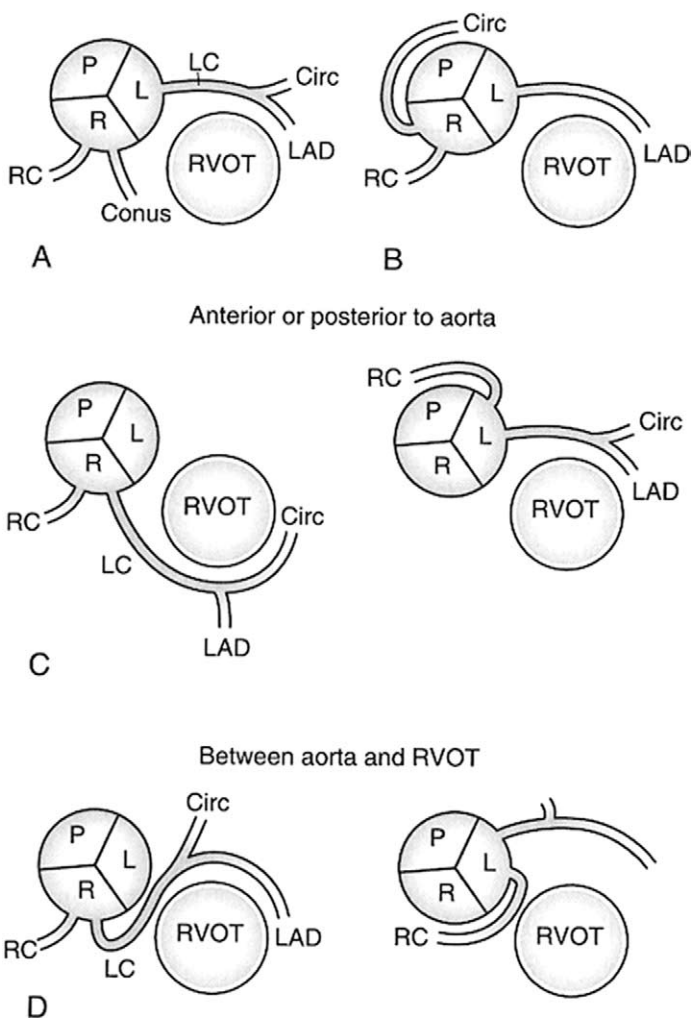
## Case 7: Congenital Coronary Artery Anomalies

A 52-year-old physician complained of intermittent chest pain only during high intensity exercise. Besides a positive family history, he had no other cardiac risk factors. A nuclear stress test (treadmill Myoview) showed a small-to-moderate region of reversible ischemia at the anterior wall along with ECG changes of 1-mm ST-depression. Cardiac angiogram showed no coronary arterial obstructions but there was an abnormal take-off of the left coronary artery from the right aortic sinus. MRI showed an aberrant left coronary artery passing between the aorta and the right ventricular outflow tract (RVOT). Surgery was recommended but he chose medical management with a beta-blocker and avoidance of strenuous exertion.

The incidence and prevalence of coronary artery anomalies are uncertain, but estimated at 1%, possibly as high as 5.6%, in a prospective angiographic study of 1950 consecutive cases.<sup>62</sup> Males and females are equally affected. Coronary artery anomalies are due to variations in number, origin and position, or distribution of the arteries. A recent consensus report categorizes the following groups of coronary artery anomalies: (1) anomalous pulmonary origins of the coronaries; (2) anomalous aortic origins of the coronaries; (3) congenital atresia of the left main coronary artery; (4) coronary arteriovenous fistula; (5) coronary artery bridging; (6) coronary artery aneurysms; and (7) coronary stenosis.<sup>63</sup>

Most coronary artery anomalies do not cause myocardial ischemia and are often found incidentally during angiographic evaluation for other cardiac diseases. The artery may pass anterior to the RVOT, posterior to the aorta, or between the aorta and RVOT<sup>11</sup> (Fig 15). The course taken by the anomalous coronary artery is the single most important factor in determining cardiac risks. Reported cases of bad outcome occur mostly in those with the artery passing *between* the aorta and RVOT and in younger patients despite the fact that they have lower frequency of atherosclerotic coronary artery disease.<sup>64</sup> These pathologic anomalies may be present from early infancy and can result in angina, congestive heart failure, myocardial infarction, cardiomyopathy, ventricular aneurysms, or sudden death. Although the exact etiology of ischemia is unknown, potential mechanisms include (1) compression of the artery between the aorta and RVOT during exercise; (2) stretching of the artery because of the abnormal course; (3) kinking of an acutely angled artery with an intramural course; and (4) occlusion of the coronary ostium because of its slit-like orifice.<sup>25</sup>





**FIG 15.** Schema of different variations of congenital coronary artery anomalies. (A) Normal origin of the left coronary artery (LC) and the right coronary artery (RC). A conus artery arises by a separate ostium from the right aortic sinus. (B) The left anterior descending coronary artery (LAD) arises normally from the left aortic sinus, and the circumflex coronary artery (Circ) arises aberrantly from the right aortic sinus. (C) First illustration shows an aberrant LC passing anterior to the right ventricular outflow tract (RVOT), and second illustration shows an aberrant RC passing posterior to the RVOT. (D) First illustration shows an aberrant LC passing between the aorta and the RVOT, and the second illustration shows an aberrant RC passing between the aorta and the RVOT. L, left aortic sinus; P, posterior aortic sinus; R, right aortic sinus. (Adapted from Perloff JK. *Clinical Recognition of Congenital Heart Disease*. Philadelphia, PA: Saunders, 2003.)

Physical examination is often unremarkable except for those with coronary arteriovenous fistula, which can produce a continuous murmur. Echocardiography, particularly TEE, has had some success in identifying the abnormal take-off and initial course of the coronary arteries.<sup>5,13</sup> Screening with treadmill exercise is not worthwhile because of its high incidence of false-positive and false-negative results. Exercise stress testing in conjunction with an imaging test (eg, echocardiography or nuclear perfusion) may reveal ischemia, wall motion abnormality, or perfusion deficits, which are strong reasons for surgical intervention. MRI may be the gold standard for imaging since it may show the origin, caliber, and position relative to the outflow tracts.<sup>65</sup>

## Management

Diagnosis of coronary anomalies often occurs during incidental work-up. Unfortunately, an estimated 50 to 90% of patients who die suddenly of a coronary anomaly have no forewarning, and fewer than 10% are known to have had a pre-mortem cardiac evaluation for symptoms related to the anomaly.<sup>66</sup> Once the diagnosis is made, surgical intervention is recommended for those at high risk (eg, history of progressive exertional angina, myocardial infarction, and aborted sudden cardiac death).<sup>67</sup> However, bypass surgery often does not last for the expected lifetime of those patients diagnosed at an early age and re-do bypass may be needed in later years. The bypass artery may also create competitive flow, leading to further narrowing of the native proximal artery. Therefore, for low risk patients, one can also advise medical therapy with beta-blocker and limitation of strenuous physical activity.<sup>65</sup> Because the left coronary artery courses between the aorta and RVOT, our surgical colleagues recommended our patient to undergo a one-vessel bypass (left internal mammary artery to the LAD), but he opted for medical management.

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**Dr. Gary Webb:** I am uncertain that the incidence of coronary artery anomalies is as high as 5.6%.

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**Dr. Gary Webb:** There are certain anomalies that should be seen as placing the patient at risk of premature death. Origin of the left main coronary artery from the right sinus of Valsalva and origin of the right coronary artery from the left sinus of Valsalva are two such entities. Anomalous origin of a coronary artery from the pulmonary artery is another anomaly requiring treatment. Coronary arteriovenous fistulae can also be clinically important and require treatment, but do not particularly predispose to sudden death.

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## Case 8: Ebstein's Anomaly

A 20-year-old college student was referred to the cardiology clinic by student health center with a diagnosis of "palpitations." She stated that she had been experiencing rapid heartbeats on a monthly basis with a rate up to 150 s and lasting 3 to 5 minutes. The baseline 12-lead ECG showed normal sinus rhythm, tall peaked P waves, a prolonged PR interval, and RBBB morphology. Examination revealed a wide split S1 and S2 with a 2/6 systolic murmur at the LLSB. Echocardiogram showed a 22-mm apical displacement of the septal tricuspid leaflet with moderate tricuspid regurgitation, consistent with Ebstein's anomaly.

Ebstein's anomaly occurs in only 0.5% of patients with CHD but accounts for 40% of congenital malformations of the tricuspid valve.<sup>68</sup> It is characterized by an abnormal septal tricuspid leaflet (and often the posterior leaflet) that is *apically* displaced from the atrioventricular ring and attaches to the junction of the inlet and trabecular septum of the right ventricle (Fig 16). This causes a portion of the right ventricle to be located at the atrial side of the tricuspid valve (ie, "atrialized"). The displaced septal leaflet is associated with discontinuity of the central fibrous body, which causes a potential substrate for accessory pathways and pre-excitation.<sup>69</sup> Other associated abnormalities include PFO, ASD, PS, VSD, PDA, and MVP. Ebstein's anomaly must be differentiated from acquired tricuspid regurgitation (eg, endocarditis, RV infarction, traumatic rupture of the tricuspid valve) and Uhl's anomaly (or right ventricular dysplasia).<sup>11</sup>

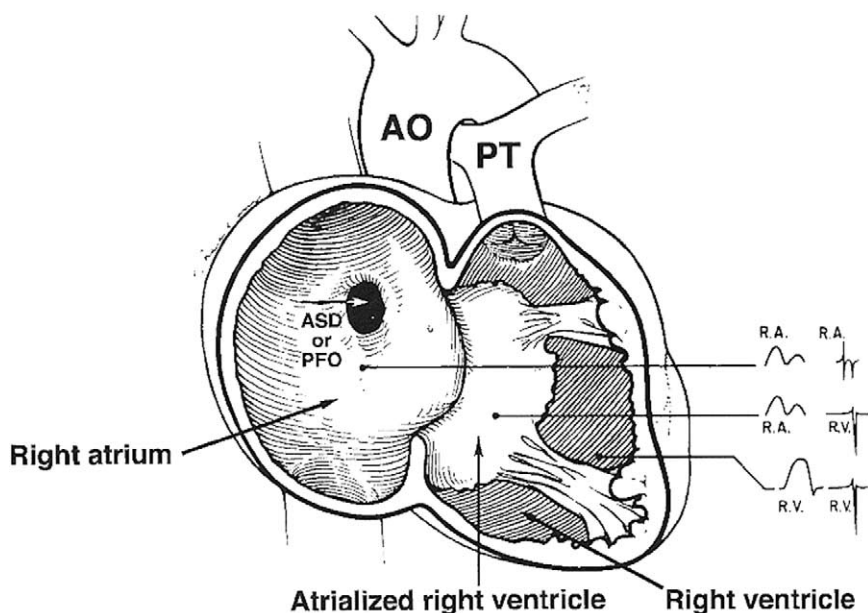
The hemodynamic consequences of Ebstein's anomaly vary considerably. If the apical displacement is mild, the valve essentially functions normally. With more severe apical displacement, significant hemodynamic changes can occur. Chronic severe tricuspid regurgitation can cause a mild increase in right atrial pressure and a decrease in right ventricular diastolic distensibility, which leads to an interatrial right-to-left shunt via a stretched PFO or pre-existing ASD, resulting in peripheral cyanosis. Classically, the cyanosis is intense for a neonate when the PVR is still elevated, resolves as an infant when the PVR falls, and reappears during adulthood when tricuspid regurgitation and RV compliance deteriorate.<sup>70</sup>

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**Dr. Gary Webb:** The right atrial pressure, and thus the JVP, is seldom elevated in patients with Ebstein anomaly. This is because the huge right atrium is very compliant even in the face of substantial regurgitation. JVP is typically normal in Ebstein patients.

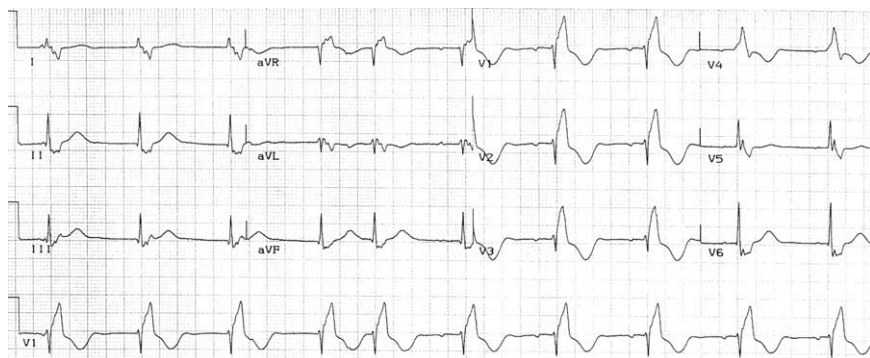
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On physical examination, the first heart sound is widely split primarily



**FIG 16.** Schema of the anatomic, functional, and electrophysiologic features of Ebstein's anomaly. In the right atrium (RA), the pressure pulse and intracardiac electrogram are both right atrial. In the functional right ventricle (RV), the pressure pulse and the intracardiac electrogram are both right ventricular. In the atrialized right ventricle, the pressure pulse is atrial but the intracardiac electrogram is ventricular. ASD, atrial septal defect; PFO, patent foramen ovale. (Adapted from Perloff JK: *Clinical Recognition of Congenital Heart Disease*. Philadelphia, PA: Saunders, 2003.)

due to an increased excursion time needed for the large anterior leaflet to reach a closed position. The second heart sound is widely split due to a delay in the pulmonary component caused by complete RBBB. Third and fourth heart sounds may also be present, resulting in a distinctive triple or quadruple rhythm. A tricuspid regurgitant murmur at the LLSB is often early systolic with a decrescendo configuration and may not increase during inspiration if the RV is functionally inadequate. The diagnosis of Ebstein's anomaly can sometimes be based on the ECG per se. Major ECG abnormalities include the following<sup>11</sup>: (1) tall peaked P waves ("Himalayan") and PR interval prolongation; (2) right bundle branch block (75-95% of cases) due to prolonged activation of the atrialized RV; (3) Wolff-Parkinson-White preexcitation (5-25% of cases) from a right sided bypass tract (type B); (4) supraventricular tachycardia, atrial fibrillation, or atrial flutter (25-30%); and (5) deep Q waves in leads V<sub>1-4</sub> and II, III, aVF, mimicking old anterior or inferior infarctions (Fig 17).



**FIG 17.** ECG from a 21-year-old acyanotic woman with Ebstein's anomaly. The rhythm shows 4 junctional beats with retrograde P wave (notch inside the QRS), followed by a premature atrial conduction beat, and then 5 sinus conducted beats. Note the presence of right bundle branch block (most common) which appears as though a second QRS had been attached to an initially normal QRS and the absence of pathognomonic (but less common) features such as "Himalayan" P waves and Wolff-Parkinson-White preexcitation.

The CXR can vary from normal to diagnostic with enlarged RA silhouette to the right of the vertebra (Fig 18). In severe cases, the pulmonary vascularity is reduced due to marked right-to-left shunt. Echocardiogram with color-flow imaging and Doppler interrogation establishes the diagnosis and severity of Ebstein's anomaly. Both TTE and TEE can be used to assess RA dilatation, septal tricuspid leaflet displacement and distortion, tricuspid regurgitation or stenosis, interatrial shunting, and associated cardiac abnormalities.<sup>71,72</sup> For mildly cyanotic patients, exercise testing with monitoring of arterial saturation can be useful to define the degree of desaturation during daily activities.

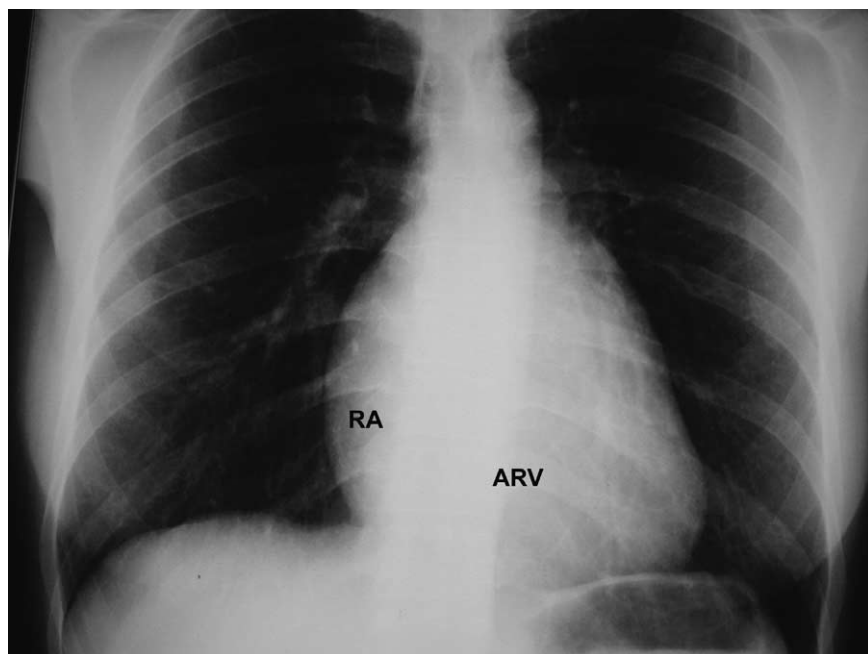
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**Dr. Gary Webb:** Pulmonary vascularity is typically seen as reduced in many patients with Ebstein anomaly due to very low pulmonary flow rates and corresponds to very low systemic cardiac outputs reflected in the characteristically small aortic knuckle seen on chest X-ray in these patients.

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## Management

Severe Ebstein's anomaly often causes high rates of intrauterine mortality. Older children with Ebstein's anomaly often come to medical attention because of an incidental murmur, whereas adolescents and adults frequently present with a supraventricular arrhythmia.<sup>73</sup> In a study following 72 unoperated survivors of Ebstein anomaly aged over 25



**FIG 18.** CXR from an acyanotic 25-year-old woman with mild Ebstein's anomaly. The right atrial contour is almost invariably enlarged (RA). The left upper cardiac border is enlarged due to a prominent right ventricular infundibulum. ARV, atrialized right ventricle.

years, morbidity was mainly related to late-onset arrhythmia and refractory hemodynamic deterioration. The magnitude of tricuspid regurgitation, cyanosis, and the New York Heart Association (NYHA) functional class were also considered significant risk factors.<sup>74</sup> Patients with atrial arrhythmias may be treated pharmacologically or with radiofrequency ablation if an accessory pathway is present. In one study, the success rate of radiofrequency ablation was 76% (16 of 21 patients) with a recurrence rate of 25% (4 of 16 patients).<sup>75</sup>

Repair or replacement of the tricuspid valve in conjunction with closure of an interatrial communication is recommended for patients who are in NYHA functional class III-IV despite medical therapy. In one study involving 189 postoperative patients, 93% were in NYHA class I-II after one year. The atrial arrhythmias occurred less frequently, heart sizes were reduced, and exercise testing showed significant improvement in performance.<sup>76</sup> However, potential complications include complete heart block, persistence of supraventricular arrhythmias, residual tricuspid regurgitation, and prosthetic valve dysfunction. Thus, intraoperative TEE is

important in verifying satisfactory reduction in tricuspid regurgitation with minimal or no stenosis. An anterior leaflet that is elongated, un-tethered, and freely mobile is suitable for repair; conversely, a significantly dysplastic, tethered, or fenestrated valve is undesirable. When valve replacement is required, a bioprosthetic valve is preferable to a mechanical valve because of the high risk of thrombosis at the low-flow RV chamber.<sup>77</sup> A concomitant Maze procedure should also be considered in patients with chronic atrial flutter or atrial fibrillation.<sup>78</sup>

For high-risk patients with severe tricuspid regurgitation and hypoplastic RV, a total cavopulmonary connection (modified Fontan) may be needed to adequately perfuse the lungs and to reduce RV preload. The original Fontan procedure was conceived in 1971 for repair of tricuspid atresia by passing the small RV using a surgically constructed atriopulmonary connection.<sup>79</sup> Since then, the procedure has undergone several modifications, and along with it, the various names associated with the procedure (eg, classic Fontan, lateral tunnel, extracardiac Fontan, Kawashima operation, bi-directional cavopulmonary anastomosis, and hemi-Fontan). Despite the success of this procedure for patients with complex single-ventricle physiology, it has also opened up a “Pandora’s box” of complications, which include right atriomegaly, hepatic dysfunction, systemic venous collateralization, atrial arrhythmias, protein-losing enteropathy, pulmonary arteriovenous malformations, thromboembolic events, and systemic outflow tract obstruction.<sup>80</sup>

For our patient, her atrial arrhythmia was not inducible on electrophysiologic study and she was treated medically with beta-blocker. She was also placed on ACE inhibitors empirically to reduce her tricuspid regurgitation and improve RV function. As in the case of all Ebstein’s anomaly, this patient was advised to take IE prophylaxis.

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**Dr. Gary Webb:** The use of ACE inhibitors to reduce TR and improve RV function is entirely speculative.

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## *Case 9: Transposition of Great Arteries (TGA)*

A 30-year-old man complained of increasing abdominal girth. He was born with TGA, VSD, and PS. He underwent a left Blalock–Taussig shunt at 15 months and a Rastelli operation at 12 years of age. Over the past 2 years, he had been noticing palpitations, fatigue, and dyspnea on exertion. Examination showed a prominent RV impulse, a 2/6 holosystolic murmur at the LLSB, and a 4/6 crescendo-decrescendo murmur at the LUSB.



Echocardiogram revealed RV hypertrophy and dilatation with an estimated ejection fraction of 35%. RHC showed RVSP of 86 mmHg with an end-diastolic pressure of 9 mmHg. The main PAP was 17 mmHg with a mean of 12 mmHg. The peak systolic gradient across the RV to pulmonary artery conduit was estimated at 69 mmHg. The patient was referred for surgery to replace the valved conduit obstruction.

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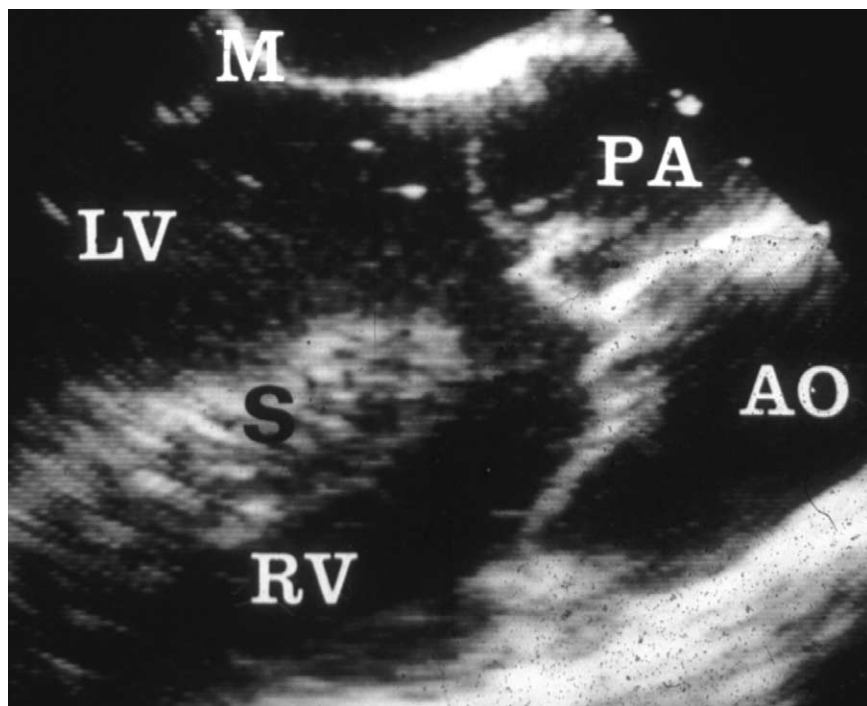
**Dr. Gary Webb:** The use of the term “RV” should be used carefully in patients with AV or VA discordance. If the RV is a systemic ventricle, then the term RVSP is incorrect as the term to assess pulmonary artery pressures.

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TGA represents approximately 5 to 8% of CHDs but accounts for 25% of deaths in the first year of life.<sup>11</sup> It is associated with other cardiac defects, including VSD (40-45% of cases), LVOT obstruction (25%), and CoA (5%).<sup>81</sup> TGA results from abnormal conal development and cono-ventricular positioning. Instead of the normal crossover or spiral relationship, the ascending aorta and main pulmonary artery run parallel to each other. The aorta is located *anterior* and *rightward* of the pulmonary artery, which is the reason the term “D-transposition” has sometimes been used to denote TGA. At the aortic valve, the posterior cusp gives rise to the right coronary artery (RCA); the left cusp gives rise to LAD and left circumflex (LCX); and the right cusp is noncoronary. Deoxygenated blood flows from the SVC and IVC → RA → RV → aorta, while oxygenated blood flows from lung → LA → LV → pulmonary artery. Thus, there is *ventriculoarterial discordance*, whereby the aorta arises from the morphologic RV via a muscular septum and the pulmonary artery arises from the morphologic LV with fibrous continuity to the mitral valve<sup>11</sup> (Fig 19). This creates two circuits that are in *parallel* rather than in *series* as in a normal individual. Therefore, early survival depends on bi-directional shunting between the two sides of the heart, at either the atrial, the ventricular, or the arterial level.

In repaired adults, the physical examination will reveal a loud S2 because of the anterior aorta. Those with a Blalock–Taussig shunt (subclavian artery to pulmonary artery) will have diminished brachial and radial pulses at the respective arm. The ECG and CXR will show changes corresponding to the hemodynamic consequences due to the associated cardiac lesions. Echocardiogram with color-flow imaging and Doppler interrogation can establish the ventricular origins of the great arteries, their spatial relationships, and the presence of associated defects and is crucial in follow-up of the various postoperative categories.<sup>5,13,82</sup>





**FIG 19.** TEE of a patient with transposition of great arteries (TGA). Note the anterior aorta (AO) and posterior pulmonary artery (PA) run parallel to each other and do not cross as in the normal heart. The atria and ventricles are properly located. The discordance occurs at the ventriculo-arterial level.

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**Dr. Gary Webb:** Patients with classic Blalock–Taussig shunts lack pulses in the ipsilateral arm. More recent techniques for Blalock–Taussig shunts have used Gore-Tex grafts between subclavian and pulmonary arteries and do not affect the pulses in the arms.

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## *Management*

TGA without intracardiac shunts (the so-called “simple form”) is incompatible with life unless early palliation is performed. Clinically, the infant becomes cyanotic quickly within the first 3 to 4 days when the ductus arteriosus closes. To achieve acceptable oxygen saturation prior to definitive surgery, a balloon atrial septostomy (disruption of the foramen flap) is performed to allow interatrial mixing of blood between the two

parallel circuits.<sup>83</sup> This procedure will maintain the arterial oxygen saturation between 50 and 80%, which is adequate for growth until the atrial switch operation can be performed later, often beyond 6 months of age provided this is the best strategy for that patient's complex.<sup>81</sup> In the older strategy using an *atrial* switch operation, a baffle is created in the atria so that blood from the SVC and IVC is directed through the mitral valve to the LV and blood from the pulmonary veins is directed through the tricuspid valve to the RV. In this new circuit, blood then flows from the SVC and IVC → RA → intraatrial baffle → LV → pulmonary artery → lung → LA → intraatrial baffle → RV → aorta. The two variations of atrial switch operation were the Mustard procedure, which used pericardial tissue to construct the baffle, and the Senning procedure, which used the atrial septum and right atrial free wall to create the baffle.<sup>84,85</sup>

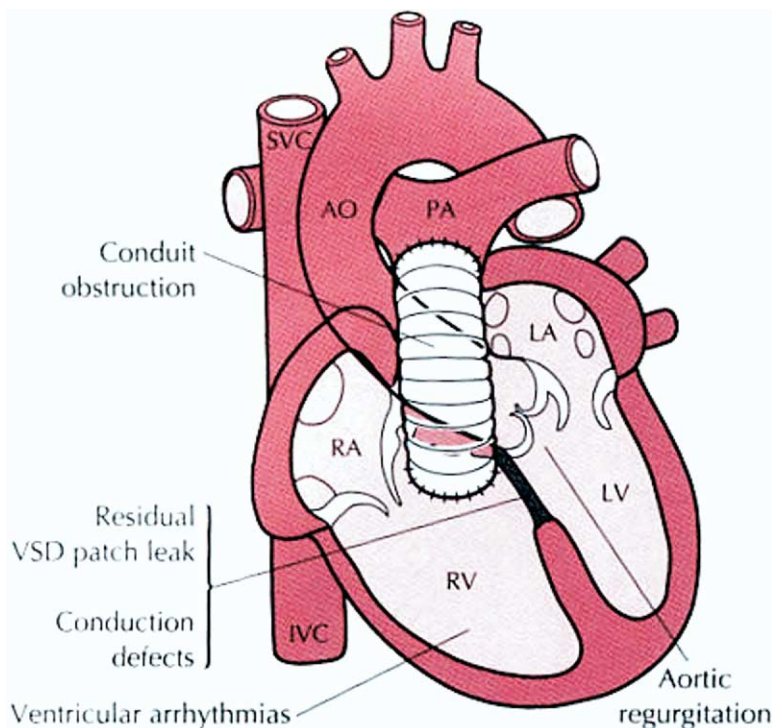
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**Dr. Gary Webb:** The atrial switch is no longer the procedure of choice.

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The main disadvantage of the atrial switch operation is that the RV is still subjected to systemic pressure (RV → aorta) and will often deteriorate over time. Other long-term complications include the following: (1) baffle obstruction causing impaired systemic or pulmonary return; (2) cardiac arrhythmias including sick sinus syndrome, junctional rhythm, and supraventricular tachycardia; and (3) progression of pulmonary vascular disease due to microthrombi, hypoxemia, or polycythemia.<sup>81</sup> For these reasons, the *arterial* switch operation has been advocated and in several large series, has shown better short-, mid-, and long-term results than atrial switch.<sup>86</sup> This procedure involves the transection of the aorta and pulmonary artery at the level above the valve sinuses. The coronary arteries are detached from the aorta with a surrounding "button" of aortic wall and sutured into place in the neo-aorta. Last, the pulmonary trunk is moved forward into its new position anterior to the aorta.<sup>87</sup> This procedure is technically challenging but has the advantage that the LV now becomes the systemic ventricle (LV → aorta). A recent study confirmed that the quality of life and health status as perceived by children 11 to 15 years after TGA repair is better after arterial switch operation than after atrial repair.<sup>88</sup>

Our patient was born with TGA, VSD, and PS. He underwent a palliative procedure with the Blalock–Taussig shunt first in order to increase pulmonary blood flow (bypasses the PS). At a later age, a Rastelli was performed. This procedure involves (1) closing the VSD so



**FIG 20.** Schema of a classic Rastelli procedure and potential complications that may occur at later years. (With permission, from Child JS, Alpert JS. Congenital heart disease in the postoperative patient. Chapter 31, In: Alpert JS, editor. *Cardiology for the Primary Care Physician*. Current Medicine; Philadelphia, PA; 1996.)

LV blood is diverted to aorta, (2) placing a valved conduit connecting the RV and main pulmonary artery, and (3) oversewing the pulmonary valve (Fig 20). The main disadvantage of this procedure is conduit obstruction, which may need to be surgically replaced several times in a patient's lifetime. In one study involving 101 patients, the repair was performed with low early mortality (7%). However, substantial late morbidity and mortality were due to conduit obstruction (44%), left ventricular outflow tract obstruction (11%), arrhythmia (11%), and sudden cardiac deaths (5%).<sup>89</sup>

### *Case 10: Congenitally Corrected Transposition of Great Arteries (CCTGA)*

A 28-year-old woman suffered a syncopal episode while watching television. She had been healthy previously with no complaints or

limitations. In the emergency room, her 12-lead ECG showed complete atrio-ventricular heart block. A 2/6 holosystolic murmur at the LLSB was heard. An echocardiogram showed the left-sided “LV” to have an apically displaced “mitral valve” as well as a prominent moderator band. After further review, the diagnosis of CCTGA was correctly made.

CCTGA is a relatively rare cardiac malformation, representing <1% of all CHDs with a male-to-female ratio of approximately 1.5:1.<sup>90</sup> Physiologically, blood flows from the RA → right-sided morphologic LV → pulmonary artery → lungs → LA → left-sided morphologic RV → aorta. Thus, there is *atrioventricular discordance* (RA → right-sided morphologic LV) as well as *ventriculoarterial discordance* (right-sided morphologic LV → pulmonary artery). In essence, the “two wrongs make one right” and allows the patient to survive. The term L-TGA (“L” stands for levo, or leftward aorta) is oftentimes used to denote CCTGA but should be avoided because many other complex conditions, including univentricular hearts, have an “L” positioned aorta.

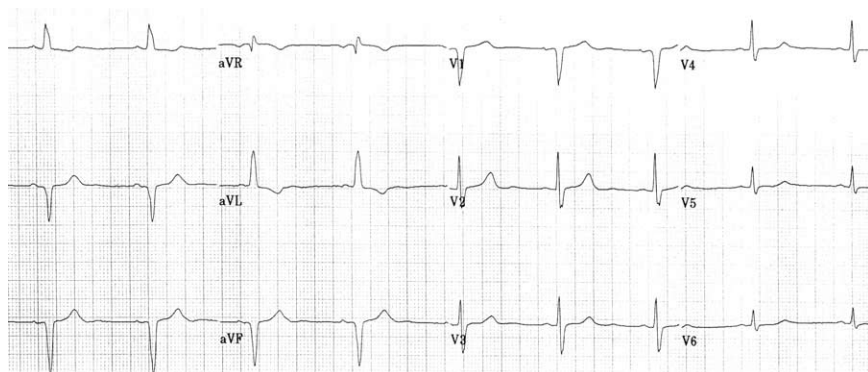
In CCTGA, not only are the ventricles inverted, so are the great arteries, the atrioventricular valves, and the coronary arteries. The two main arteries run parallel to each other and do not cross as in normal heart; the aorta is *anterior* and *leftward*, whereas the pulmonary trunk is *posterior* and *rightward*. For coronary arteries, the posterior aortic cusp gives rise to the LAD and “RCA” (morphologic LCX), while the left cusp gives rise to the “LCX” (morphologic RCA). The anterior cusp is noncoronary. The morphologic mitral valve is on the right side, and the morphologic tricuspid valve is on the left side. Most CCTGA patients also have co-existing cardiac malformations, including VSD (60-80%), PS (30-50%), Ebstein’s anomaly (15-45%), and less commonly ASD, PDA, double-outlet RV, and subaortic stenosis.<sup>91</sup> The conduction system is also affected because the AV node and bundle of His can have an unusual course and location, predisposing patients to high incidence of atrioventricular conduction block with increasing age at ~2%/year.<sup>92</sup>

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**Dr. Gary Webb:** Even though the incidence of complete heart block in patients with congenitally corrected TGA may average out at 2% per year, most heart blocks occur at the time of cardiac surgery.

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On physical examination, the S2 is loud (because the aortic valve is situated anterior to and left of the pulmonic valve) and may be mistaken for a sign of pulmonary hypertension. If VSD and PS coexist, a holosystolic murmur at the LLSB and a crescendo-decrescendo “mid”

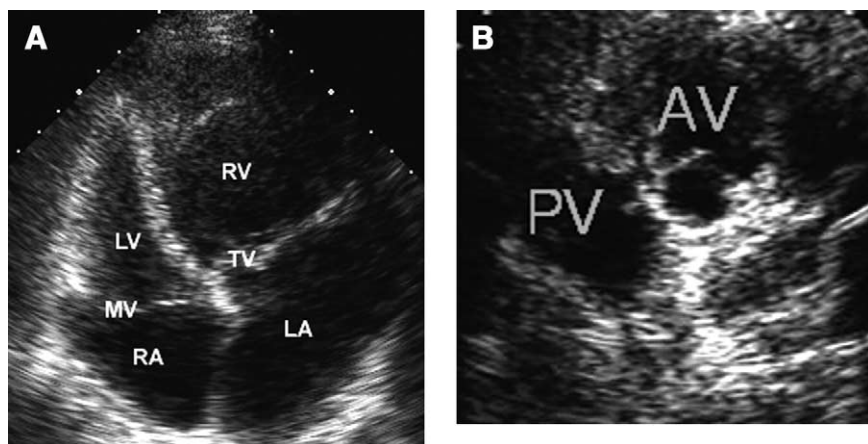


**FIG 21.** ECG of a 30-year old man with congenitally corrected transposition of great arteries (CCTGA). There is left axis deviation. Prominent Q waves appear in inferior leads, but Q waves do not appear in left precordial leads (V6) because septal depolarization is reversed (from right-to-left instead) due to “ventricular inversion.”

systolic murmur at the LUSB can be heard, respectively. A left-sided tricuspid regurgitation murmur can be prominent, especially in those with morphologic RV failure. The ECG may show first-degree atrioventricular block, 2:1 second-degree, or complete heart block.<sup>11</sup> Reversed septal activation (right to left) causes absence of Q waves in the left precordial leads (Fig 21). For echocardiography, clues to the diagnosis are (1) the morphologic tricuspid valve always lies closer to the apex when compared to the morphologic mitral valve, and this will be apparent on the left side of the heart (left-sided morphologic RV); (2) a moderator band and thicker trabeculation, indicators of RV morphology, are seen on the left side of the heart; (3) a “five chamber view” will not be possible on the left side; and (4) mitral papillary/muscles always insert into the free walls, whereas tricuspid valves insert into one free wall and the septum<sup>93</sup> (Fig 22). MRI and CT are also useful modalities for anatomic assessment in patients with CCTGA, but provide less functional data compared to echocardiography.

## Management

The natural history of CCTGA is quite variable and is related to the presence of associated lesions. In infants and children with symptoms, surgery is advocated at the earliest time possible. Several techniques are available, although the double-switch repair approach has shown more favorable results than conventional biventricular repair (8%



**FIG 22.** Echocardiogram of congenitally corrected transposition of great arteries (CCTGA). (A) Apical four-chamber view shows a morphologic right atrium (RA) aligned with a morphologic right-sided left ventricle (LV) and a morphologic left atrium (LA) aligned with a morphologic left-sided right ventricle (RV). The left-sided tricuspid leaflets can be identified by their more apical insertion compared to right-sided mitral valve. The RV also has moderator bands in the apex. (B) Parasternal short-axis view shows cross sections of the anterior leftward aortic valve (AV) and the posterior rightward pulmonary valve (PV).

versus 13% mortality).<sup>94</sup> The *double-switch* operation corrects the atrioventricular discordance by an *atrial* switch (eg, Senning or Mustard) and the ventriculoarterial discordance by an *arterial* switch. For those with a large VSD, atrial baffle, and Rastelli (see Case 9) are performed instead.<sup>95</sup>

Surprisingly, a few patients with uncomplicated CCTGA can function normally. They may be diagnosed as adults only after complaining of changes in symptoms.<sup>96</sup> For example, symptomatic CHF becomes extremely common by the 3rd and 4th decade because the systemic left-sided morphologic RV cannot perform the usual job of the muscular LV. Moderate and severe tricuspid regurgitation may ensue, leading to further deterioration of the left-sided morphologic RV. We routinely treat these patients with afterload reducing agents such as angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), although data have not yet confirmed clinical efficacy.<sup>97,98</sup> Patients who present with symptomatic 2:1 atrioventricular block and complete heart block should have permanent pacemakers, as was the case for our patient. Finally, all patients with CCTGA should have IE prophylaxis due to the high rates of VSD and valvular regurgitation.



## Case 11: Tetralogy of Fallot (TOF)

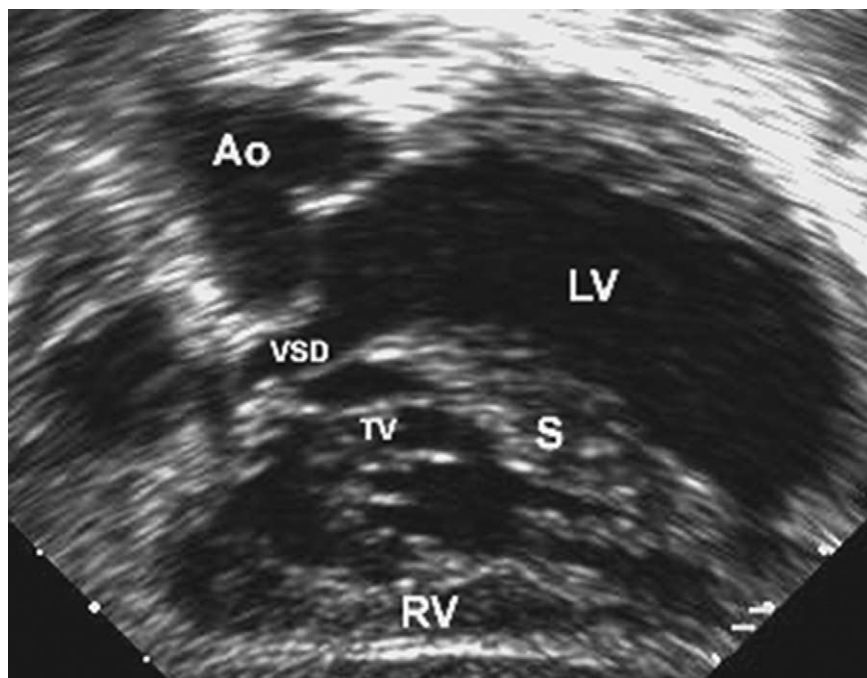
A 34-year-old lawyer with a history of TOF was seen at the ACHD clinic. She recalled frequent squatting as a toddler. She underwent an intracardiac repair at age 7 and subsequently had normal growth. She had no physical limitations and was on the soccer team in college. On examination, there was a 2/6 mid-diastolic medium frequency murmur at LUSB and LLSB. The ECG showed a RBBB with QRS width of 178 ms. Her signal-averaged ECG was positive, indicating an area of slow conduction that potentially could be a substrate for monophormic ventricular tachycardia and a cause of sudden cardiac death. TTE disclosed severe pulmonary regurgitation and a dilated RV. Her chest CT also showed a RVOT aneurysm at the incision site of the right ventriculotomy. Based on these findings, the patient was recommended to undergo an operation for replacement of her pulmonary valve and revision of the RVOT aneurysm.

TOF is caused by an anterocephalad deviation of the outlet septum resulting in four features: (1) a non-restrictive VSD; (2) an overriding aorta (<50% override); (3) obstruction of the RVOT, which may be infundibular, valvar, or usually both, with or without supra-valvar or branch pulmonary artery stenosis; and consequently (4) right ventricular hypertrophy<sup>99</sup> (Fig 23). Associated conditions include (1) right aortic arch in 25% of patients; (2) ASD in 10% of patients, or the so-called “pentalogy of Fallot”; (3) coronary arterial anomalies in 10% of patients; (4) left superior vena cava in 5% of patients; and (5) less commonly, enlarged bronchial arteries.<sup>100</sup>

The hemodynamic changes depend on several variables. In the presence of the usual large nonobstructive malaligned VSD, the systolic pressures in the RV and LV are equal. If the RVOT obstruction is mild, the shunt through the VSD may be left-to-right, resulting in a condition called “acyanotic tetralogy” or “*pink tet.*” If the RVOT obstruction is moderate, bi-directional shunting occurs, yielding a “*balanced tet.*” In typical TOF patients, however, the RVOT obstruction is severe with a right-to-left shunt, creating a “*cyanotic tet.*”<sup>25</sup> Typical clinical features include (1) cyanosis and clubbing by 6 months of age; (2) hypoxic “spells” (characterized by abrupt onset of tachypnea, dyspnea, and cyanosis and in some cases, unconsciousness, seizures, and even death); and (3) frequent squatting (contraction of leg muscles increases SVR, decreases the right-to-left shunt, and lessens the cyanosis).<sup>11</sup>

Without surgical intervention, the rate of survival is dismal—66% at 1 year of age, 50% at 3 years, 11% at 20 years, 6% at 30 years, and 3% at





**FIG 23.** Echocardiogram (apical four-chamber view) showing characteristic features of tetralogy of Fallot (TOF): malaligned ventricular septal defect, overriding aorta, right ventricular hypertrophy (and obstruction of the right ventricular outflow tract not seen in this view).

40 years.<sup>101</sup> Nevertheless, TOF remains the most common type of CHD in cyanotic children after 4 years of age and represents a large proportion of adults with cyanotic CHD. In our clinic, we have a patient with repaired TOF who underwent orthotopic heart transplantation at age 64 and another patient who was newly diagnosed at age 39. For unoperated patients, the physical examination may reveal digital and oral cyanosis, a palpable RV impulse, a single S2 (pulmonic component is not audible), an aortic ejection click (from a dilated overriding aorta), and a systolic outflow murmur (from the RVOT obstruction). The ECG may show right-axis deviation and RV hypertrophy. The CXR may show a “boot-shaped” heart with an upturned cardiac apex and a concave pulmonary artery segment. Echocardiography and MRI can both be used to establish the diagnosis.

## Management

Most adult patients will have had surgery by the time they present to the adult cardiologist. Since cyanosis in infancy is primarily due to some

form of PS (eg, narrowed RVOT) causing right-to-left shunting, *palliative* surgery is directed at augmenting pulmonary blood perfusion. These include the classic and modified Blalock–Taussig shunt (subclavian artery joined to the pulmonary artery), Waterston shunt (right pulmonary artery joined to the ascending aorta), and Pott shunt (left pulmonary artery joined to the descending thoracic aorta) (see Tables 3-5). At a later age, *reparative* surgery is needed to close the VSD and relieve the RVOT obstruction.<sup>102</sup> The latter may involve using pulmonary valvotomy, resection of infundibular muscle, RVOT patch, transannular patch, pulmonary valve implantation, extracardiac conduit between the RV and pulmonary artery, and patch augmentation of central pulmonary arteries.<sup>103</sup>

Although surgical results are excellent with a operative mortality of less than 2 to 3%, late complications of TOF repair can still occur, including inadequate repair with recurrent RVOT obstruction, VSD patch leak, and significant residual pulmonary regurgitation. In addition, operated TOF patients can be at increased risk of sudden cardiac death. This is often attributed to ventricular arrhythmias due to either residual hemodynamic compromises (eg, diminished RV function, increased RVSP > 60 mmHg, and pulmonary regurgitation) or electrophysiological abnormalities (inducible sustained ventricular tachycardia, conduction defects, and prolonged ventricular depolarization and repolarization).<sup>104</sup> Frequency of atrial arrhythmias is estimated at ~12% and is also associated with substantial morbidity, including congestive heart failure, reoperation, subsequent ventricular tachycardia, stroke, and death.<sup>105</sup> Thus, all post-operative patients should undergo yearly follow-up with thorough screenings. Echocardiography with Doppler imaging should assess for RV size and function, septal motion, RVOT obstruction, residual VSD, and valvular regurgitation. ECG should be obtained to assess PR interval, QRS duration (ventricular depolarization), QT interval (ventricular repolarization), and if abnormal, a signal averaged ECG is needed to assess QT dispersion. QT dispersion (the difference between the shortest and longest QT interval in any of the 12 leads on standard surface ECG) is a marker of inhomogeneous repolarization and has been shown to be predictive of sustained monomorphic ventricular tachycardia. One study showed that a QRS duration of >180 ms and a QT dispersion of >60 ms further refine the risk stratification<sup>106</sup> (Fig 24). Electrophysiologic testing is needed for those with positive signal average ECG or symptomatic arrhythmias. Treatment often involves repeat surgery to relieve the hemodynamic compromises and remove the electrophysiological substrates, as was the case in our 34-year-old patient.



**FIG 24.** ECG of ventricular fibrillation converted to normal sinus rhythm after cardioversion. This 39-year-old man with a history of repaired tetralogy of Fallot with right ventricular outflow tract aneurysm presented to the emergency room after complaining of palpitation and presyncope symptoms. He was subsequently treated with catheter ablations and placement of an automatic implantable cardioverter defibrillator (AICD). Ventricular arrhythmia is a common cause of sudden cardiac death in these patients.

## Case 12: Eisenmenger Syndrome

A 23-year-old man with a history of Down's syndrome was referred to our ACHD clinic for evaluation of a cardiac murmur. The patient was born in Mexico and had no routine follow-up. The mother reported that the patient had become physically less active for the past 3 years and lately had frequent lung infections. Cardiac examination showed a normal jugular venous waveform, palpable RV parasternal impulse, loud S2, and 3/6 high-frequency diastolic murmur at LUSB and LLSB. Echocardiogram revealed a D-shaped LV due to RV pressure overload, a large atrioventricular septal defect, tricuspid regurgitant velocity of 4.3 m/s (estimated RVSP of 83 mmHg, assuming RA pressure of 10 mmHg), and severe pulmonary regurgitation with end-diastolic velocity of 3.2 m/s (estimated pulmonary artery end diastolic pressure of 50 mmHg). These findings confirm the diagnosis of Eisenmenger syndrome.

Eisenmenger syndrome is a complex disease. Proper evaluation and treatment require an understanding of the pathophysiology, clinical presentation, natural history, and complications. The syndrome can be summarized as chronic systemic-to-pulmonary communication causing → left-to-right shunting of blood → increased pulmonary blood flow → irreversible pulmonary vascular injury → increased PVR → reversed right-to-left shunting of blood → hypoxia and erythrocytosis.<sup>107</sup> The nonrestrictive communications encompass many types of CHD reviewed earlier and may occur at the atrial level (eg, ASD), ventricular level (eg, VSD or atrioventricular septal defect), or arterial level (eg, PDA, truncus arteriosus, or aortopulmonary window). It may also result from ventriculoarterial discordance (eg, TGA), atrioventricular and ventriculoarterial discordances (eg, CCTGA) with VSD, or even surgically created connections (eg, Potts and Waterston anastomoses).



**FIG 25.** Chest computed tomography (CT) of an Eisenmenger patient with in situ thrombus in the right pulmonary artery (RPA). MPA, main pulmonary artery; Ao, aorta.

Physical examination usually reveals central cyanosis, digital clubbing, a RV impulse, a palpable pulmonary closure sound, and a high-pitched decrescendo Graham Steel murmur from pulmonary regurgitation. There may be a holosystolic murmur of tricuspid regurgitation or a right ventricular S4 gallop when RV decompensation occurs. ECG may show biventricular hypertrophy. CXR may show prominently dilated central pulmonary arteries with pruning of peripheral vessels. Echocardiogram with Doppler imaging is helpful in visualizing the intra- or extra-cardiac shunts causing the syndrome. CT or MRI can also provide excellent visualization of the defects, but is most valuable in evaluating for pulmonary arterial in situ thrombi, quality of pulmonary tissue, and for intrapulmonary hemorrhage<sup>108,109</sup> (Fig 25).

## Management

Depending on the pathophysiology, patients may present with severe heart failure during infancy, dyspnea on exertion during childhood, or progressive cyanosis during adulthood. Survival is infrequent beyond the late 5th decade of life, though our oldest patient died of Legionnaire's disease at 78 years of age. Death may be due to RV failure, pulmonary thrombi or hemorrhage, cerebral infarct, tachyarrhythmias, or renal

dysfunction.<sup>110</sup> The long-term prognosis of Eisenmenger patients however is substantially better than primary pulmonary hypertension (PPH) patients. In one study, survival was 97% at 1 year, 89% at 2 years, and 77% at 3 years for Eisenmenger patients compared to 77, 69, and 35%, respectively, for PPH patients.<sup>111</sup> The long list of medical complications that plague adult Eisenmenger patients, include the following: (1) secondary erythrocytosis due to increased erythropoietin production in response to chronic hypoxemia; (2) hyperviscosity symptoms such as headache, dizziness, visual disturbance, fatigue, and paresthesia; (3) hemostatic disorders such as easy bruising, epistaxis, and hemoptysis due to thrombocytopenia and prolonged coagulation times; (4) high incidence of stroke and cerebral abscess; (5) pulmonary thromboembolism and rupture of pulmonary artery aneurysm; (6) coronary artery ectasia; (7) proteinuria due to glomerular abnormality; (8) hyperuricemia from increased production and decreased renal clearance; and (9) hypertrophic osteoarthropathy.<sup>108</sup>

Because of these potential complications, all patients should have periodic physical examination, ECG, CXR, echocardiogram, Holter monitoring, and blood work (including CBC, mean corpuscular volume, ferritin, creatinine, INR, and PTT).<sup>112</sup> In general, an increased hematocrit in Eisenmenger patients is *not* a justification for prophylactic phlebotomy and can cause relative iron deficiency anemia.<sup>108</sup> When phlebotomy is occasionally indicated (eg, to relieve severe hyperviscosity symptoms or to improve hemostasis preoperatively), patients must receive adequate volume replacement (eg, 500-1000 mL isotonic saline) to avoid dehydration. Oxygen therapy is usually not needed for patients at baseline since it does not increase exercise capacity or quality of life and can cause epistaxis if the oxygen is non-humidified.<sup>113</sup> Travel to high-altitude locations may pose a major risk because of decreased inspired oxygen. Hypoxic pulmonary vasoconstriction may worsen pulmonary hypertension, increase right-to-left shunting, causing acute right heart failure and systemic arterial desaturation.<sup>107</sup> In contrast, commercial flights (with the cabin pressure altitude usually maintained between 1800 and 2400 meters above sea level) is considered safe for the patients.<sup>112</sup> Pregnancy should be avoided because it is considered high risk for both the mother and the fetus. Prophylactic treatment for in situ thrombus with anticoagulation is controversial because these patients are also at higher risk for intrapulmonary hemorrhage.<sup>108</sup>

The cause of Eisenmenger physiology for our patient is due to his nonrestrictive atrioventricular septal defect. Remarkably, about 50% of Down's patients are born with CHD (Fig 26). The most frequent lesions



**FIG 26.** Nine-year-old female with Down syndrome. The inner epicanthic fold is subtle. The nose is short and flat with depressed nasal bridge. The corners of the mouth turn downward, creating an expression of sadness. (Adapted from Perloff JK. *Clinical Recognition of Congenital Heart Disease*. Philadelphia, PA: Saunders, 2003.)

are atrioventricular septal defect (45%), VSD (35%), isolated secundum ASD (8%), isolated persistent PDA (7%), isolated TOF (4%), and other lesions (1%).<sup>114</sup> Additionally, adolescents and young adults with no known intracardiac disease can later on develop MVP (46%) and aortic regurgitation (17%). Therefore, it is recommended that all Down's patients receive detailed cardiac examination as well as an echocardiogram.<sup>115</sup>

## Conclusions

In summary, there is a large and growing population of adults with CHD. Most will need life-long cardiac care by physicians cognizant of their conditions and adept at managing their medical needs. Surgical cures



are rare and most repairs leave behind (residua) or cause (sequelae) some abnormality, whether major or minor.<sup>5</sup> We hope this brief synopsis will help familiarize readers with CHD and at the same time arouse their interest in this intellectually stimulating field.

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**Dr. Gary Webb:** Drs. Wu and Child have presented an excellent review and discussion of congenital heart diseases that are commonly seen in adults.

The delivery of high-quality care of the adult patient with congenital heart defects can be difficult. While management of the classic cases can be stated fairly easily, most cases are not “classic,” and it is variations on the themes that make the assessment and management of individual patients so challenging.

In my opinion, ACDH patients with lesions of moderate or great complexity should see ACDH experts. Individual cardiologists and other medical practitioners should have a referral relationship with ACDH experts in the interest of best patient care. Presently, such experts are not always easy to find (Webb GD: *Cardiol Young* 2004;14:6-14). Once identified, they need the support of their medical communities to foster their expertise.

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## REFERENCES

1. Hoffman JI, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol* 2002;39:1890-900.
2. Warnes CA, Liberthson R, Danielson GK, et al. Task force 1: the changing profile of congenital heart disease in adult life. *J Am Coll Cardiol* 2001;37:1170-5.
3. Child JS, Collins-Nakai RL, Alpert JS, et al. Task force 3: workforce description and educational requirements for the care of adults with congenital heart disease. *J Am Coll Cardiol* 2001;37:1183-7.
4. Summary of recommendations—care of the adult with congenital heart disease. *J Am Coll Cardiol* 2001;37:1167-9.
5. Child JS. Echocardiographic evaluation of the adult with postoperative congenital heart disease. In: Otto CM, editor. *The Practice of Clinical Cardiology*. 2nd ed. Philadelphia, PA: Saunders, 2002. p. 901-21.
6. Romano-Zelekha O, Hirsh R, Blieden L, Green M, Shohat, T. The risk for congenital heart defects in offspring of individuals with congenital heart defects. *Clin Genet* 2001;59:325-9.
7. Connolly HM, Warnes CA. Pregnancy and contraception. In: Gatzoulis MA, Webb GD, Daubeney PEF, editors. *Diagnosis and Management of Adult Congenital Heart Disease*. St. Louis, MO: Churchill Livingstone, 2003. p. 135-44.
8. Perloff JK, Koos B. Pregnancy and congenital heart disease: the mother and the fetus. In: Child JS, editor. *Congenital Heart Disease in Adults*. 2nd ed. Philadelphia, PA: Saunders, 1998. p. 144-64.
9. Oakley C, Child A, Lung B, et al. Expert consensus document on management of cardiovascular diseases during pregnancy. *Eur Heart J* 2003;24:761-81.
10. Dodo H, Child JS. Infective endocarditis in congenital heart disease. *Cardiol Clin* 1996;14:383-92.
11. Perloff JK. *Clinical Recognition of Congenital Heart Disease*. 5th ed. Philadelphia, PA: Saunders, 2003.



12. Triedman JK. Arrhythmias in adults with congenital heart disease. *Heart* 2002;87:383-9.
13. Child JS. Transthoracic and transesophageal echocardiographic imaging: anatomic and hemodynamic assessment. In: Perloff JK, Child JS, editors. *Congenital Heart Disease in Adults*. 2nd ed. Philadelphia, PA: Saunders, 1998. p. 91-128.
14. Moodie DS, Sterba R. Long-term outcomes excellent for atrial septal defect repair in adults. *Cleve Clin J Med* 2000;67:591-7.
15. Moodie DS. Diagnosis and management of congenital heart disease in the adult. *Cardiol Rev* 2001;9:276-81.
16. Vogel M, Berger F, Kramer A, Alexi-Meskishvili V, Lange PE. Incidence of secondary pulmonary hypertension in adults with atrial septal or sinus venosus defects. *Heart* 1999;82:30-3.
17. 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;68:75-8.
18. 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;333:469-73.
19. 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;38:2035-42.
20. 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;340:839-46.
21. 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;39:1061-5.
22. Brandt RR, Neumann T, Neuzner J, Rau M, Faude I, Hamm CW. Transcatheter closure of atrial septal defect and patent foramen ovale in adult patients using the Amplatzer occlusion device: no evidence for thrombus deposition with antiplatelet agents. *J Am Soc Echocardiogr* 2002;15:1094-8.
23. Li W, Somerville J. Infective endocarditis in the grown-up congenital heart (GUHC) population. *Eur Heart J* 1998;19:166-73.
24. Dajani AS, Taubert KA, Wilson W, et al. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. *Circulation* 1997;96:358-66.
25. Amplatzer K, Moller J. *Radiology of Congenital Heart Disease*. St. Louis, MO: Mosby Year Book, 1993.
26. Roguin N, Du ZD, Barak M, Nasser N, Hershkowitz S, Milgram E. High prevalence of muscular ventricular septal defect in neonates. *J Am Coll Cardiol* 1995;26:1545-8.
27. Neumayer U, Stone S, Somerville J. Small ventricular septal defects in adults. *Eur Heart J* 1998;19:1573-82.
28. Redington A, Shore D, Oldershaw P. *Congenital heart disease in adults: a practical guide*. Philadelphia, PA: Saunders, 1994.
29. McDaniel NL, Gutgesell HP. Ventricular septal defects. In: Allen HD, Gutgesell HP, Clark EB, Driscoll DJ, editors. *Moss and Adams' Heart Disease in Infants, Children and Adolescents: Including the Fetus and Young Adult*. 5th ed. Baltimore, MD: Williams & Wilkins, 2001. p. 636-51.

30. Pienvichit P, Piemonte TC. Percutaneous closure of postmyocardial infarction ventricular septal defect with the CardioSEAL septal occluder implant. *Cathet Cardiovasc Interv* 2001;54:490-4.
31. Levi DS, Alejos JC, Moore JW. Future of interventional cardiology in pediatrics. *Curr Opin Cardiol* 2003;18:79-90.
32. Reller MD, Ziegler ML, Rice MJ, Solin RC, McDonald, RW. Duration of ductal shunting in healthy preterm infants: an echocardiographic color flow Doppler study. *J Pediatr* 1988;112:441-6.
33. Therrien J, Dore A, Gersony W, et al. CCS Consensus Conference 2001 update: recommendations for the management of adults with congenital heart disease. Part I. *Can J Cardiol* 2001;17:940-59.
34. Fisher RG, Moodie DS, Sterba R, Gill CC. Patent ductus arteriosus in adults—long-term follow-up: nonsurgical versus surgical treatment. *J Am Coll Cardiol* 1986;8:280-4.
35. Brili SV, Toutouzas P. Patent arterial duct and aortopulmonary window. In: Gatzoulis MA, Webb GD, Daubeney PEF, editors. *Diagnosis and Management of Adult Congenital Heart Disease*. St. Louis, MO: Churchill Livingstone, 2003. p. 247-52.
36. Faella HJ, Hijazi ZM. Closure of the patent ductus arteriosus with the amplatzer PDA device: immediate results of the international clinical trial. *Cathet Cardiovasc Interv* 2000;51:50-4.
37. Sabet HY, Edwards WD, Tazelaar HD, Daly RC. Congenitally bicuspid aortic valves: a surgical pathology study of 542 cases (1991 through 1996) and a literature review of 2,715 additional cases. *Mayo Clin Proc* 1999;74:14-26.
38. Whittemore R, Wells JA, Castellsague X. A second-generation study of 427 probands with congenital heart defects and their 837 children. *J Am Coll Cardiol* 1994;23:1459-67.
39. Niwa K, Perloff JK, Bhuta SM, et al. Structural abnormalities of great arterial walls in congenital heart disease: light and electron microscopic analyses. *Circulation* 2001;103:393-400.
40. Dall'Agata A, Cromme-Dijkhuis AH, Meijboom FJ, et al. Use of three-dimensional echocardiography for analysis of outflow obstruction in congenital heart disease. *Am J Cardiol* 1999;83:921-5.
41. Morris CD, Reller MD, Menashe VD. Thirty-year incidence of infective endocarditis after surgery for congenital heart defect. *JAMA* 1998;279:599-603.
42. Child JS, Perloff JK, Kubak B. Infective endocarditis: risks and prophylaxis. In: Perloff JK, Child JS, editors. *Congenital Heart Disease in Adults*. 2nd ed. Philadelphia, PA: Saunders, 1998. p. 129-143.
43. Child JS. Risks for and prevention of infective endocarditis. *Cardiol Clin* 1996;14:327-43.
44. Brickner ME. Valvar aortic stenosis. In: Daubeney PEF, editor. *Diagnosis and Management of Adult Congenital Heart Disease*. St. Louis, MO: Churchill Livingstone, 2003. Pp. 213-21.
45. Bonow RO, Carabello B, de Leon AC Jr, et al. Guidelines for the management of patients with valvular heart disease: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients with Valvular Heart Disease). *Circulation* 1998;98:1949-84.

46. Takkenberg JJ, Dossche KM, Hazekamp MG, et al. Report of the Dutch experience with the Ross procedure in 343 patients. *Eur J Cardiothorac Surg* 2002;22:70-7.
47. Waller BF, Howard J, Fess S. Pathology of pulmonic valve stenosis and pure regurgitation. *Clin Cardiol* 1995;18:45-50.
48. Nishimura RA, Pieroni DR, Bierman FZ, et al. Second natural history study of congenital heart defects. Pulmonary stenosis: echocardiography. *Circulation* 1993;87:I73-9.
49. Dore A. Pulmonary stenosis. In: Gatzoulis MA, Webb GD, Daubeney PEF, editors. *Diagnosis and Management of Adult Congenital Heart Disease*. St. Louis, MO: Churchill Livingstone, 2003. p. 299-303.
50. Mandell VS. Interventional procedures for congenital heart disease. *Radiol Clin North Am* 1999;37:439-61, vii.
51. Chen CR, Cheng TO, Huang T, et al. Percutaneous balloon valvuloplasty for pulmonic stenosis in adolescents and adults. *N Engl J Med* 1996;335:21-5.
52. Elzenga NJ, Gittenberger-de Groot AC. Localised coarctation of the aorta. An age dependent spectrum. *Br Heart J* 1983;49:317-23.
53. Baron MG. Plain film diagnosis of common cardiac anomalies in the adult. *Radiol Clin North Am* 1999;37:401-20, vi.
54. Muhler EG, Neuerburg JM, Ruben A, et al. Evaluation of aortic coarctation after surgical repair: role of magnetic resonance imaging and Doppler ultrasound. *Br Heart J* 1993;70:285-90.
55. Soler R, Rodriguez E, Requejo I, Fernandez R, Raposo I. Magnetic resonance imaging of congenital abnormalities of the thoracic aorta. *Eur Radiol* 1998;8:540-6.
56. McCrindle BW. Coarctation of the aorta. *Curr Opin Cardiol* 1999;14:448-52.
57. Beekam RH. Coarctation of the aorta. In: Allen HD, Gutgesell HP, Clark EB, Driscoll DJ, editors. *Moss and Adams' Heart Disease in Infants, Children and Adolescents: Including the Fetus and Young Adult*. 5th ed. Baltimore, MD: Williams & Wilkins, 2001. p. 988-1010.
58. Connolly HM, Huston J 3rd, Brown RD Jr, Warnes CA, Ammass NM, Tajik AJ. Intracranial aneurysms in patients with coarctation of the aorta: a prospective magnetic resonance angiographic study of 100 patients. *Mayo Clin Proc* 2003;78:1491-9.
59. Kaemmerer H. Aortic coarctation and interrupted aortic arch. In: Gatzoulis MA, Webb GD, Daubeney PEF, eds. *Diagnosis and Management of Adult Congenital Heart Disease*. St. Louis, MO: Churchill Livingstone, 2003. p. 253-64.
60. Walhout RJ, Lekkerkerker JC, Oron GH, Hitchcock FJ, Meijboom EJ, Bennink GB. Comparison of polytetrafluoroethylene patch aortoplasty and end-to-end anastomosis for coarctation of the aorta. *J Thorac Cardiovasc Surg* 2003;126:521-8.
61. Hamdan MA, Maheshwari S, Fahey JT, Hellenbrand WE. Endovascular stents for coarctation of the aorta: initial results and intermediate-term follow-up. *J Am Coll Cardiol* 2001;38:1518-23.
62. Angelini P, Villason S, Chan AVJ, Diez JG. Normal and anomalous coronary arteries in humans. In: Angelini P, editor. *Coronary Artery Anomalies: A Comprehensive Approach*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 1999. p. 27-150.
63. Dodge-Khatami A, Mavroudis C, Backer CL. Congenital Heart Surgery Nomenclature and Database Project: anomalies of the coronary arteries. *Ann Thorac Surg* 2000;69:S270-97.

64. Taylor AJ, Rogan KM, Virmani R. Sudden cardiac death associated with isolated congenital coronary artery anomalies. *J Am Coll Cardiol* 1992;20:640-7.
65. Liberthson R. Congenital anomalies of the coronary arteries. In: Gatzoulis MA, Webb GD, Daubeney PEF, editors. *Diagnosis and Management of Adult Congenital Heart Disease*. 5th ed. St. Louis, MO: Churchill Livingstone, 2003. p. 425-431.
66. Angelini P. Coronary artery anomalies—current clinical issues: definitions, classification, incidence, clinical relevance, and treatment guidelines. *Tex Heart Inst J* 2002;29:271-8.
67. Reul RM, Cooley DA, Hallman GL, Reul GJ. Surgical treatment of coronary artery anomalies: report of a 37 1/2-year experience at the Texas Heart Institute. *Tex Heart Inst J* 2002;29:299-307.
68. Hauck AJ, Freeman DP, Ackermann DM, Danielson GK, Edwards WD. Surgical pathology of the tricuspid valve: a study of 363 cases spanning 25 years. *Mayo Clin Proc* 1988;63:851-63.
69. Frescura C, Angelini A, Daliento L, Thiene G. Morphological aspects of Ebstein's anomaly in adults. *Thorac Cardiovasc Surg* 2000;48:203-8.
70. Radford DJ, Graff RF, Neilson GH. Diagnosis and natural history of Ebstein's anomaly. *Br Heart J* 1985;54:517-22.
71. Shiina A, Seward JB, Edwards WD, Hagler DJ, Tajik AJ. Two-dimensional echocardiographic spectrum of Ebstein's anomaly: detailed anatomic assessment. *J Am Coll Cardiol* 1984;3:356-70.
72. Ahmed S, Nanda NC, Nekkanti R, Pacifico AD. Transesophageal three-dimensional echocardiographic demonstration of Ebstein's anomaly. *Echocardiography* 2003;20:305-7.
73. Brickner ME, Hillis LD, Lange RA. Congenital heart disease in adults. Second of two parts. *N Engl J Med* 2000;342:334-42.
74. Attie F, Rosas M, Rijlaarsdam M, et al. The adult patient with Ebstein anomaly. Outcome in 72 unoperated patients. *Medicine (Baltimore)* 2000;79:27-36.
75. Cappato R, Schluter M, Weiss C, et al. Radiofrequency current catheter ablation of accessory atrioventricular pathways in Ebstein's anomaly. *Circulation* 1996;94:376-83.
76. Danielson GK, Driscoll DJ, Mair DD, Warnes CA, Oliver WC Jr. Operative treatment of Ebstein's anomaly. *J Thorac Cardiovasc Surg* 1992;104:1195-202.
77. Kiziltan HT, Theodoro DA, Warnes CA, O'Leary PW, Anderson BJ, Danielson GK. Late results of bioprosthetic tricuspid valve replacement in Ebstein's anomaly. *Ann Thorac Surg* 1998;66:1539-45.
78. Theodoro DA, Danielson GK, Porter CJ, Warnes CA. Right-sided maze procedure for right atrial arrhythmias in congenital heart disease. *Ann Thorac Surg* 1998;65:149-53; discussion 153-4.
79. Fontan F, Baudet E. Surgical repair of tricuspid atresia. *Thorax* 1971;26:240-8.
80. Freeman RM, Li J, Yoo SJ. Late complications following the Fontan operation. In: Gatzoulis MA, Webb GD, Daubeney PEF, editors. *Diagnosis and Management of Adult Congenital Heart Disease*. St. Louis, MO: Churchill Livingstone, 2003. p. 85-91.
81. Hornung T. Transposition of the great arteries. In: Gatzoulis MA, Webb GD, Daubeney PEF, editors. *Diagnosis and Management of Adult Congenital Heart Disease*. St. Louis, MO: Churchill Livingstone, 2003. p. 349-62.

82. Ho S, McCarthy KP, Josen M, Rigby ML. Anatomic-echocardiographic correlates: an introduction to normal and congenitally malformed hearts. *Heart* 2001;86(Suppl. 2):II3-11.
83. Rashkind WJ, Miller WW. Creation of an atrial septal defect without thoracotomy. A palliative approach to complete transposition of the great arteries. *JAMA* 1966;196:991-2.
84. Mustard WT. Successful two-stage correction of transposition of the great vessels. *Surgery* 1964;55:469-72.
85. Senning A. Correction of the transposition of the great arteries. *Ann Surg* 1975;182:287-92.
86. Losay J, Touchot A, Serraf A, et al. Late outcome after arterial switch operation for transposition of the great arteries. *Circulation* 2001;104:II21-6.
87. Jatene AD, Fontes VF, Paulista PP, et al. Anatomic correction of transposition of the great vessels. *J Thorac Cardiovasc Surg* 1976;72:364-70.
88. Culbert EL, Ashburn DA, Cullen-Dean G, et al. Quality of life of children after repair of transposition of the great arteries. *Circulation* 2003;108:857-62.
89. Kreutzer C, De Vive J, Oppido G, et al. Twenty-five-year experience with Rastelli repair for transposition of the great arteries. *J Thorac Cardiovasc Surg* 2000;120:211-23.
90. Rutledge JM, Nihill MR, Fraser CD, Smith OE, McMahon CJ, Bezold LI. Outcome of 121 patients with congenitally corrected transposition of the great arteries. *Pediatr Cardiol* 2002;23:137-45.
91. Graham TPJ. Congenitally corrected transposition. In: Gatzoulis MA, Webb GD, Daubeney PEF, editors. *Diagnosis and Management of Adult Congenital Heart Disease*. St. Louis, MO: Churchill Livingstone, 2003. p. 379-87.
92. Huhta JC, Maloney JD, Ritter DG, Ilstrup DM, Feldt RH. Complete atrioventricular block in patients with atrioventricular discordance. *Circulation* 1983;67:1374-7.
93. Deepak SM, Royle M, Goode GK. Congenitally corrected transposition of the great arteries (L transposition). *Heart* 2003;89:976.
94. Yeh T Jr, Connelly MS, Coles JG, et al. Atrioventricular discordance: results of repair in 127 patients. *J Thorac Cardiovasc Surg* 1999;117:1190-203.
95. Imamura M, Drummond-Webb JJ, Murphy DJ Jr, et al. Results of the double switch operation in the current era. *Ann Thorac Surg* 2000;70:100-5.
96. Presbitero P, Somerville J, Rabajoli F, Stone S, Conte MR. Corrected transposition of the great arteries without associated defects in adult patients: clinical profile and follow up. *Br Heart J* 1995;74:57-9.
97. Lester SJ, McElhinney DB, Vilorio E, et al. Effects of losartan in patients with a systemically functioning morphologic right ventricle after atrial repair of transposition of the great arteries. *Am J Cardiol* 2001;88:1314-6.
98. Hechter SJ, Fredriksen PM, Liu P, et al. Angiotensin-converting enzyme inhibitors in adults after the Mustard procedure. *Am J Cardiol* 2001;87:660-3, A11.
99. Therrien J, Webb G. Clinical update on adults with congenital heart disease. *Lancet* 2003;362:1305-13.
100. Dabizzi RP, Teodori G, Barletta GA, Caprioli G, Baldrighi G, Baldrighi V. Associated coronary and cardiac anomalies in the tetralogy of Fallot. An angiographic study. *Eur Heart J* 1990;11:692-704.
101. Bertranou EG, Blackstone EH, Hazelrig JB, Turner ME, Kirklin JW. Life expectancy without surgery in tetralogy of Fallot. *Am J Cardiol* 1978;42:458-66.

102. Dittrich S, Vogel M, Dahnert I, Berger F, Alexi-Meskishvili V, Lange PE. Surgical repair of tetralogy of Fallot in adults today. *Clin Cardiol* 1999;22:460-4.
103. Gatzoulis MA. Tetralogy of Fallot. In: Gatzoulis MA, Webb GD, Daubeney PEF, editors. *Diagnosis and Management of Adult Congenital Heart Disease*. St. Louis, MO: Churchill Livingstone, 2003. p. 315-26.
104. Bricker JT. Sudden death and tetralogy of Fallot. Risks, markers, and causes. *Circulation* 1995;92:158-9.
105. Harrison DA, Siu SC, Hussain F, MacLoughlin CJ, Webb GD, Harris L. Sustained atrial arrhythmias in adults late after repair of tetralogy of fallot. *Am J Cardiol* 2001;87:584-8.
106. Gatzoulis MA, Till JA, Redington AN. Depolarization-repolarization inhomogeneity after repair of tetralogy of Fallot. The substrate for malignant ventricular tachycardia? *Circulation* 1997;95:401-4.
107. Vongpatanasin W, Brickner ME, Hillis LD, Lange RA. The Eisenmenger syndrome in adults. *Ann Intern Med* 1998;128:745-55.
108. Perloff JK, Rosove MH, Sietsema KE, Territo MC. Cyanotic congenital heart disease: a multisystem disorder. In: Child JS, editor. *Congenital Heart Disease in Adults*. 2nd ed. Philadelphia, PA: Saunders, 1998. p. 199-226.
109. Pignatelli RH, McMahon CJ, Chung T, Vick GW 3rd. Role of echocardiography versus MRI for the diagnosis of congenital heart disease. *Curr Opin Cardiol* 2003;18:357-65.
110. Daliento L, Somerville J, Presbitero P, et al. Eisenmenger syndrome. Factors relating to deterioration and death. *Eur Heart J* 1998;19:1845-55.
111. Hopkins WE, Ochoa LL, Richardson GW, Trulock EP. Comparison of the hemodynamics and survival of adults with severe primary pulmonary hypertension or Eisenmenger syndrome. *J Heart Lung Transplant* 1996;15:100-5.
112. Oechslin E. Eisenmenger's syndrome. In: Gatzoulis MA, Webb GD, Daubeney PEF, editors. *Diagnosis and Management of Adult Congenital Heart Disease*. St. Louis, MO: Churchill Livingstone, 2003. p. 363-77.
113. Sandoval J, Aguirre JS, Pulido T, et al. Nocturnal oxygen therapy in patients with the Eisenmenger syndrome. *Am J Respir Crit Care Med* 2001;164:1682-7.
114. Roizen NJ, Patterson D. Down's syndrome. *Lancet* 2003;361:1281-9.
115. American Academy of Pediatrics Committee on Genetics, Health supervision for children with Down syndrome. *Pediatrics* 2001;107:442-9.