Congenital Heart Disease

20

Matina Prapa, Dimitra Krexi, Anselm Uebing,
and Michael A. Gatzoulis

Introduction

Congenital heart disease (CHD) is defined as a cardiovascular defect that is present since birth and has an estimated incidence of up to 75/1,000 live births including trivial lesions [1]. Isolated ventricular septal defect (VSD) is one of the most common forms of CHD; approximately 3 % of infants have a tiny muscular VSD with spontaneous closure in 85–90 % of cases by the first year of life [1]. Another 1 % have a bicuspid but non-stenotic aortic valve that seldom causes problems in childhood, but may calcify or degenerate later in life [1] (Table 20.1).

Major chromosomal abnormalities account for 8–13 % of CHD with important implications in prognosis and family counseling [2]. Such an example is the presence of 22q11 deletion in approximately 90 % of patients with DiGeorge syndrome and lesions including Tetralogy of Fallot or VSD, who have a 50 % chance of transmitting the disease to their offsprings [2]. A few congenital anomalies are due to teratogens, such as alcohol, lithium, or retinoic acid, or to single gene defects. However, most cases of non-syndromic CHD are likely to be owing to the complex interplay of genetic aberrations with environmental factors.

Due to medical and surgical advances, 85 % of children born with congenital heart defects now survive into adulthood [3]. Adults with CHD can be divided into those with previous repair or palliation and those with unrepaired defects. While patients with repaired CHD are more likely to have improved outcomes, residual hemodynamic lesions and sequelae from previous interventions, such as scar-related arrhythmias, are frequent. The following sections will provide an introduction to the most prevalent CHD lesions and summarize specific issues which are topical to adult patients with CHD.

M. Prapa, MD (✉) • D. Krexi, MD • A. Uebing, MD, PhD
M.A. Gatzoulis, MD, PhD
Adult Congenital Heart Disease, Royal Brompton Hospital,
Sydney Street, London, SW3 6NP, UK
e-mail: m.prapa@rbht.nhs.uk

Classification

Congenital heart disease defects can be classified into mild, moderate, or severe with regard to clinical management and appropriate access of patients to tertiary care [4]. A more physiological classification is that of acyanotic CHD, where there is no communication between the systemic and pulmonary circulation or there is a left-to-right shunt, and cyanotic CHD with right-to-left shunting. Finally, a useful approach to accurate description of CHD lesions is "sequential segmental analysis" according to which the heart is broken down into three segments (the atrial chambers, the ventricular mass, and the great arteries; Fig. 20.1) and the relationship between adjacent chambers is described (Table 20.2).

Specific Lesions

Atrial Septal Defect

Atrial septal defect (ASD) is defined as a direct communication between the atrial chambers and can be divided into four morphological types: ostium secundum defect of the oval fossa,

Table 20.1 Incidence of congenital heart disease lesions per 1,000 live births

Lesion	Incidence
Bicuspid aortic valve	9.2
Ventricular septal defect	2.8
Patent ductus arteriosus	0.6
Atrial septal defect	0.6
Pulmonary stenosis	0.5
Aortic coarctation	0.3
Tetralogy of Fallot	0.3
Atrioventricular septal defect	0.3
Transposition of the great arteries	0.3
Aortic valve stenosis	0.2

Modified from Hoffman and Kaplan [1]. With permission from Elsevier

C. Rosendorff (ed.), *Essential Cardiology*,
DOI 10.1007/978-1-4614-6705-2_20,

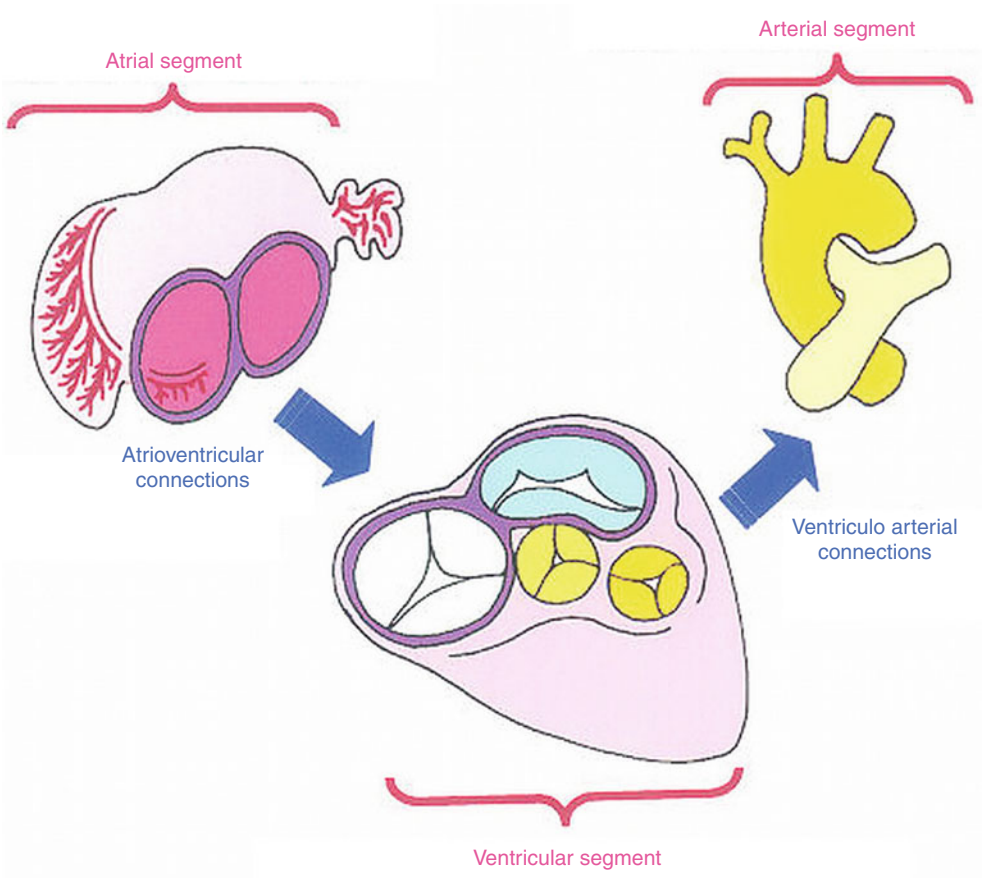

Fig. 20.1 The three segments of the heart used for sequential segmental analysis of congenital heart defects (see Table 20.1) (Image courtesy of S.Y. Ho)

Table 20.2 Sequential segmental analysis of congenital heart disease

1. Arrangement of the atrial chambers (situs)
Situs solitus = morphologically right atrium on the right and morphologically left atrium on the left
Situs inversus = mirror image of the usual arrangement (atria on the wrong sides)
Isomerism = morphological right or left atria bilaterally
2. Atrioventricular (AV) connections
Concordant = appropriate connection of atria to ventricles
Discordant = atria connected to inappropriate ventricles (e.g., right atrium connected to left ventricle)
3. Ventriculoarterial (VA) connections
Concordant = appropriate connection of ventricles to great arteries
Discordant = ventricles connected to inappropriate arteries (e.g., right ventricle connected to aorta)
4. Associated malformations
5. Examples
Atrial septal defect = situs solitus, concordant AV connections, concordant VA connections and atrial septal defect
Complete transposition of the great arteries = situs solitus, concordant AV connections, discordant VA connections

Modified from Ho [5]. With permission from Elsevier

which is the commonest; superior sinus venosus defect overriding the superior vena cava, often associated with partial anomalous pulmonary venous drainage; ostium primum or partial atrioventricular defect, discussed later; and coronary sinus defect, in which there is a deficiency of the wall between the coronary sinus and the left atrium (Fig. 20.2). Left-to-right shunting occurs across an ASD or through anomalous pulmonary veins when the right ventricle becomes more distensible than the left ventricle a few weeks after birth. When pulmonary blood flow (Qp) is more than twice the systemic blood flow (Qs), the right atrium and ventricle are enlarged and hyperactive, with prominent pulsation over the lower left sternal border, and cardiomegaly and increased pulmonary arterial markings on chest X-ray. The relationship between pulmonary and systemic blood flow (Qp/Qs) can be estimated in the catheter laboratory using the Fick principle or noninvasively using cardiac magnetic resonance and echocardiography.

Children with a secundum ASD or partial anomalous pulmonary veins are usually asymptomatic and form one of the largest groups of patients with untreated CHD seen in adult clinics. Adult patients rarely have symptoms before the third or fourth decade of life and may present with exertional dyspnea or palpitations due to atrial tachyarrhythmias. Late complications of unrepaired ASDs include development of right heart failure, atrial flutter or fibrillation, pulmonary hypertension, and paradoxical embolism. Cardinal signs of an ASD on examination include a wide fixed split second heart sound and right ventricular lift. Increased pulmonary

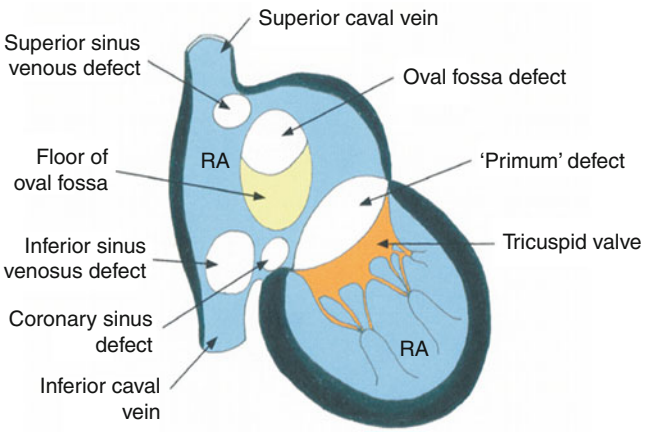

Fig. 20.2 Different types of atrial septal defects (as seen from the right side of the heart)

blood flow may cause a moderately loud pulmonary ejection systolic murmur and a tricuspid mid-diastolic murmur.

The ECG in ASD often shows right-axis (secundum ASD) or superior left-axis (primum ASD) deviation, right atrial enlargement, prolonged PR interval, and right bundle branch block pattern (RBBB). The chest X-ray reveals cardiomegaly (right heart dilation), signs of increased pulmonary blood flow with dilated central pulmonary arteries, and a small aortic knuckle due to persistent low systemic cardiac output. Transthoracic echocardiography is the main diagnostic imaging tool for ASD and demonstrates the location and size of the defect, the direction of the shunt, and a Doppler estimate of the pulmonary artery pressures (PAP). Transesophageal echocardiography (TOE) may be necessary to visualize the pulmonary veins and septal rims of the defect to determine suitability for device closure. Cardiac magnetic resonance imaging (CMR) is useful in the instance of inadequate echocardiographic images and provides information on pulmonary venous anatomy and right ventricular size and function. Diagnostic cardiac catheterization is now rarely performed unless there is suspicion of significant pulmonary arterial hypertension or an indication for assessment of coronary artery disease.

Indications for ASD closure are summarized in Table 20.3; closure of ASDs with right heart dilatation is recommended irrespective of symptoms on the merits of better prognostication. In many centers, percutaneous transcatheter closure has become the recommended treatment for uncomplicated secundum ASDs with suitable anatomy. Surgical closure is required for ostium primum, sinus venosus, and coronary sinus defects. Arrhythmia targeted interventions should be considered at the time of ASD closure, especially in patients older than 40 years who are at a higher risk of developing late atrial flutter or fibrillation following surgical repair [6]. Prophylactic anticoagulation is recommended for 3–6 months following percutaneous closure.

Table 20.3 Indications for closure of atrial septal defect (ASD)

ASD closure	
Indications:	Contraindications:
ASD associated with RA and RV enlargement, irrespective of symptoms	Advanced pulmonary arterial hypertension
Paradoxical embolism	Severe LV dysfunction
Documented orthodeoxia-platypnea	

Abbreviations: *LV* left ventricle, *RA* right atrium, *RV* right ventricle

Ventricular Septal Defect

Ventricular septal defects are divided into (1) perimembranous, (2) muscular, and (3) doubly committed subarterial. Muscular VSDs are bordered completely by myocardium, whereas perimembranous VSDs are partially bordered by the central fibrous body, in continuity between the leaflets of an atrioventricular and an arterial valve. Spontaneous closure of VSDs at both of the above sites is common in childhood. Doubly committed subarterial VSDs are located in the outlet septum in close proximity with the aortic and pulmonary valves. These defects leave the aortic valve cusp (noncoronary or sometimes right coronary cusp) unsupported; the cusp prolapses into the defect and partly occludes it so that the left-to-right shunt is small even if the VSD is large. Progressive aortic regurgitation in this type of VSD is common and replacement of the valve may be needed.

Clinical presentation of a VSD is dependent on the size of the defect, the right and left ventricular pressures, and the pulmonary vascular resistance. Small restrictive VSDs produce a significant pressure gradient between the two ventricles with a small left-to-right shunt ($Qp/Qs < 1.5/1.0$) and no hemodynamic derangement; these defects usually present as systolic murmurs in the absence of symptoms. Moderately restrictive VSDs result in moderate left-to-right shunt ($Qp/Qs = 1.5–2.5/1.0$) with mild to moderate volume overload of the left ventricle; patients with this defect may develop mild congestive heart failure. Finally, large nonrestrictive VSDs ($Qp/Qs > 2.5/1.0$) can lead to Eisenmenger syndrome (discussed later) with progressive pulmonary vascular disease and reversal of the left-to-right shunting.

On examination, a small- or medium-sized VSD has a typical harsh loud systolic murmur, usually pansystolic, obscuring the first heart sound, and heard best at the left lower sternal border. The size of the VSD and the amount of shunting must be judged not on the murmur but on the activity of the heart and precordium. Large nonrestrictive VSDs may produce an apical diastolic rumble of increased mitral flow or signs of pulmonary arterial hypertension (PAH), including a right ventricular heave and a palpable loud P2.

The ECG may reveal left atrial hypertrophy and signs of left ventricular overload in moderate-sized VSDs and signs of right ventricular hypertrophy in large nonrestrictive VSDs with PAH. The chest X-ray in moderate-sized VSDs

Table 20.4 Indications for closure of ventricular septal defect (VSD)

VSD closure	
Indications:	Contraindications:
Left-to-right shunt (Qp:Qs) > 2.0 and evidence of LV volume overload	Pulmonary arterial hypertension
Qp:Qs > 1.5:1 with pulmonary artery pressure < 2/3 of systemic pressure and PVR < 2/3 of systemic vascular resistance	
Qp:Qs > 1.5:1 with LV systolic or diastolic failure	
Previous episode of endocarditis	
Aortic regurgitation	

Abbreviations: *LV* left ventricle, *PVR* pulmonary vascular resistance

shows cardiomegaly (left ventricular dilatation) and pulmonary plethora and in large VSDs with PAH, dilated central pulmonary arteries and right heart enlargement. Transthoracic echocardiography establishes the size, location, and hemodynamic consequences of the defect as well as associated lesions such as aortic regurgitation. Cardiac catheterization can be performed when noninvasive data are inadequate and further information is needed, such as quantification of the shunt and assessment of pulmonary vascular resistance.

Due to spontaneous closure of 70–80 % of VSDs, initial treatment is conservative. Small defects need only prophylaxis against infective endocarditis. Timely surgical closure is required in moderate restrictive and large nonrestrictive defects with a Qp/Qs > 2.0/1.0 and clinical evidence of left ventricular volume overload [4] (Table 20.4). Transcatheter device closure may be considered in selected cases of muscular and perimembranous VSDs. Late complications related to small unoperated VSDs or residual defects following surgery include infective endocarditis, aortic regurgitation secondary to leaflet involvement, and symptomatic arrhythmias [7]. Life expectancy following surgical correction of VSD is close to normal in patients with good left ventricular function prior to surgery.

Atrioventricular Septal Defect

Atrioventricular septal defect (AVSD) comprises a spectrum of abnormalities of the atrioventricular valves (AVV) characterized by the presence of a common atrioventricular junction. In partial AVSD (also known as ostium primum ASD), the right and left AVVs have separate orifices and the ventricular septum is intact. In complete AVSD, there is a contiguous primum ASD and a large VSD, separated only by a common AVV with five leaflets (a trileaflet left and quadrileaflet right AVV). An unwedged position of the aortic valve is also common which results to an elongated left ventricular outflow tract (LVOT) with a risk of subaortic obstruction [8].

The clinical course of patients with partial AVSD is similar to that of secundum ASD with potentially earlier presentation due to development of left AVV regurgitation. The majority of complete AVSDs occur in patients with Down syndrome (>75 %); these patients have large volume loads early in life and develop congestive heart failure and pulmonary vascular disease by a few months after birth. On physical examination, partial AVSDs will have similar signs to ASDs (described above) along with a holosystolic murmur in the instance of significant left AVV regurgitation. Patients with complete AVSDs will be cyanosed and clubbed with a single first heart sound (common AVV) and signs of pulmonary hypertension (discussed later).

Common ECG findings of AVSDs include left-axis deviation and first-degree atrioventricular block due to congenital abnormalities of the conduction system [9]. The chest X-ray will reveal cardiomegaly and increased pulmonary vascular markings. Transthoracic echocardiography can establish an accurate diagnosis with identification of the anatomical defect along with the magnitude of left-to-right shunting and estimation of pulmonary artery pressure. Cardiac catheterization has a limited role in the diagnostic and preoperative evaluation of AVSDs unless there is a need to formally assess the pulmonary vascular resistance and vasoreactivity [4].

Survival without surgery is relatively short [10]. Surgery involves closing the atrial and ventricular defects and repairing the atrioventricular valves. Early surgical repair of complete AVSD is indicated in the absence of irreversible pulmonary hypertension. Late valve problems and even reoperation are relatively common, and complete atrioventricular block may occur. Recurrent left AVV regurgitation is the most common postoperative complication requiring reoperation in 5–10 % of patients [4].

Left Ventricular Outflow Tract Disorders

Left ventricular outflow tract obstruction (LVOTO) is a group of stenotic lesions that can occur at supravalvar, valvar, or subvalvar level. Irrespective of the site of obstruction, significant LVOTO imposes an increase in left ventricular afterload leading to concentric hypertrophy, dilatation, and eventual failure of the left ventricle.

Supravalvar Aortic Stenosis

This is rare and often associated with Williams syndrome (infantile hypercalcemia, mental retardation, elfin facies). The stenosis may be localized or long and diffuse and can extend into the coronary ostia with a worse prognosis in the instance of coronary involvement (Fig. 20.3). Clinical features resemble those of valvar aortic stenosis (described later), but with no ejection click. Frequently, systolic blood pressure is about 15 mmHg higher in the right than in the left arm

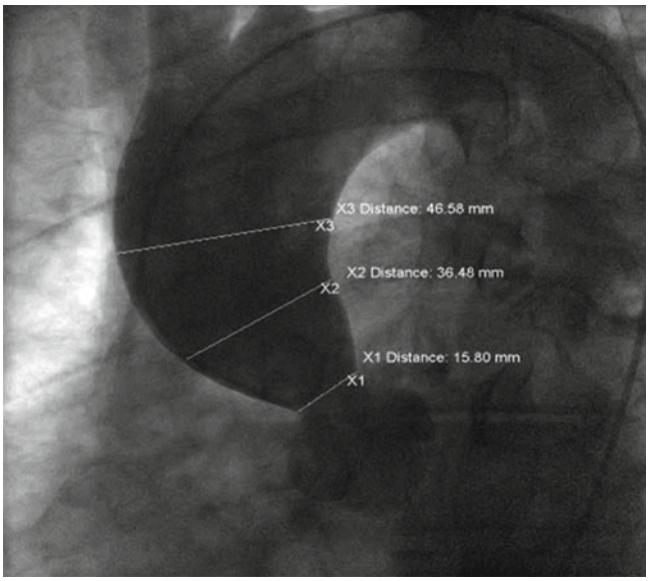

Fig. 20.3 Angiogram of a patient with Williams syndrome. Note marked native supra-aortic valve stenosis with post-stenotic aortic dilatation

because of the direction of the jet coming through the stenosis. Surgical repair is indicated in the presence of a catheter or mean echocardiographic gradient of >50 mmHg. Stenoses of other arteries may occur with Williams syndrome, including the abdominal aorta and peripheral pulmonary arteries.

Valvar Aortic Stenosis and Bicuspid Aortic Valve

Valvar aortic stenosis may occur due to a wide spectrum of congenitally malformed valves, most commonly a bicuspid aortic valve (BAV) comprising of two full-developed leaflets (true BAV) or three leaflets, two of which have been fused together (functional BAV) [11]. Bicuspid aortic valve has a prevalence of 0.5–2 % with a male/female ratio of 3:1 [12]. It is a heritable condition with an incidence of a BAV in approximately 9 % of first-degree relatives of affected individuals. Development of a BAV predisposes to several complications, including valvar dysfunction, infective endocarditis, and structural pathologies of the aortic wall, such as coarctation of the aorta and dilatation of the aortic root. Aortic dilatation in BAV is progressive and may be related to hemodynamic abnormalities or intrinsic structural defects of the aortic wall [12].

Clinical presentation depends on the severity of obstruction and may vary from none to dyspnea, angina, syncope, or chest pain. On examination, there will be an ejection systolic murmur maximal anywhere between the apex and the upper right sternal border and, in the same region, an early systolic ejection click that does not vary with respiration. Left ventricular hypertrophy may be palpable or shown on the electrocardiogram. The chest X-ray may show cardiomegaly and dilatation of the ascending aorta (common with a BAV). Echocardiography is the most effective noninvasive test for identification and quantification of the severity of aortic valve disease and aortic root dilatation. MRI and CT angiography are useful for visualization of the entire thoracic aorta, whereas cardiac catheterization may be needed before aortic valve replacement to determine the presence of coexistent coronary artery disease.

The majority of BAV patients will require valve surgery during their lifetime, predominantly due to significant aortic stenosis in early childhood, aortic regurgitation into adolescence, and calcific valve disease later in adulthood [13]. Intervention on the valve is required for severe aortic stenosis with or without symptoms, and severe aortic regurgitation associated with symptoms, or progressive left ventricular dilatation (LV end-diastolic diameter 4 SDs above normal) [4]. Prophylactic surgery for aortic dilatation is recommended when the ascending aorta diameter is >5.0 cm or when there is progressive dilatation at a rate ≥5 mm/year [4]. Balloon valvotomy is effective if there is minimal aortic incompetence and no significant calcification of the aortic valve. Choice of valve for surgical replacement depends on the patient's lifestyle and includes use of an aortic homograft, a mechanical valve, or the Ross procedure (especially for young women of reproductive age). Lifelong cardiology follow-up is recommended for all patients with aortic valve disease as progressive or recurrent AS, AR, or aortic enlargement (in the presence of a BAV) may occur.

Subaortic Stenosis

Subvalvar LVOTO may develop due to presence of a discrete membranous or fibromuscular ring just below the aortic valve or, less frequently, in relation to a tunnel-like fibromuscular band. The lesion has a male predominance (2:1) and may coexist with other lesions, especially a VSD. There may be mild to moderate aortic incompetence due to valve damage from the high-velocity jet through the stenosis. Clinically these lesions resemble valvar aortic stenosis, and echocardiography is needed to distinguish them. Balloon valvotomy is less useful than in valvar stenosis, and surgical excision may be needed. Indications for surgery include presence of a peak gradient of >50 mmHg or a mean gradient of 30 mmHg on echocardiography or if LVOTO is combined with progressive AR and left ventricular dysfunction or dilatation [4].

Coarctation of the Aorta

This is a localized narrowing of the aorta just beyond the origin of the left subclavian artery with development of an extensive collateral arterial network to supply the lower body. Associated abnormalities include intracranial berry aneurysms, anomalies of the head and neck vessels, VSD, PDA, and Turner syndrome. Multiple left heart lesions, including aortic stenosis and parachute mitral valve, may be

present, whereas a bicuspid aortic valve can be found in up to 85 % of patients. Aneurysm formation is a known clinical feature of the disease and may occur at the site of previous surgical repair or in the proximal ascending aorta [14].

Coarctation of the aorta may present acutely in the neonatal period and early childhood with heart failure or ductal shock following closure of the arterial duct. Milder lesions are frequently missed in childhood and form a large proportion of patients with CHD seen by adult cardiologists. In the latter instance, patients often come to medical attention with systemic hypertension, murmurs, and other related symptoms such as headache, epistaxis, intermittent leg claudication, cerebral vascular accidents (especially subarachnoid hemorrhage), infective endocarditis, rupture of the aorta, or premature coronary artery disease.

Clinical features of the lesion include hypertension in the upper body (blood pressure should be taken in the right arm) with decreased pulses and pressure in the legs; diastolic pressures are often similar in arms and legs, but systolic pressures differ markedly. Most have palpable collateral arteries around the scapula. There is left ventricular hypertrophy clinically and on electrocardiogram, but no T-wave inversion. A systolic or continuous murmur is heard best in the mid-back, and sometimes there is a mid-diastolic rumble at the apex even though there is no mitral stenosis.

On chest X-ray, the ascending aorta is dilated, as is the descending aorta below the constricted site of the coarctation; the hourglass pattern shows a "3" sign on plain X-ray. Confirmation by echocardiography should include demonstration of delayed acceleration of flow in the descending aorta by Doppler study. MRI and computed tomography (CT) angiography are the imaging modalities of choice for evaluation of the lesion pre- and post-repair and when urgent aortic imaging is required in the instance of hemoptysis (suspected aortic dissection or ruptured aneurysm) (Fig. 20.4). Cardiac catheterization is employed for percutaneous intervention and screening for coronary artery disease.

Repair of coarctation may be achieved surgically or percutaneously by angioplasty or stent implantation. Indications for repair include a peak-to-peak coarctation gradient ≥20 mmHg or a peak-to-peak coarctation gradient <20 mmHg in the presence of significant coarctation based on imaging with radiological evidence of significant collateral flow [4]. The choice of catheter versus surgical treatment should be determined jointly by a team of cardiologists, interventionalists, and surgeons specialized in adult CHD. Systemic hypertension, even after adequate repair, is common and should be treated medically.

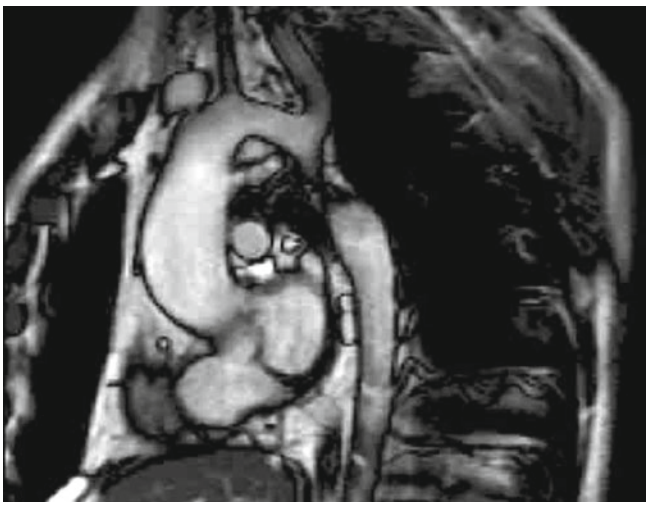

Fig. 20.4 Magnetic resonance imaging of native coarctation of the aorta. Note moderate ascending aortic dilatation secondary to presence of a bicuspid aortic valve. Also marked dilatation of left subclavian artery due to significant collateral blood flow (Image courtesy of PJ Kilner)

Patent Arterial Duct

Patent arterial duct (PDA) is a communication between the proximal left pulmonary artery and the descending aorta distally to the left subclavian artery. This structure is vital in fetal life but may persist postpartum with hemodynamic consequences corresponding to the size of the PDA; small communications can present with a murmur in the absence of symptoms, whereas moderate-large PDAs can lead to left-to-right shunting with excessive pulmonary flow and left heart volume overload.

On clinical examination, there is a continuous "machinery" or "train in a tunnel" murmur heard best below the left clavicle. The size of the PDA and the amount of shunting are diagnosed not from the murmur but from associated features: a big duct has a loud second heart sound, bounding pulses, and left ventricular dilation and hypertrophy on clinical, radiological, electrocardiographic, and echocardiographic examination. Large PDAs can lead to development of Eisenmenger syndrome with absence of murmurs and characteristically differential cyanosis (cyanosis and clubbing of toes but not fingers).

Indications for PDA closure include significant left-to-right shunting and left heart enlargement or prior endarteritis [4]. Closure of the communication is contraindicated in the presence of pulmonary vascular disease. Percutaneous closure at cardiac catheterization by coils or other devices is the preferred method because of its high success and few complications. Surgical closure is reserved for large or distorted defects which are unsuitable for transcatheter closure. Life expectancy after closure is essentially normal with worse prognosis in the instance of pulmonary vascular disease.

Tetralogy of Fallot and Right Ventricular Outflow Tract Disorders

Tetralogy of Fallot (TOF) is the commonest form of cyanotic heart disease, comprised from four features: a large VSD, an

Table 20.5 Late complications following radical repair of Tetralogy of Fallot (TOF)

Late complications after TOF repair
Residual pulmonary regurgitation
Residual RVOT obstruction
Branch pulmonary artery stenosis/hypoplasia
RV dysfunction/RVOT aneurysm
Residual VSD
AR ± aortic root dilatation
LV dysfunction
Endocarditis
Supraventricular arrythmia
Ventricular tachycardia/sudden death
Heart block (uncommon)

overriding aorta, right ventricular outflow tract obstruction from infundibular and/or valvar PS, and right ventricular hypertrophy. Pulmonary artery hypoplasia or stenosis may also be present. The lesion has a wide degree of morphological variation, from mild PS to pulmonary atresia and from minimal degree of aortic override to double-outlet right ventricle (>50 % coming from the RV). Associated cardiac abnormalities include right aortic arch (~25 %), ASD, AVSD, and coronary anomalies, with the left anterior descending coronary artery arising from the right coronary artery and crossing the RV outflow in approximately 3–7 % of patients [4]. Up to 35 % of patients with TOF have a 22q11 deletion; genetic screening should be offered in these patients due to high risk of recurrence of CHD in their offsprings [2].

The clinical presentation of TOF depends on the degree of right ventricular outflow tract (RVOT) obstruction; significant obstruction leads to right-to-left shunting with cyanosis, whereas mild obstruction, the so-called pink tetralogy, may present with dyspnea and minimal cyanosis. The majority of adult patients will have undergone radical repair in childhood and present with symptoms related to late complications (discussed below, see Table 20.5), such as palpitations, syncope, or heart failure. On physical examination, repaired TOF may reveal a right ventricular lift with an ejection systolic murmur of residual RVOT obstruction. A diastolic murmur of pulmonary regurgitation or aortic regurgitation (due to aortic root dilatation) may also be heard. The pulmonary component of the second sound is often not audible.

The electrocardiogram commonly reveals right bundle branch block (RBBB) in patients with previous surgery. The length of QRS reflects the degree of right ventricular dilatation and, when prolonged, is an adverse prognostic marker for sustained ventricular tachycardia and sudden cardiac death [15]. The chest X-ray shows a right-sided aortic arch in ~25 % of patients. Dilatation of the ascending aorta and cardiomegaly from right ventricular enlargement may also be seen. Echocardiography is used following repair to assess the presence of residual pulmonary stenosis or regurgitation, residual VSD, biventricular size and function, the size of the aortic root, and the degree of aortic regurgitation. Magnetic resonance imaging can accurately assess right ventricular size and volumes and with late gadolinium enhancement can identify the presence of ventricular fibrosis, a marker of adverse outcome [16]. Cardiac catheterization is infrequently used but may be used for assessment pulmonary blood flow and resistance and identification of anomalies of the coronary arteries or residual septal defects [4].

Definitive surgical treatment of TOF involves closure of the VSD with a patch and relief of the RVOT obstruction with resection of the hypertrophied infundibular muscle and insertion of an RVOT or transannular patch; a preliminary palliative systemic artery-pulmonary shunt is occasionally needed. Late complications of radical repair are included in Table 20.4; in the instance of transannular patch repair technique, significant pulmonary regurgitation is almost always encountered. Indications for pulmonary valve replacement in the latter instance include the presence of severe pulmonary regurgitation with symptoms or decreased exercise tolerance, RV enlargement/dysfunction, moderate or severe tricuspid regurgitation, or development of clinical arrhythmias (atrial or ventricular). Residual RVOT obstruction can occur at subvalvar, valvar level, or more distally with the following indications for reintervention: peak echocardiography gradient >50 mmHg, RV/LV pressure ratio >7, residual VSD with Qp:Qs > 1.5:1, and severe AR with symptoms or LV enlargement/dysfunction [4]. The proper risk stratification for major cardiac arrhythmias (atrial flutter/fibrillation or sustained VT) remains a matter of debate; high-risk patients for sustained VT and/or sudden death with right ventricular dilatation and QRS duration ≥180 ms will require electrophysiological assessment and are increasingly managed with implantable cardioverter defibrillators [4].

Ebstein's Anomaly of the Tricuspid Valve

Ebstein's anomaly of the tricuspid valve (TV) is defined as an apical displacement of the septal and posterolateral leaflets away from the atrioventricular junction into the right ventricle resulting to "atrialization" of the RV inflow with a smaller functional RV and an enlarged right atrium. The malformed TV can lead to varying degrees of tricuspid regurgitation (TR) exaggerating right heart enlargement. Associated lesions include ASD or patent foramen ovale (up to 94 % of patients) and Wolf-Parkinson-White syndrome, often with multiple accessory atrioventricular pathways [17]. Ebstein's anomaly can also be part of other complex lesions such as congenitally corrected transposition of the great arteries, pulmonary stenosis/atresia, BAV, coarctation, or VSD [17].

Clinical presentation of the lesion depends on its severity and may vary from intrauterine death to manifestation of the disease in late adulthood. Severe Ebstein's anomaly will present in infancy with congestive heart failure and failure to thrive. Adult patients may remain asymptomatic or present with exercise intolerance, palpitations, cyanosis, or

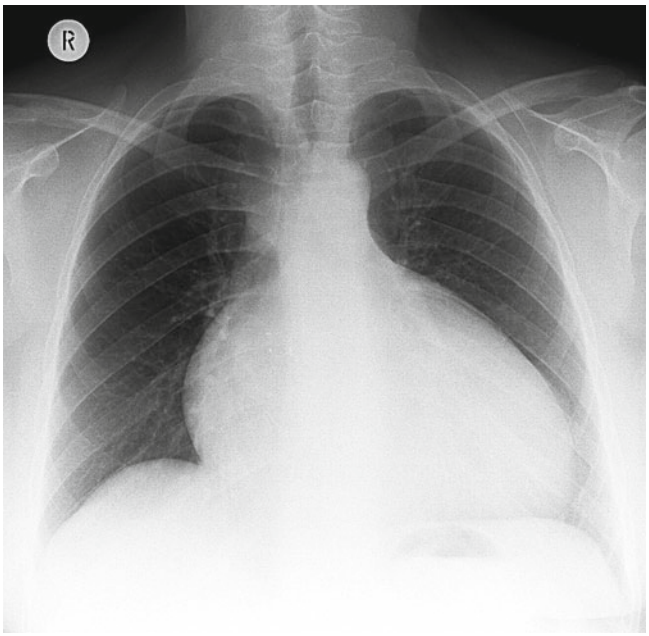

Fig. 20.5 Chest X-ray of a patient with Ebstein's anomaly of the tricuspid valve. Note marked cardiomegaly with globular shape of the cardiac silhouette, small aortic knuckle, and reduced pulmonary vascular markings

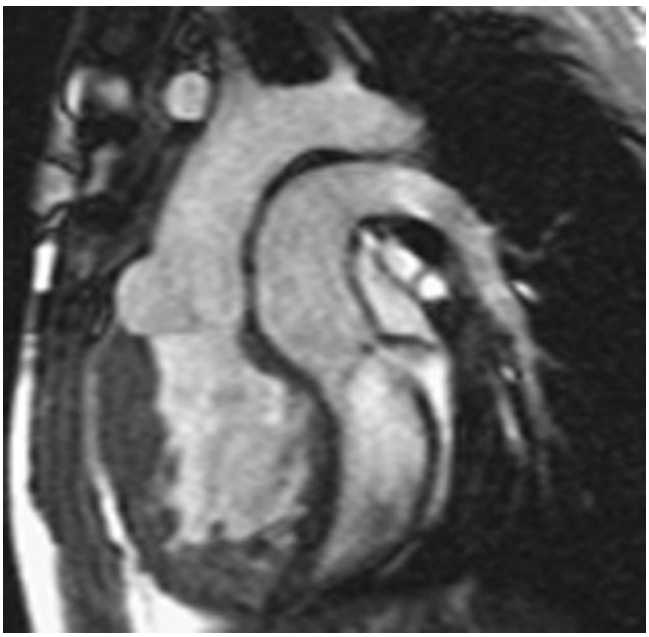

Fig. 20.6 Magnetic resonance imaging of complete transposition of the great arteries. Note anterior aorta arising from a hypertrophied systemic right ventricle and posterior pulmonary artery arising from the left ventricle

paradoxical emboli due to a right-to-left shunt present at atrial level. Physical examination will reveal cyanosis and clubbing in patients with right-to-left shunting. Late signs of Ebstein's anomaly include elevated JVP, hepatomegaly, ascites, and peripheral edema. On auscultation, there will be a widely split S1 and S2 and a holosystolic murmur of TR best heard at the lower left sternal border.

Typical findings of the lesion on electrocardiogram include low QRS voltage, tall P-waves reflective of right atrial enlargement, prolonged PR interval, RBBB, and a delta-wave secondary to an accessory pathway. Supraventricular tachyarrhythmias and atrial fibrillation are frequent in adult patients. The chest X-ray will reveal cardiomegaly due to right heart enlargement with a globular shape of the cardiac silhouette and a small aortic knuckle (Fig. 20.5). Echocardiography can confirm the diagnosis via visualization of apical displacement of the septal leaflet of the TV by >8 mm/m^2 [17].

Surgical procedures for Ebstein's anomaly may involve repair or replacement of the TV, plication of the atrialized portion of the right ventricle, and procedures to ablate arrhythmogenic foci. Indications for intervention include presence of symptoms or deteriorating exercise capacity, significant cyanosis, paradoxical embolism, and progressive right heart enlargement with impaired RV systolic function [4]. Anticoagulation with warfarin is recommended for patients with a history of paradoxical embolism or atrial fibrillation and catheter ablation for treatment of tachyarrhythmias secondary to accessory pathways.

Transposition of the Great Arteries

There are two types of transposition of the great arteries (TGA), complete TGA and congenitally corrected TGA.

Complete Transposition

In complete TGA, there is atrioventricular concordance and ventriculoarterial discordance; in other words, the right atrium connects to the morphological right ventricle which gives rise to the aorta and the left atrium connects to the morphological left ventricle which gives rise to the pulmonary artery (Fig. 20.6). As the systemic and pulmonary circulations run in parallel, complete TGA is incompatible with life unless there is a communication between the two circuits (ASD, VSD, PDA). The lesion is often associated with VSD (~40–45 %), LVOT obstruction (~25 %), and aortic coarctation (~5 %) [18].

Infants with complete TGA become progressively cyanotic as the arterial duct closes and require early surgical intervention. Mortality without intervention reaches 90 % by the first year of life; a few unoperated patients with large VSDs may survive into adulthood and develop Eisenmenger syndrome. Clinical presentation of adult operated patients is related to the type of surgical technique (see below).

Atrial Switch Procedure

This procedure involves redirection of the blood at the atrial level with use of a baffle made of synthetic material or pericardium (Mustard procedure) or atrial flaps (Senning procedure),

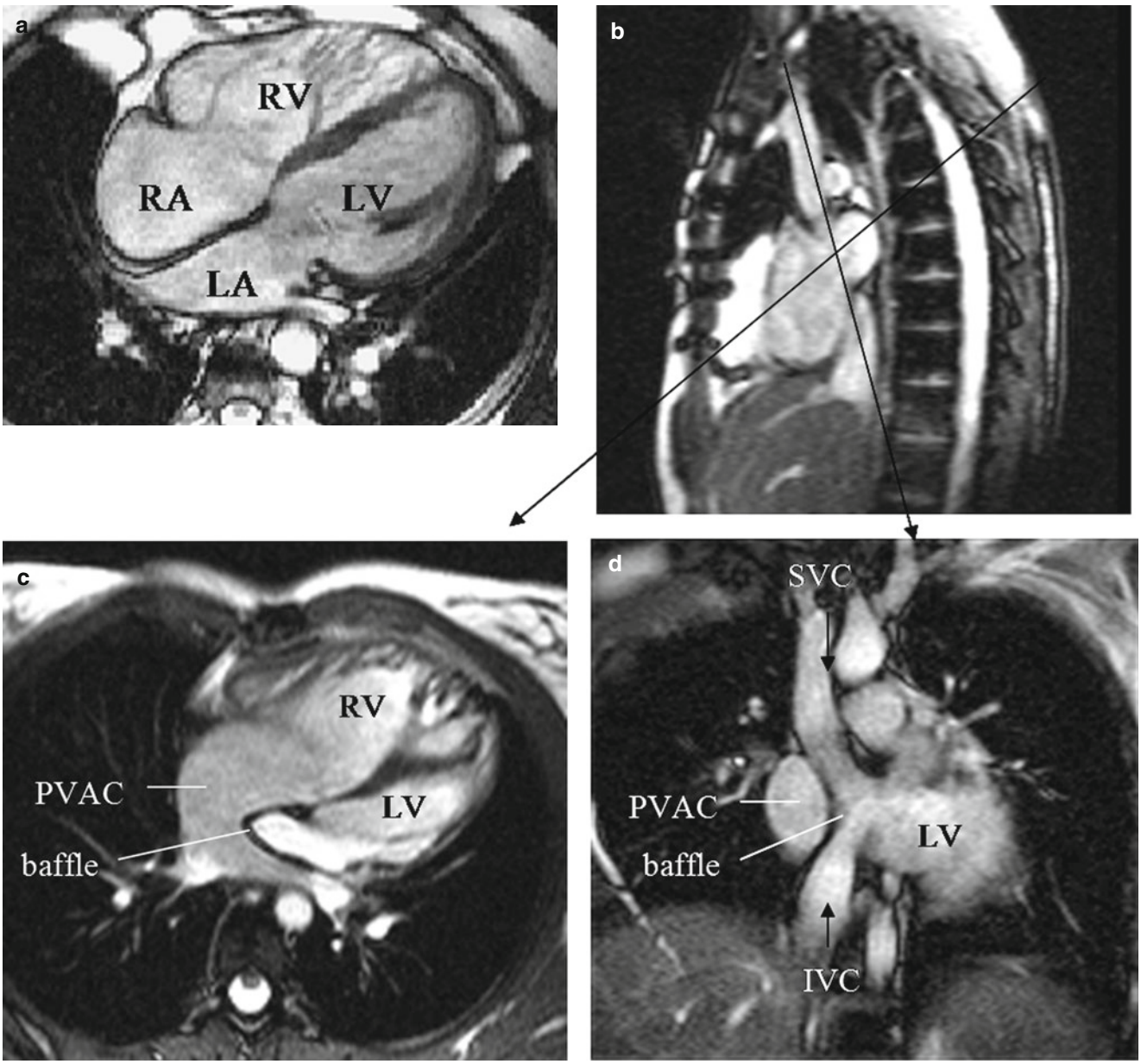

Fig. 20.7 Atrial switch procedure (Mustard) for complete transposition of the great arteries. (**a**) Four-chamber image showing usual atrioventricular connections in a patient with repaired Tetralogy of Fallot. (**b**) A sagittal image though the reconstructed atrial compartments in a patient after Mustard operation. The *black arrows* show the location of: (**c**) an oblique transaxial slice aligned with the pulmonary venous atrial compartment (*PVAC*) and (**d**) an oblique coronal image aligned with superior and inferior vena cava (*SVC* and *IVC*), redirected by the baffle to the left ventricle (*LV*). *LA* left atrium, *RA* right atrium, *RV* right ventricle (Images courtesy of SV Babu-Narayan & PJ Kilner)

achieving a physiological-type repair. The systemic venous return is directed to the left ventricle and thence to the pulmonary artery, and the pulmonary venous return to the right ventricle and thence to the aorta (Fig. 20.7). Common complications of atrial redirection procedures include progressive dysfunction of the right ventricle (which supports the systemic circulation) and high arrhythmic burden due to extensive atrial suture lines. Atrial flutter and fibrillation develops in 14 % of patients and sinus node dysfunction in 48 % [19, 20]. Progressive tricuspid regurgitation is frequent and may require surgical intervention if moderate to severe. Other complications include superior or inferior vena cava pathway obstruction and atrial baffle leak, both of which may require surgical intervention if not amenable to percutaneous repair.

Arterial Switch Procedure

This is an anatomical type repair with redirection of blood flow at the level of the great arteries by switching the

pulmonary artery and aorta, including the coronaries, to their normal position. Arterial switch offers the advantage of a systemic left ventricle. The long-term sequelae of the procedure include development of neoaortic regurgitation, progressive dilatation of the neoaortic root, myocardial ischemia due to stenosis of the coronary ostia, and RVOT obstruction, which is the commonest cause for reoperation.

Rastelli Procedure

This is a procedure used for patients with TGA, pulmonary/subpulmonary stenosis, and a large VSD. Blood flow is redirected at the ventricular level with an intracardiac baffle which tunnels the LV to the aorta via the VSD and with an extracardiac conduit which is placed between the RV and the pulmonary artery. Similarly to arterial switch, this procedure has the advantage of a systemic left ventricle. However, it is not without late complications such as conduit stenosis requiring reoperation and atrial and ventricular arrhythmias.

Congenitally Corrected Transposition

In congenitally corrected TGA (ccTGA), the atrioventricular and ventriculoarterial connections are discordant; the right atrium is connected to the morphological LV and thence to the pulmonary artery and the left atrium is connected to the morphological RV and thence to the aorta. Therefore, in ccTGA, "physiological" correction of the circulation occurs but with presence of a systemic right ventricle. Up to 98 % of patients have associated malformations such as VSD, pulmonary or subpulmonary stenosis, "Ebstein-like" anomalies of the systemic atrioventricular valve, and complete atrioventricular block [21].

Adult patients with isolated ccTGA (~1 %) may remain undiagnosed until late adulthood with usual manifestation of systemic right ventricular failure by the fourth to fifth decade of life and palpitations related to atrial arrhythmias by the sixth decade. Patients with a VSD and pulmonary stenosis will present earlier with cyanosis, congestive heart failure, palpitations, or syncope (due to complete atrioventricular block). On physical examination, there will be a characteristically loud aortic second sound heard best at the upper left sternal border due to the abnormal aortic position (anterior and to the left). Similarly, the abnormal position of the great vessels produces a characteristic straight segment at the left upper heart border on chest X-ray which reflects the ascending aorta. The electrocardiogram can show complete atrioventricular block and prominent Q-waves in the right chest leads, leading often to the mistaken diagnosis of anterior myocardial infarction. Echocardiography can detect the presence of double discordance and associated malformations, whereas MRI can provide an accurate assessment of the systemic right ventricle.

Double-switch procedures, combining an atrial switch with an arterial switch, aim at restoration of the left ventricle in the systemic position and have been performed in infants and young children with encouraging early outcomes [4]. Adult patients usually undergo surgery for significant left atrioventricular valve regurgitation, ideally before deterioration of systemic right ventricular function (EF <45 %). The status of atrioventricular conduction must be monitored regularly as there is a 2 % annual risk of spontaneous heart block [4].

Univentricular Physiology and Fontan Procedure

The term "univentricular heart" describes a variety of rare complex cardiac malformations in which there is a single functional ventricular cavity and biventricular repair is not feasible. Common types of univentricular defects include tricuspid and mitral atresia, double inlet left ventricle, and hypoplastic left heart syndrome. Clinical presentation occurs in infancy with cyanosis due to mixing of systemic and pulmonary blood in a single ventricle. Depending on the underlying anatomy, increased pulmonary blood flow will lead to mild cyanosis and congestive heart failure, whereas decreased pulmonary blood flow will result in profound hypoxemia. Survival without treatment is poor and therapeutic options can only be palliative [22].

A staged approach is taken to achieve a Fontan-type circulation. Initially, palliative procedures are performed in the neonatal period to control pulmonary blood flow, involving either a pulmonary artery band to decrease flow or a systemic to pulmonary artery shunt to increase flow. During the second stage (~4–12 months of age) a bidirectional Glenn shunt is created consisting of an end-to-side anastomosis of the superior vena cava to the top of the right pulmonary artery. The classic Fontan operation, performed in the final stage (18 months to 4 years of age or later), consists of an atriopulmonary connection with anastomosis of the right atrium to the pulmonary artery. However, the current technique of choice is total cavopulmonary connection (TCPC) which can be performed as a single or two-staged procedure and combines a bidirectional Glenn with connection of the inferior vena cava to the pulmonary artery via an intracardiac or extracardiac conduit (Fig. 20.8). A fenestration between the Fontan circuit and the pulmonary atrium is frequently created to prevent excessive elevation of right atrial pressure and improve systemic cardiac output in exchange for a degree of hypoxemia at the immediate postoperative period. The fenestration can be closed at a later stage with a catheter approach.

Clinical presentation of adult patients with Fontan circulation relates to the long-term complications of the procedure, as discussed below. On physical examination there may be cyanosis and clubbing due to presence of a fenestration or collateral vessels. Jugular venous pressure is often elevated. Auscultation will not reveal murmurs but a single second

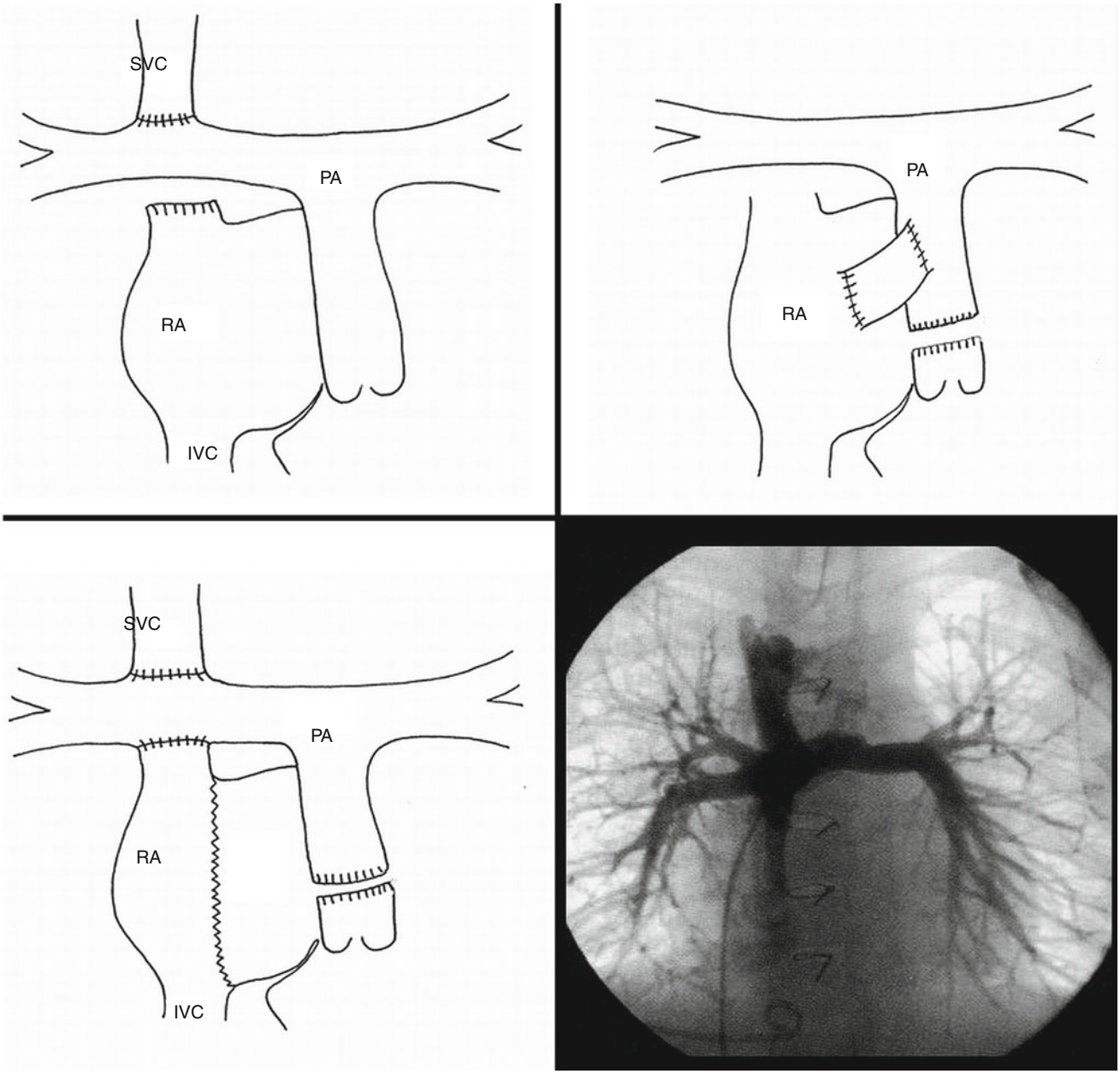

Fig. 20.8 Types of venous anastomoses and Fontan procedures. *Right lower panel* shows an angiogram of a patient with tricuspid atresia and total cavopulmonary connection (lateral tunnel). *IVC* inferior vena cava, *PA* pulmonary artery, *RA* right atrium, *SVC* superior vena cava

heart sound may be heard. The electrocardiogram may reveal intra-atrial reentry tachycardia, sinus node dysfunction, or axis deviation (type depending on the dominant ventricle). The chest X-ray and echocardiographic findings depend on the underlying anatomy. Cardiac MRI is useful for assessment of blood flow in the Fontan circuit.

The modified Fontan procedure with use of intracardiac or extracardiac conduit seems to result in better outcomes and improved survival compared to earlier versions of the technique [23]. However, the complexity of the underlying lesions along with the chronic passive pulmonary blood flow and low cardiac output leads to a number of late complications. Supraventricular tachycardias are an important cause of late morbidity and mortality and should be treated promptly and may require radio-frequency ablation [24]. Underlying hemodynamic lesions precipitating tachyarrhythmias should be excluded [4]. Sinus node dysfunction is common and may require atrial pacing if the atrioventricular node is intact. Intracardiac thrombus formation may occur due to sluggish blood flow in an enlarged right atrium or tachyarrhythmias and will require anticoagulation. Other complications include progressive atrioventricular valve

regurgitation, hepatic congestion, systemic ventricular dysfunction, and obstruction or leaks in the Fontan circuit. Protein losing enteropathy is an additional serious complication of the Fontan physiology with severe protein loss into the intestine due to high mesenteric venous pressure. Clinical manifestations include generalized edema, ascites, pleural effusions, and diarrhea. Reoperation should be considered in patients with failing Fontan circulation and heart transplantation may be an option in the instance of severe ventricular dysfunction or refractory protein-losing enteropathy [4].

Eisenmenger Syndrome

Eisenmenger syndrome is a pathophysiologic condition consisting of PAH with a reversed (right-to-left) central shunt and cyanosis. Patients with Eisenmenger physiology have an uncorrected large communication between the systemic and pulmonary circulations at the atrial, ventricular, or arterial level resulting to high pulmonary blood flow and progressive pulmonary vascular disease. A number of lesions can cause Eisenmenger syndrome, the commonest of which are AVSD, VSD, PDA, and ASD [4]. With large shunts at arterial or ventricular level, the syndrome is frequently established during the first 2 years of life, whereas with shunts at atrial level, pulmonary vascular disease develops later during adult life.

Children with Eisenmenger syndrome may be asymptomatic or present with mild exertional dyspnea. Cyanosis and impaired exercise capacity gradually become more prominent as pulmonary vascular resistance increases and bidirectional shunting develops. Adults with Eisenmenger syndrome may remain clinically stable due to chronic adaptation to their limited exercise capacity with lower activity levels. However, they may also present with symptoms related to complications of the syndrome, such as palpitations, chest pain, edema, syncope, or hemoptysis (discussed later). On clinical examination, there will be central cyanosis and clubbing. Signs of elevated pulmonary vascular pressure include right ventricular heave, loud P2, and occasionally a pulmonary ejection click. Murmurs of pulmonary or tricuspid regurgitation may also be present.

Pulse oximetry should be assessed at least annually in patients with Eisenmenger syndrome [4]. The electrocardiogram may reveal right-axis deviation with signs of right ventricular hypertrophy and right atrial enlargement. The chest X-ray often shows augmented proximal pulmonary arteries andcardiomegaly(rightheartenlargement).Echocardiography will identify the underlying lesion and site of the shunt and estimate pulmonary arterial pressure. MRI is useful for establishment of the diagnosis, while CT can be used to assess the lung parenchyma, aneurysms of the proximal pulmonary arteries, in situ thrombosis, and sites of pulmonary hemorrhage. Cardiac catheterization will establish the diagnosis of Eisenmenger syndrome with potential vasodilator testing or anatomic intervention. Routine laboratory testing is also necessary (see complications) and should include assessment of full blood count, liver function tests, urea, creatinine, electrolytes, uric acid, and iron status (transferrin saturation and ferritin).

Complications of the Eisenmenger syndrome and their management are outlined in Table 20.6. The general care of patients with Eisenmenger syndrome consists of preservation of fluid balance, management of secondary erythrocytosis, appropriate iron supplementation, and abolition of routine phlebotomies. Anticoagulation may be indicated, especially for patients with documented pulmonary thrombosis and embolic phenomena, in the absence of prior severe hemoptysis. Targeted pharmacological therapies have recently become available for patients with PAH and are recommended for symptomatic patients with Eisenmenger syndrome (NYHA functional class ≥ III) [25]. Reparative surgery is indicated only in patients with evidence of pulmonary arterial reactivity and/or at least 1.5:1 left-to-right shunting. Survival of patients with Eisenmenger syndrome has been reported to be 55 % to the age of 50 years, although these data are highly selective as they refer to patients who have survived to adulthood [26].

Issues in Adults with Congenital Heart Disease

Numerous issues should be considered when caring for adult patients with CHD, many of which are unique to this population.

Exercise Intolerance

Exercise intolerance is a common cause of suboptimal quality of life and a strong predictor of outcome in CHD [27]. It may result from a variety of cardiac mechanisms, such as persistent or residual defects, coronary anomalies, and arrhythmias or extracardiac factors including pulmonary parenchymal and vascular disease, cyanosis, and pulmonary arterial hypertension. Subjective evaluation of exercise intolerance using the NYHA classification appears to underestimate the severity of functional impairment in adult CHD [27]. Cardiopulmonary exercise testing is ideally suited for objective evaluation of the cardiovascular, respiratory, and muscular systems and is now becoming part of the routine clinical assessment of adult CHD patients [27]. Echocardiography and MRI are a fundamental part of the long-term follow-up of adult patients, with the latter being particularly suited for assessment of right ventricular function. The primary aim when managing an adult CHD patient with exercise intolerance is to identify and treat residual

Table 20.6 Complications of Eisenmenger syndrome

Complications	Management
Cardiac:	Heart failure: medical treatment (give diuretics with care to avoid dehydration)
Progressive heart failure	Arrhythmias: consider anticoagulation (atrial flutter/fibrillation), give antiarrhythmics (amiodarone), unknown role of implantable defibrillators in this setting
Arrhythmias (supraventricular or ventricular)	Endocarditis: meticulous prophylaxis
Angina	Paradoxical embolism: use air filters on IV lines/infusion pumps with bubble detector
Syncope	Angina: markedly enlarged pulmonary artery aneurysms may rarely cause chest pain by compression of the left main coronary artery
Endocarditis	
Paradoxical embolism	
Progressive pulmonary artery enlargement	
Hematologic:	Hyperviscosity: routine phlebotomy is contraindicated and restricted to patients with hemoglobin >20 g/dL and hematocrit >65 %, associated with severe hyperviscosity symptoms, in the absence of dehydration and iron deficiency
Erythrocytosis	Anemia and dehydration should be avoided and treated promptly
Hyperviscosity syndrome	Iron deficiency: treat with iron supplementation
Iron deficiency	
Neutropenia and thrombocytopenia	
Bleeding disorder	
Pulmonary:	Hemoptysis: chest X-ray and CT scan to determine extent of hemorrhage; embolization of culprit vessels
Hemoptysis	Thrombosis: consider anticoagulation if recurrent events, in the absence of dehydration and iron deficiency
Intrapulmonary bleeding	
Pulmonary artery thrombosis	
Central nervous system:	Stroke: inappropriate repeated phlebotomies increase risk
Stroke/TIA	Cerebral abscess: urgent contrast enhanced CT and blood cultures
Cerebral abscess	
Renal:	Avoid iatrogenic renal dysfunction
Proteinuria and hematuria	
Mildly elevated creatinine	
Progressive renal failure	
Metabolic:	Treat symptomatic hyperuricemia
Hyperuricemia and gout	
Hyperbilirubinemia and gallstones	
Nephrolithiasis	

hemodynamic lesions, especially those potentially amenable to surgical or percutaneous repair.

Arrhythmias

Atrial arrhythmias become more frequent with age, particularly in patients with atrial dilatation (e.g., previous ASD, Ebstein's anomaly) and those with history of surgery involving extensive atrial incisions (e.g., Mustard procedure). Ventricular arrhythmias can also occur in patients with previous ventriculotomy, such as repaired TOF, due to macro-reentrant circuits [28]. Sinus node dysfunction can be present at birth due to congenital abnormalities (e.g., sinus venosus ASD) or following cardiac surgery (e.g., Mustard, Senning, or Fontan procedures) (Fig. 20.9). Atrioventricular block can occur spontaneously in congenital defects with conduction system abnormalities (e.g., AVSD, ccTGA) or postoperatively.

Clinical manifestation of arrhythmias in patients with CHD ranges from absence of symptoms to rapid deterioration or sudden cardiac death. The onset of arrhythmia often reflects hemodynamic abnormalities which require prompt identification and correction with catheter ablation or surgical interventions. Patients with atrial tachycardia will often require long-term anticoagulation to prevent thrombus formation. Antiarrhythmic agents such as amiodarone and beta blockers are commonly used. Pacing for bradyarrhythmias can prove challenging in adults with CHD due to limited access to the heart (e.g., congenital venous anomalies, surgical conduits and baffles). Implantable cardioverter defibrillators (ICD) are increasingly implanted in CHD; indications include patients who survived a cardiac arrest, those with spontaneous ventricular tachycardia (VT) which could not be ablated, and in patients with inducible VT, concomitant unexplained syncope, and impaired right or left ventricular function [29].

Pregnancy

Preconceptual counseling should start in adolescence with timely pre-pregnancy assessment of cardiac status and close follow-up during pregnancy and postpartum. The risk of maternal death is less than 1 % for the majority of parturients with CHD. However, certain conditions are associated with significantly higher risk, such as PAH of any etiology, poor systemic ventricular function, and severe left heart obstructive lesions. Effective contraception is imperative in the latter cases although some women will decide to become pregnant

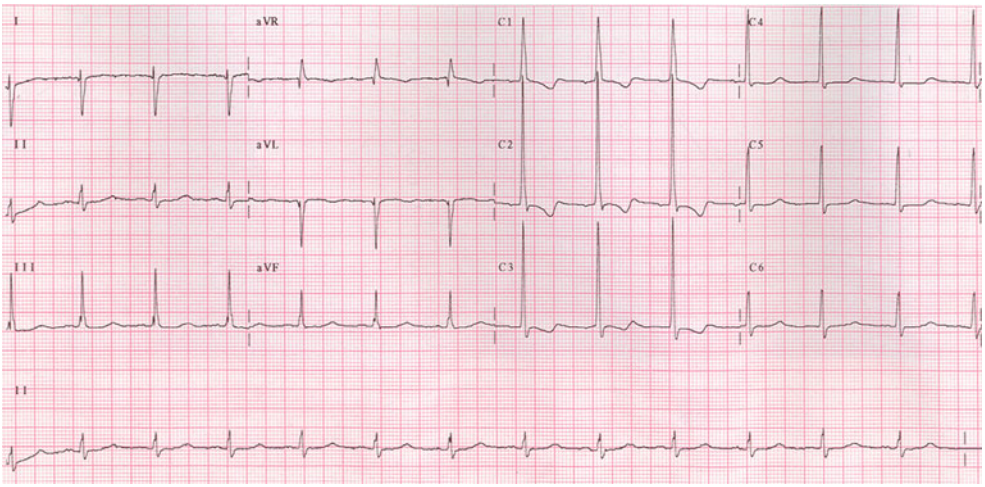

Fig. 20.9 Electrocardiogram of a patient with Mustard procedure for complete transposition of the great arteries. Sinus rhythm with low-amplitude P-waves. Maintenance of sinus rhythm is relatively uncommon in Mustard patients; common rhythms include junctional rhythm and intra-atrial reentrant tachycardia. Note typical findings of marked right-axis deviation and tall dominant R-waves in the anteroseptal chest leads, with T-wave inversion in V1 and V2, reflecting hypertrophy of the systemic right ventricle

regardless of the risks to their health. Minimization of risk by optimization of cardiac function before pregnancy is, thus, essential.

Patients with left-sided obstructive lesions should be identified and offered balloon valvotomy or surgery before pregnancy. Women with lesions associated with aortic root dilatation, such as BAV and aortic coarctation, require careful pregestation assessment of their aortic dimensions and, potentially, elective aortic root replacement. Likewise, women with repaired TOF, pulmonary regurgitation and right ventricular enlargement may be considered for pulmonary valve replacement before pregnancy [30]. Arrhythmia is a common complication during pregnancy; DC cardioversion is safe, whereas antiarrhythmic drug therapy should be used with care [31]. Anticoagulation is an additional issue, especially in parturients with mechanical valves. Low molecular weight heparin can be used during the first trimester, substituted by warfarin during the second and early third trimesters. Warfarin is again replaced by unfractioned heparin at approximately 35 weeks of gestation. Common indications for cardiac intervention during pregnancy include stenotic valve disease, acute dissection of the aorta, pacemaker insertion, and insertion of an inferior vena cava filter.

References

1. Hoffman JI, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol. 2002;39(12):1890–900.
2. Pierpont ME, Basson CT, Benson Jr DW, et al. Genetic basis for congenital heart defects: current knowledge: a scientific statement from the American Heart Association Congenital Cardiac Defects Committee, Council on Cardiovascular Disease in the Young: endorsed by the American Academy of Pediatrics. Circulation. 2007;115(23):3015–38.
3. Gatzoulis MA, Hechter S, Siu SC, Webb GD. Outpatient clinics for adults with congenital heart disease: increasing workload and evolving patterns of referral. Heart. 1999;81(1):57–61.
4. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease). Developed in Collaboration With the American Society of Echocardiography, Heart Rhythm Society, International Society for Adult Congenital Heart Disease, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2008;52(23):e143–263.
5. Ho SY. Cardiac morphology and nomenclature. In: Gatzoulis MA, Webb GD, Daubeney PEF, editors. Diagnosis and management of adult congenital heart disease. 2nd ed. Philadelphia: WB Saunders; 2011. p. 5–13.
6. Gatzoulis MA, Freeman MA, Siu SC, Webb GD, Harris L. Atrial arrhythmia after surgical closure of atrial septal defects in adults. N Engl J Med. 1999;340(11):839–46.
7. Neumayer U, Stone S, Somerville J. Small ventricular septal defects in adults. Eur Heart J. 1998;19(10):1573–82.
8. Suzuki K, Ho SY, Anderson RH, et al. Morphometric analysis of atrioventricular septal defect with common valve orifice. J Am Coll Cardiol. 1998;31(1):217–23.
9. Feldt RH, DuShane JW, Titus JL. The atrioventricular conduction system in persistent common atrioventricular canal defect: correlations with electrocardiogram. Circulation. 1970;42(3):437–44.
10. Berger TJ, Blackstone EH, Kirklin JW, Bargeron Jr LM, Hazelrig JB, Turner Jr ME. Survival and probability of cure without and with operation in complete atrioventricular canal. Ann Thorac Surg. 1979;27(2):104–11.
11. Roberts WC, Ko JM. Frequency by decades of unicuspid, bicuspid, and tricuspid aortic valves in adults having isolated aortic valve replacement for aortic stenosis, with or without associated aortic regurgitation. Circulation. 2005;111(7):920–5.
12. Prapa M, Ho SY. Risk stratification in bicuspid aortic valve disease: still more work to do. Eur J Cardiothorac Surg. 2012;41(2):327–8.
13. Lewin MB, Otto CM. The bicuspid aortic valve: adverse outcomes from infancy to old age. Circulation. 2005;111(7):832–4.
14. Oliver JM, Gallego P, Gonzalez A, Aroca A, Bret M, Mesa JM. Risk factors for aortic complications in adults with coarctation of the aorta. J Am Coll Cardiol. 2004;44(8):1641–7.
15. Gatzoulis MA, Till JA, Somerville J, Redington AN. Mechanoelectrical interaction in tetralogy of Fallot. QRS prolongation relates to right ventricular size and predicts malignant ventricular arrhythmias and sudden death. Circulation. 1995;92(2):231–7.
16. Babu-Narayan SV, Kilner PJ, Li W, et al. Ventricular fibrosis suggested by cardiovascular magnetic resonance in adults with repaired tetralogy of fallot and its relationship to adverse markers of clinical outcome. Circulation. 2006;113(3):405–13.

17. Attenhofer Jost CH, Connolly HM, Dearani JA, Edwards WD, Danielson GK. Ebstein's anomaly. Circulation. 2007;115(2):277–85.
18. Hornung TS, Derrick GP, Deanfield JE, Redington AN. Transposition complexes in the adult: a changing perspective. Cardiol Clin. 2002;20(3):405–20.
19. Gelatt M, Hamilton RM, McCrindle BW, et al. Arrhythmia and mortality after the Mustard procedure: a 30-year single-center experience. J Am Coll Cardiol. 1997;29(1):194–201.
20. Dos L, Teruel L, Ferreira IJ, et al. Late outcome of Senning and Mustard procedures for correction of transposition of the great arteries. Heart. 2005;91(5):652–6.
21. Warnes CA. Transposition of the great arteries. Circulation. 2006;114(24):2699–709.
22. Ammash NM, Warnes CA. Survival into adulthood of patients with unoperated single ventricle. Am J Cardiol. 1996;77(7):542–4.
23. d'Udekem Y, Iyengar AJ, Cochrane AD, et al. The Fontan procedure: contemporary techniques have improved long-term outcomes. Circulation. 2007;116(11 Suppl):I157–64.
24. Gatzoulis MA, Munk MD, Williams WG, Webb GD. Definitive palliation with cavopulmonary or aortopulmonary shunts for adults with single ventricle physiology. Heart. 2000;83(1):51–7.
25. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. J Am Coll Cardiol. 2009;53(17):1573–619.
26. Cantor WJ, Harrison DA, Moussadji JS, et al. Determinants of survival and length of survival in adults with Eisenmenger syndrome. Am J Cardiol. 1999;84(6):677–81.
27. Dimopoulos K, Diller GP, Piepoli MF, Gatzoulis MA. Exercise intolerance in adults with congenital heart disease. Cardiol Clin. 2006;24(4):641–60, vii.
28. Horton RP, Canby RC, Kessler DJ, et al. Ablation of ventricular tachycardia associated with tetralogy of Fallot: demonstration of bidirectional block. J Cardiovasc Electrophysiol. 1997;8(4):432–5.
29. Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). J Am Coll Cardiol. 2006;48(5):e247–346.
30. Khairy P, Ouyang DW, Fernandes SM, Lee-Parritz A, Economy KE, Landzberg MJ. Pregnancy outcomes in women with congenital heart disease. Circulation. 2006;113(4):517–24.
31. Joglar JA, Page RL. Antiarrhythmic drugs in pregnancy. Curr Opin Cardiol. 2001;16(1):40–5.

Recommended Reading

Gatzoulis MA, Webb GD, Broberg C, Uemura H, editors. Cases in adult congenital heart disease. Philadelphia: Churchill Livingstone; 2010.

Gatzoulis MA, Webb GD, Daubeney PEF, editors. Diagnosis and management of adult congenital heart disease. 2nd ed. Philadelphia: WB Saunders; 2011.

Steer PJ, Gatzoulis MA, Baker P, editors. Heart disease and pregnancy. London: The Royal College of Obstetricians and Gynaecologists; 2006.