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ESSENTIALS Adults with congenital heart disease are a growing population, and now outnumber children with congenital heart disease in the United Kingdom. Many patients with repaired hearts can now, with spe- cialist care, expect to live a normal or near normal lifespan. Other survivors have complex, surgically altered hearts and circulations that reflect the surgical and interventional practices of the preceding two decades. Their long-term outlook is unknown and they remain at lifelong risk of complications that may require further intervention. The organization of services to provide specialist care is key to their long-term survival. The language of congenital heart disease The classification and description of complex congenital heart disease can appear intimidating, but should be easily understood by using a simple physiological approach that takes into account whether a condition is cyanotic or acyanotic, whether there is a shunt, and the implications of the morphology for pulmonary blood flow. The description of the congenitally malformed heart is aided by a sequential segmental analysis of the relationship of the three cardiac segments, which makes it possible to understand and describe how a complex heart is connected. The three segments to be considered are: (1) the atriums; (2) the ventricles; (3) the great vessels. The next step is to describe how each segment connects to the others. Cyanosis and pulmonary hypertension Cyanosis occurs as a result of a right-to-left shunt, with its natural history determined by the pulmonary blood flow. If pulmonary blood flow is limited (e.g. by pulmonary stenosis in the presence of a large ventricular septal defect), then pulmonary blood flow and ar- terial oxygen will be low, as will pulmonary artery pressure. Cyanotic patients with low or normal pulmonary artery pressure are usually amenable to surgical repair that abolishes the cyanosis. By con- trast, if the pulmonary circulation is unprotected (e.g. if the defect includes a large ventricular septal defect and no pulmonary stenosis), then pulmonary blood flow will be high and at high pressure, pul- monary vascular remodelling will occur, and—without intervention— pulmonary vascular disease will eventually develop (pulmonary arterial hypertension; the Eisenmenger syndrome). Once

pulmonary vascular disease is established, it is not possible to repair the defect and abolish the right-to-left shunt. The right ventricle Preservation of ventricular function is fundamental in allowing long- term survival with a good quality of life. The right ventricle is a key factor in the long-term outcome of many congenital cardiac condi- tions. It may fail as a result of either long-standing pressure or volume overload. (1) Pressure loading—this occurs in patients in whom the right ventricle supports the systemic circulation, such as those with congenitally corrected transposition of the great arteries, and in those who underwent interatrial repair (Mustard or Senning operation) of simple transposition of the great arteries. The right ventricle is hyper- trophied, and ultimately fails, with tricuspid regurgitation secondary to annular dilatation hastening the decline. (2) Volume loading—this commonly occurs as a result of pulmonary regurgitation secondary to pulmonary valvotomy or repair of tetralogy of Fallot in early life. There may be no audible murmur because there are often only remnants of pulmonary valve tissue, such that the regurgitant flow is laminar. Partly because of the lack of physical signs, and partly because pulmonary regurgitation is usually tolerated for many years before the right ven- tricle begins to fail, patients may present very late with a very dilated and impaired ventricle. Long-standing large atrial septal defects pro- duce similar right ventricular volume loading effects. The right ven- tricle may be inherently abnormal, as in Ebstein anomaly where a combination of a functionally small ventricle and volume loading from tricuspid regurgitation may cause the right ventricle to fail. The Fontan circulation Hearts which have only one functional ventricle present a par- ticularly difficult challenge. Patients are cyanosed, and only a few will reach adulthood if left unoperated. The ultimate aim for pa- tients with only one functional ventricle is a Fontan circulation: a palliative approach that reduces ventricular volume loading and abolishes cyanosis. It is critically dependent on a low pulmonary vascular resistance, hence early control of pulmonary blood flow is paramount. If pulmonary blood flow is too high, it is controlled by placing a pulmonary artery band (i.e. by the creation of iatrogenic, protective pulmonary stenosis). If pulmonary blood flow is too low, the infant will not thrive, and pulmonary blood supply is augmented 16.12 Congenital heart disease in the adult
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 by means of a systemic to pulmonary artery shunt. There are many variations of the Fontan operation, but all involve the separation of pulmonary and systemic circulations by using the single ventricle to support the systemic circulation and by connecting the systemic veins directly (or via the right atrium) to the pulmonary artery. There is thus no ‘pump’ in the pulmonary circulation, so although cyan- osis is abolished, the Fontan circulation is one of a chronic low output state. Thus, although the Fontan approach enables most pa- tients with a single ventricle to reach adulthood, they have a fragile circulation and will develop a range of complications. They are par- ticularly at risk if they have a tachyarrhythmia or acute noncardiac illness, since they tolerate such insults poorly and are dependent on their medical teams’ understanding of their circulation to ensure good hydration, avoidance of vasodilatation, and rapid restoration of sinus rhythm. Tachyarrhythmia Tachyarrhythmias are a major cause of sudden death in patients with congenital heart disease, with scar-related atrial tachyarrhythmias being common in those who have had previous cardiac surgery, and probably a commoner cause of death than ventricular arrhythmias. Atrial tachyarrthymias are the reason that patients who underwent interatrial repair (Mustard or Senning operations) of transposition of the great arteries are the congenital cardiac group with the highest incidence of sudden death. Their surgically created atrial ‘baffles’ mean that atrial function is abnormal, and ventricular filling is im- paired, particularly at high heart rates. Atrial flutter is common post Mustard or Senning, and patients are

usually able to conduct 1:1 at a rate of 300 bpm, resulting in cardiovascular collapse. Correct management is rapid restoration of sinus rhythm, followed by flutter ablation. Patients with a Fontan circulation are similarly vulner- able to interatrial re-entry tachyarrhythmias. Ventricular and atrial tachycardias may both occur in most survivors of complex con- genital heart disease, particularly after repair of tetralogy of Fallot. If ablation is not successful, consideration should be given to an internal cardioverter defibrillator. Pregnancy and contraception Many women with congenital heart disease wish to consider preg- nancy. For most this can be undertaken with only a small increased risk, but for some pregnancy carries a significant risk of compli- cation, long-term morbidity, and death. Outcomes can be opti- mized by preconception counselling and specialist joint cardiac and obstetric care. Access to safe and effective contraception is important to allow patients to avoid potentially high-risk pregnan- cies. Estrogen-containing preparations are not suitable for those at risk of intracardiac thrombus or who have a right-to-left shunt; long-acting progestogen-only methods offer safe and effective alternatives Heart failure and end-of-life care As the population of adults with congenital heart disease ages, so the number developing heart failure increases. Conventional heart failure drugs have not been shown to have much benefit in this situ- ation, and there is a lack of clear guidance as to who will benefit from interventions such as cardiac resynchronization therapy. Cardiac transplantation is associated with a worse early mortality than acquired heart disease, but the long-term outcome is as good. Transplantation is limited both by suitability of the recipient with a complex, surgically modified heart, and by donor availability. Services caring for patients need to develop a robust end-of-life pathway that focuses on symptoms and quality of life, and runs in parallel with other therapies. Introduction The growing number of adult survivors of congenital heart dis- ease will encounter medical staff from all areas of medicine and surgery. It is therefore important that all doctors have an under- standing of the principles of congenital heart disease and enough knowledge to know when to refer such patients to a specialist centre. As a result of advances in paediatric cardiac surgery and inter- vention, the outlook for the approximately 8 per 1000 babies born with congenital heart disease has changed dramatically in the last half-century. Fifty years ago, 70% of children born with congenital heart disease died before their tenth birthday; now more than 80% survive to adulthood and in the United Kingdom there are more adults than children living with congenital heart disease. Despite such advances, only those with the simplest conditions (e.g. isolated secundum atrial septal defect or anomalous pul- monary venous drainage successfully repaired in childhood) may be considered cured of their heart disease. Most patients need con- tinued specialist follow-up since they have residual lesions that may progress over many years and require timely intervention. Surgical techniques evolve continually, creating new populations with different surgically modified conditions and long-term out- comes. Careful follow-up is therefore crucial, not only to provide high standards of clinical care, but also to provide feedback about late results in order to inform initial management in infancy. As a result of such long-term follow-up information, the operation of choice for transposition of the great arteries became the arterial switch from the late 1980s, because of the late problems encountered in patients who had undergone interatrial repair with the Senning or Mustard operations. Surgical advances mean that patients with new surgically modi- fied conditions are reaching adulthood. Their outlook and the complications they may face are not known, so lifelong specialist surveillance is important. Left unoperated, hypoplastic left heart syndrome is lethal; survivors of the three-stage surgical palliation are now reaching the adult clinics. They will form the largest new population over the next decade and face a more complex future than those with a ‘standard’ Fontan circulation. Classification and nomenclature The classification and description of complex congenital heart disease can appear intimidating.

Nonetheless, a grasp of the basic principles is important to understand the anatomy and pathophysi- ology of congenital cardiac conditions. A simple physiological

16.12 Congenital heart disease in the adult 3561 approach to classifying congenital heart disease takes into account whether a condition is cyanotic or acyanotic, whether there is a shunt, and the implications of the morphology for pulmonary blood flow (Table 16.12.1). Sequential segmental analysis The description of the congenitally malformed heart is aided by a segmental approach, which makes it possible to understand and de- scribe how a complex heart is connected. Any heart can be described by considering it as three segments (the atrial chambers, the ven- tricular mass, and the great arteries) and describing in a sequential manner how each segment is arranged and connected to the next segment (Figs. 16.12.1 and 16.12.2). Atrial arrangement Situs solitus is the usual arrangement of asymmetrical structures (i.e. morphological left atrium on the left, and right atrium on the right; morphological left main bronchus on the left, and right main Table 16.12.1 Classification of congenital heart disease Acyanotic Cyanotic: obligatory right-to-left shunt No shunt Left-to-right shunt Eisenmenger syndrome right to left shunt due to raised pulmonary vascular resistance Normal or low pulmonary blood flow Level of lesion Example of specific lesion Level of shunt Example of specific lesion Level of shunt Example of specific lesion (unoperated) Level of shunt Example of specific lesion Right inflow Ebstein anomaly Atrial PAPVD ASD AVSD Atrial Large ASD (uncommon cause) Atrial, with obstruction to pulmonary blood flow Severe pulmonary stenosis with ASD Left inflow Parachute mitral valve Cor triatriatum Ventricular VSD Ventricular Large VSD Ventricular, with obstruction to pulmonary blood flow Tetralogy of Fallot, Pulmonary atresia VSD, Univentricular heart with pulmonary stenosis Right outflow Infundibular stenosis Pulmonary stenosis Arterial PDA Aortopulmonary window Arterial Large PDA Aortopulmonary window Extra cardiac Pulmonary AVM, anomalous systemic venous connection e.g. left SVC to LA, veno-venous collaterals Left outflow Subaortic stenosis Bicuspid aortic valve Multiple AVSD Multiple Large AVSD Arterial Supravalvar stenosis Coarctation of the aorta ASD, atrial septal defect; AVSD, atrioventricular septal defect; LA, left atrium; PAPVD, partial anomalous pulmonary venous drainage; SVC, superior vena cava; VSD, ventricular septal defect. Fig. 16.12.1 The segments of the heart.

section 16 Cardiovascular disorders 3562 bronchus on the right; stomach on the left, liver on the right). Situs inversus is the mirror-image arrangement of these structures. Isomerism describes abnormal symmetry of paired structures that usually show laterality, as shown in Table 16.12.2. The pres- ence of isomerism of the atrial appendages should alert the phys- ician to the coexistence of complex associated lesions, including a variety of abnormalities of venous connections that may cause technical difficulties at cardiac catheterization and permanent pacemaker insertion. Right isomerism is commoner in males and left isomerism in females. Survival to adulthood with right isomerism is uncommon because of associated asplenia and se- vere cyanotic heart disease, including obstructed anomalous pul- monary venous drainage (the pulmonary venous confluence is a left atrial structure). The lesions associated with left isomerism tend to produce left-to-right shunts and little if any cyanosis. Atrioventricular connections In the normal heart, the atrioventricular connections are con- cordant (Fig. 16.12.2): • the right atrium connects to the right ventricle via the tricuspid valve • the left atrium connects to the left ventricle via a mitral valve If the atrioventricular connections are discordant: • the right atrium connects to the left ventricle via a mitral valve • the left atrium connects to the right ventricle via a tricuspid valve Ventriculo-arterial connections In the normal heart, the ventriculo-arterial connections are

con- cordant (Fig. 16.12.2): • the left ventricle connects to the aorta via the aortic valve • the right ventricle connects to pulmonary artery via the pulmonary valve If the ventriculo-arterial connections are discordant (transposition of the great arteries), then: Fig. 16.12.2 Sequential segmental analysis.

 • the left ventricle connects to the pulmonary artery via the pul- monary valve • the right ventricle connects to the aorta via the aortic valve Cyanosis: A multisystem disorder Cyanosis occurs as a result of a right-to-left shunt. Cyanotic heart disease is a multisystem disorder; its manifestations are listed in Table 16.12.3. Secondary erythrocytosis Chronic hypoxia is the stimulus to the increased red blood cell mass and high haematocrit found in cyanotic heart disease. This physio- logical response increases the oxygen-carrying capacity of the blood and improves tissue oxygenation sufficiently to reach a new equilib-rium at a higher haematocrit. The secondary erythrocytosis of cyan- otic heart disease is a physiological response, often associated with thrombocytopenia. It is fundamentally different from the patho- logical generalized increase in all haemopoietic stem cell lines found in the malignant disease polycythaemia rubra vera. Table 16.12.2 Diagnosis of atrial arrangement Situs solitus (normal arrangement) Situs inversus (mirror-image arrangement) Right atrial isomerism Left atrial isomerism Atrial and appendagea morphology R-sided morphological RA and appendage L-sided morphological LA and appendage R-sided morphological LA and appendage L-sided morphological RA and appendage Bilateral morphological RA and appendages Bilateral morphological LA and appendages Pulmonary and bronchial morphologyb R lung trilobed L lung bilobed R-sided main bronchus: short, L-sided main bronchus: long R lung bilobed L lung trilobed R-sided main bronchus: long, L-sided main bronchus: short Bilateral trilobed lungs Bilateral short morphological R bronchi Bilateral bilobed lungs Bilateral long morphological L bronchi Abdominal arrangementc Aorta IVC Stomach Liver Spleen To L of spine To R of spine L-sided R-sided R-sided Normal or mirror image Aorta and IVC on same side IVC anterior to aorta Usually L-sided Midline Usually absent Aorta and azygos on same side Azygos posterior to aorta Usually R-sided Midline Often polysplenia Ao, aorta, AV, azygos vein, IVC, inferior vena cava; L, left; LA, left atrium; R right; RA, right atrium; SVC, superior vena cava. a Readily identified on transoesophageal echocardiography. b Since bronchopulmonary situs nearly always follows atrial situs, atrial situs can be inferred from the chest radiograph. c Echocardiography shows the intra-abdominal relations of the great vessels. In left isomerism, there is usually interruption of the IVC, and the abdominal venous return connects to the heart via a (right-sided) azygos or (left-sided) hemiazygos vein. The hepatic veins can be identified draining separately into the atriums. Table 16.12.3 Complications of cyanotic congenital heart disease Haematological Secondary erythrocytosis Iron deficiency (venesection, menorrhagia) Thrombocytopenia Haemorrhage Coagulopathy → Hyperviscosity symptoms? ↑ Risk of CVA Neurological CVA Cerebral abscess 2° to paradoxical embolism Hyperuricaemia Impaired renal clearance of uric acid Increased uric acid production? → Gout Renal abnormalities ↓ Uric acid clearance Glomerular proteinuria Mesangial matrix thickening Capillary and hilar arteriole dilatation → High risk of iatrogenic renal failure Bilirubin kinetics ↑ Haem breakdown → Pigment gallstones Digits and long bones Clubbing Hypertrophic osteoarthropathy Dental Gingival hypertrophy →↑ Risk of endocarditis Infection Endocarditis Cerebral abscess Skin Acne CVA, cardiovascular accident.

 Venesection was advocated historically to reduce the haematocrit to less than 65% in patients with cyanotic heart disease because of con- cerns about

the effects of hyperviscosity. However, although a raised haematocrit is associated with increased blood viscosity, it also cor- relates with improved exercise tolerance, and does not correlate well with symptoms classically regarded as those of hyperviscosity (Box 16.12.1). Conversely, iron deficiency brought about by venesection is associated with increased symptoms akin to those of hyperviscosity (but does not cause an actual increase in viscosity) as well as an in- creased risk of stroke. Restoration of iron stores improves exercise tol- erance and symptoms. Cyanotic patients with iron deficiency should therefore have the cause of the deficiency treated and be given iron supplements sufficient to render them iron replete over a course of months. A prolonged course of low-dose iron should allow iron stores to be replenished without causing a rapid rise in haematocrit. There is no evidence that venesection improves symptoms beyond a few days, nor that it carries any prognostic benefit. Thus, venesection to reduce elevated haemoglobin and haematocrit is rarely, if ever, indicated for the physiological erythrocytosis of cyanotic heart disease. Menorrhagia is common in women with cyanotic heart disease and may be sufficient to cause iron deficiency anaemia. It may be difficult to manage, the combined oral contraceptive pill being contraindicated because of the prothrombotic effects of the estro gen it contains, and tranexamic acid may similarly be associated with thrombosis. Norethisterone may provide short-term relief. Progestogen-only contraceptives have unpredictable effects on men- struation: the subdermal implant (e.g. Nexplanon®) is safe and causes oligomenorrhoea in some women. Mirena® IUS is a progestogen- eluting intrauterine device that causes oligomenorrhoea in most women, but great care is needed for those with cyanotic heart dis- ease or who have not undergone previous vaginal delivery because insertion may cause a vasovagal response and cardiovascular col- lapse. If menorrhagia is due to uterine fibroids, catheter emboliza- tion of the feeding uterine artery is safe and may be successful. Disorders of coagulation and blood vessels It is poorly understood why patients with cyanotic disease are at in- creased risk of haemorrhage and thrombosis. There is often a mild thrombocytopenia that may be due partly to shortened platelet survival time, and the large multimeric forms of von Willebrand factor and other clotting factors may be depleted. Coagulation testing may yield spurious results in patients with haematocrit over 55% unless the amount of citrate anticoagulant in the sample bottle is reduced. Bleeding may be minor and mucocutaneous, but major haemor- rhage may occur during surgery, or from the lungs. Pulmonary artery thrombosis is discussed next (see ‘Eisenmenger syndrome: defects with secondary pulmonary vascular disease’). Interestingly, sys- temic arterial atherosclerosis is rare in the cyanotic population, per- haps because of a combination of thrombocytopenia, upregulated nitric oxide, hyperbilirubinaemia, and hypocholesterolaemia. Other complications of cyanotic heart disease The risk of stroke is increased in cyanotic heart disease, with in- dependent risk factors being intravenous lines, arterial hyperten- sion, atrial fibrillation, iron deficiency, and prosthetic intravascular material such as endocardial pacing systems. The mechanism of stoke is often paradoxical embolism due to right-to-left shunting. Paradoxical air emboli are a cause of stroke in patients whose venous lines are not fitted with filters. Patients who require transvenous pacing should be anticoagulated to prevent paradoxical thrombo- embolism from pacing leads. Cerebral abscess is an uncommon but potentially devastating complication of cyanosis, with a mortality of around 13%. The right- to-left shunt allows systemic venous blood to avoid passing through the lungs, where bacteria are removed by phagocytosis. The diagnosis should be considered in all cyanotic patients who present with fever, headache, and malaise, neurological signs, or altered consciousness. Similarly, patients who present with cerebral abscess of apparently unknown cause should have a right-to-left shunt excluded. The right-to-left shunt may be extracardiac: for example, pulmonary arteriovenous malformation, or a persistent left superior vena cava (SVC)

draining to the left atrium. A bubble contrast echocardiogram without Valsalva manoeuvre, via the left brachial vein, will detect such right-to-left shunting. Empirical treatment is usually a third-generation cephalosporin and metronidazole; blood cultures, and if possible stereotactic aspiration of pus with narrow antibiotic therapy and surgical drainage may be necessary for large abscesses. Despite the high incidence of hyperuricaemia, attacks of acute gout are uncommon and asymptomatic hyperuricaemia does not require treatment. Acute attacks should be treated with colchicine, avoiding nonsteroidal anti-inflammatory agents (NSAIDs) because of their detrimental effects on haemostasis and renal function. As in primary hyperuricaemia, allopurinol is useful in preventing recurrence. The renal abnormalities outlined in Table 16.12.3 are frequently not associated with abnormal baseline renal function. However, renal failure may be precipitated by hypotension and dehydra- tion, especially in combination with radiographic contrast media, NSAIDs, or aminoglycoside antibiotics. The mode of decline and eventual death is a combination of heart and renal failure in many patients with cyanotic heart disease, and care should be taken to titrate diuretic therapy cautiously to minimize worsening renal function. Renal dialysis or filtration is very poorly tolerated in this patient group and should be avoided: the failing cyanotic circulation does not cope with the haemodynamic demands of renal support, and deterioration and death are likely to occur rapidly. Acne is a common complaint in adolescents and adults with cyan- otic disease and may be widespread and psychologically debilitating. When severe it may also increase the risk of bacteraemia and endocarditis. Digital clubbing is almost universal in cyanotic heart disease, and some degree of hypertrophic osteoarthropathy of the long bones may occur in up to one-third of patients. Symptoms include aching and tenderness of the long bones of the forearms and legs. Box 16.12.1 Symptoms of hyperviscosity • Headache • Faint, dizzy, light-headed • Depressed mentation, sense of distance • Blurred vision, amaurosis fugax • Paraesthesiae • Tinnitus • Fatigue, lethargy • Myalgia, muscle weakness • Chest and abdominal pain • Restless legs

 There is oedema and cellular infiltration, causing lifting of the peri- osteum that is visible radiographically, with new bone formation and resorption. Localized activation of endothelial cells by an ab- normal platelet population, with the ensuing release of fibroblast growth factors, may play a central role in the pathogenesis of both phenomena. Cyanotic patients become more hypoxic during air travel, as the partial pressure of oxygen in a pressurized aircraft is lower than that at sea level. However, such travel seems to be well tolerated at least for short and medium haul journeys and supplemental oxygen should not normally be necessary. Travellers should be warned to avoid dehydration and to plan their journeys to avoid having to carry baggage for long distances within large airports. Cyanotic patients are at risk of iatrogenic complications if they require surgery or intervention for noncardiac conditions. See Box 16.12.2. Eisenmenger syndrome: Defects with secondary pulmonary vascular disease Eisenmenger syndrome is a cyanotic condition that occurs in pa- tients with a large (nonrestrictive) communication between the systemic and pulmonary circulations that results in high pul- monary vascular resistance and pulmonary arterial hypertension, so that the shunt across the communication is reversed (right-to- left) or bidirectional. The communication may be at atrial, ven- tricular, or arterial levels. In fetal life, pulmonary vascular resistance is high and there is muscularity of the pulmonary arterioles. In the normal circulation, pulmonary vascular resistance falls soon after birth and remodel- ling of the pulmonary arterioles occurs. However, if there is a large communication; for example, a ventricular septal defect, the effects of blood entering the pulmonary circulation at high volume and systemic pressure causes reverse remodelling, and instead of falling, the pulmonary vascular resistance rises. Endothelial dysfunction secondary to

changes in shear stress and circumferential wall stress is thought to mediate these changes through altered expression of vasoactive mediators and growth factors such as endothelin-1, nitric oxide, prostacyclin, and vascular endothelial and fibroblast growth factors. Corrective surgery in infancy usually prevents the development of this irreversible syndrome, so its incidence in the developed world is declining. However, when patients do present their management is dependent on a good understanding of their condition. For patients with established right-to-left shunting and pul- monary arterial hypertension, the diagnosis is clear. However, some have intermediate pathologies, and European guidelines attempt to clarify these: it is important to understand that despite the absence of a right-to-left shunt and cyanosis, potentially life-threatening pulmonary artery hypertension is present (Table 16.12.4). Clinical findings Symptoms of breathlessness relate to the degree of hypoxia; many patients feel worse in hot weather or after a hot bath because the resulting systemic vasodilatation is not accompanied by a reduction in pulmonary vascular resistance, so the right-to-left shunt is en- hanced and they become more hypoxic. Exercise-induced syncope may occur, and is exacerbated by hot weather and dehydration. Haemoptysis is common and may be fatal. Whatever the underlying defect, some examination findings are shared. Patients are cyanosed and clubbed and may be plethoric. There is a right ventricular heave and the pulmonary component of the second heart sound is palpable and loud. A pulmonary ejection click and pulmonary regurgitation may be audible. A soft systolic flow murmur may be heard from the dilated pulmonary artery. No systolic murmur can be heard from the lesion responsible for the pulmonary vascular disease since the chambers on both sides of the lesion are at equal pressure. It is frequently possible to distinguish between the common lesions associated with the Eisenmenger syndrome on clinical Box 16.12.2 Checklist for patients at high riska of iatrogenic complications during the perioperative period or during intercurrent illness • Seek advice from the patient's congenital cardiology team • Maintain hydration—intravenous fluids (via air filter if cyanotic to avoid the risk of paradoxical embolism) when nil by mouth • Maintain haemoglobin commensurate with degree of cyanosis to optimize oxygen-carrying capacity • Avoid vasodilator agents—especially at induction of anaesthesia • Protect the kidneys—maintain hydration, avoid nephrotoxic agents (NSAIDs, aminoglycosides), use minimal volumes of contrast agents a Patients at high risk include those who are cyanotic and those with Eisenmenger syndrome or Fontan circulation. Table 16.12.4 Pulmonary arterial hypertension associated with congenital heart disease A Eisenmenger syndrome A large systemic to pulmonary artery shunt leads to a severe increase in pulmonary vascular resistance such that it exceeds systemic vascular resistance, and the shunt reverses (becomes right-to-left). The patient is cyanosed B Pulmonary artery hypertension associated with systemic to pulmonary shunt A moderate–large defect causes a rise in pulmonary vascular resistance, but it remains less than systemic vascular resistance and the shunt remains left-to-right C Pulmonary artery hypertension and a small systemic to pulmonary shunt A small defect (e.g. VSD <1 cm or ASD>2 cm) coexists with pulmonary arterial hypertension. If pulmonary vascular resistance exceeds systemic vascular resistance, the shunt reverses and the patient is cyanosed. The clinical course is akin to idiopathic pulmonary arterial hypertension. It is likely that two different diagnoses are present, i.e. a patient with idiopathic pulmonary artery hypertension coincidentally has a small septal defect D Pulmonary artery hypertension after surgery to correct systemic to pulmonary artery shunt A large systemic to pulmonary shunt is surgically repaired but pulmonary artery hypertension is still present ASD, atrial septal defect; VSD, ventricular septal defect.

section 16 Cardiovascular disorders 3566 grounds. The patient with an Eisenmenger patent arterial duct has differential cyanosis and clubbing, since fully saturated blood from the left ventricle supplies the aortic arch and its branches before mixing occurs with desaturated pulmonary arterial blood via the patent duct. The right hand may therefore be pink with no clubbing, the left may be slightly more cyanosed because of the origin of the left subclavian artery opposite the duct, and the toes are more deeply cyanosed and clubbed. The second heart sound may be closely or normally split. In contrast, cyanosis and clubbing is uniform when the right-to-left shunt occurs at atrial, ventricular, or ascending aortic (as in truncus arteriosus or aortopulmonary window) levels. The second sound is single in ventricular septal defect (VSD), atrio- ventricular septal defect (AVSD), and truncus, but may be split in an atrial septal defect (ASD). Investigations The chest radiograph shows a dilated pulmonary trunk because of high pulmonary blood flow in earlier life, but reduced blood flow as pulmonary vascular resistance rose means that the lung fields are oligaemic (Fig. 16.12.3). Unless cardiac failure intervenes, the heart size is usually normal, the effects of volume overload having regressed as pulmonary vascular resistance increased and the left- to-right shunt diminished and disappeared. The electrocardiogram (ECG) shows P pulmonale and biventricular hypertrophy. The echocardiogram should establish the site of the shunt and allow an estimation of pulmonary arterial pres- sure and ventricular function. Cardiopulmonary exercise testing may be used with caution: pa- tients with Eisenmenger syndrome are among the most limited of those with congenital heart disease and maximal exercise testing may induce potentially fatal syncope. The less strenuous but still ob- jective 6-min walk or shuttle tests are preferable measures of exercise capacity in these patients. High-resolution CT scanning demonstrates the hypertensive pul- monary vasculature and any collateral vessels. It is also the investiga- tion of choice to show in situ pulmonary thrombus and pulmonary artery aneurysms, and to demonstrate the site of any pulmonary haemorrhage. Care should be taken to avoid contrast-induced neph- ropathy by ensuring adequate hydration. Cardiac catheterization is unnecessary and potentially dangerous for patients with established pulmonary vascular disease. The only indication is for those patients in whom there is doubt about the presence and severity of pulmonary vascular disease and who would be considered for selective pulmonary vasodilator therapy or (rarely) surgical repair if reversibility can be confirmed. Histologically, pulmonary vascular disease progresses from medial hypertrophy through intimal proliferation with migration of smooth muscle cells, to progressive fibrosis and obliteration, dilata- tion, the development of angiomas, and finally fibrinoid necrosis. Those who have developed fibrotic and obliterative changes are likely to have irreversible pulmonary vascular disease. Routine lung biopsy is not recommended; it carries a high risk in the pulmonary hypertensive adult and is unlikely to show reversible pathology. In addition, thoracotomy scars from open lung biopsy are a relative contraindication to heart–lung transplantation. Outcome and complications Survival into adulthood with Eisenmenger syndrome is common. Median life expectancy is around 40 years, which is better than for those with idiopathic pulmonary arterial hypertension. Markers of poorer prognosis include complex anatomy and physiology, coex- istent Down’s syndrome, decline in functional class, and the devel- opment of heart failure, renal dysfunction, and clinical arrhythmia. Serum uric acid increases with disease progression and may also be used as a long-term predictor of mortality. The patient with Eisenmenger syndrome is prone to all the complications of cyanotic heart disease: nowadays the mode of death is most commonly due to heart failure or infection (including cerebral abscess). This con- trasts with Paul Wood’s description in the mid-20th century, when pulmonary haemorrhage and periprocedural deaths predominated. Haemoptysis is usually due to rupture of small hypertensive intrapulmonary vessels, or more rarely to thrombosis in situ and pul- monary

infarction. Massive haemoptysis is a well-recognized cause of death. All patients should be admitted to hospital and the systemic pressure kept low by bed rest and β-blockade; the pulmonary ar- tery pressure being the same as that measured in the brachial artery. NSAIDs should be stopped and vasodilators should not be given. If the haemoptysis is massive, diamorphine should be administered, fresh frozen plasma or cryoprecipitate may be given, and consider- ation should be given to selectively intubating the nonbleeding lung to allow an attempt to embolize a bleeding vessel. Bronchoscopy has no role and may worsen the haemorrhage. In situ thrombosis in the dilated pulmonary arteries of adults with Eisenmenger syndrome is common (prevalence of 20–30%) and relates to the degree of cyanosis. It is best detected and quan- tified using high-resolution CT scanning. Anticoagulation of any sort has not been shown to resolve such thrombus, and patients are at risk of pulmonary embolic episodes. Warfarin may increase the risk of bleeding while failing to reduce the thrombus, and aspirin should be avoided as it may exacerbate haemorrhage associated with thrombocytopenia. Fig. 16.12.3 Chest radiograph of a 35-year-old woman with Eisenmenger secundum atrial septal defect. The aortic knuckle is small and the central pulmonary arteries enlarged, indicating pulmonary arterial hypertension; the lung fields are clear. The cardiac silhouette is not enlarged.

 Right ventricular failure may be precipitated by atrial arrhythmia and usually occurs after the age of 30 years. Decline may be her- alded by the onset of right ventricular failure, renal dysfunction, supraventricular arrhythmia, and haemoptysis. Death may be sudden and due to arrhythmia or massive haemoptysis. In some pa- tients death follows progressive hypoxia terminating in bradycardia and asystole from which they cannot be resuscitated. Intercurrent illness and noncardiac surgery may pose major risks. The latter is particularly dangerous when carried out without the benefit of expert cardiology, anaesthetic, and periopera- tive care. A sound understanding of the pathophysiology is vital (Box 16.12.2). Management Until recently, treatment of patients with Eisenmenger syndrome has been palliative and symptom led, directed at avoiding iatrogenic and natural complications. Gentle exercise should be encouraged, but strenuous exertion avoided, since it may result in syncope. Long- term oxygen therapy may improve symptoms in some patients, but has not been shown to have prognostic benefit. Although this approach is still the mainstay of treatment, selective pulmonary vasodilators including phosphodiesterase inhibitors (e.g. sildenafil) and endothelin receptor antagonists (e.g. bosentan) may improve outcome and should be considered at least for patients with New York Heart Association (NYHA) class III symptoms. These drugs have been shown to improve outcome in other forms of pulmonary hypertension. Early data from small trials suggest that bosentan helps to maintain right ventricular function, quality of life, and exercise capacity. Sildenafil improves quality of life and exercise tolerance in many patients as they reach NYHA III. Pregnancy and contraception Pregnancy carries a particularly high risk (25–40% maternal mor- tality). Pregnancy and contraception in congenital heart disease are discussed next. All women with pulmonary hypertension of any cause should be counselled about the risks and given access to safe, effective contraception. If a woman with Eisenmenger syndrome be- comes pregnant and chooses not to have a termination, she should be referred to a specialist pulmonary hypertension centre. Valve and outflow tract lesions Isolated pulmonary valve stenosis Isolated pulmonary stenosis is common, occurring in up to 10% of patients with congenital heart disease. There is usually fusion of the valve cusps leading to a doming appearance. Syndromic associ- ations are not unusual and include Noonan, Williams, and Alagille syndromes. Significant pulmonary stenosis results in right ventricular hyper- trophy and high right-sided pressures; right-to-left shunting causing cyanosis

may occur if there is a coexistent ASD or patent foramen ovale (PFO). Pulmonary stenosis is a better-tolerated lesion than aortic sten- osis, with an excellent survival. Severe pulmonary stenosis usually presents in childhood, either as an asymptomatic murmur, or with failure to thrive, chest pain, dyspnoea, or cyanosis. Physical signs Patients are acyanotic unless there is an interatrial communication, in which case cyanosis can be severe. The venous pressure is raised only if the right ventricle has begun to fail and there is tricuspid re- gurgitation. There may be a right ventricular heave. The pulmonary component of the second heart sound is soft and there is a pul- monary ejection systolic murmur. An early diastolic murmur may also be present if there is coexistent pulmonary regurgitation. Investigations The ECG may demonstrate right ventricular hypertrophy. This re- gresses after relief of the stenosis. The chest radiograph reveals poststenotic dilation of the proximal pulmonary artery, and the lung fields may be oligaemic if the pulmonary stenosis is severe. Transthoracic echocardiography confirms the diagnosis and al- lows functional assessment of the severity of pulmonary stenosis and regurgitation as well as right ventricular hypertrophy, dilatation, and function. Management Adults with trivial (<20 mm Hg) pulmonary stenosis do not require regular follow-up, since progression is unlikely. Approximately 20% of adults with mild stenosis (<50 mm Hg) may progress and ultim- ately require intervention, and most of those with a peak pulmonary valve gradient greater than 50 mm Hg require intervention. Balloon pulmonary valvotomy is the treatment of choice, unless the valve is thickened and dysplastic or regurgitant, or there are as- sociated anomalies requiring a surgical approach. Valvotomy is usu- ally successful and it is uncommon for stenosis to recur, however, the procedure invariably results in a degree of pulmonary regurgitation and so long-term follow-up is required.
Lone infundibular stenosis and double-chambered
right ventricle Abnormally placed muscle bands cause either infundibular obstruc- tion or—if placed more inferiorly—subinfundibular obstruction and a double-chambered right ventricle. The degree of obstruction may be mild in childhood, but progresses in adult life and causes symptoms as the right ventricle hypertrophies and outflow obstruc- tion becomes severe. A perimembranous VSD usually coexists and may close spontaneously. Treatment is by surgical resection of the obstructing muscle bands. Ebstein anomaly This rare, complex defect of the tricuspid valve occurs in 1 in 20 000 live births and affects both sexes equally. The risk may be increased by maternal exposure to lithium during the first trimester. In the normal heart, the tricuspid and mitral valves are formed from the endocardium of the right and left ventricles, respectively. The valve leaflets delaminate from the endocardium to form the atrioventricular valves. In Ebstein anomaly, there is failure of tri- cuspid valve leaflet delamination during fetal life, so that the leaflets adhere to the right ventricular myocardium, resulting in apical dis- placement of the functional tricuspid valve, tethering, redundancy, and fenestrations of the valve leaflets. There is a broad spectrum of severity of this condition, dependent upon the degree of failure of delamination.

 Ebstein anomaly is characterized by a spectrum of features: • Adherence of the tricuspid valve leaflets to the underlying myocardium due to failure of delamination in fetal life. • Apical displacement of the tricuspid valve hinge points and orifice: ■ As a result of the failure of delamination the septal and posterior (mural) leaflets insert further into the body of the right ventricle than in the normal heart (in which the mitral and tricuspid valves are offset so that the tricuspid valve is displaced up to 1.5 cm towards the right ventricular apex). ■ The ‘atrialized’ portion of the right ventricle is often thinner walled than the functional right ventricle due to congenital partial absence of the myocardium; as a result, the functional size of the right ventricle is reduced and that of the right atrium increased. • Dilation of the functional

right atrium. • Dilatation of the true tricuspid valve annulus at the atrioven- tricular junction. This combination of features usually results in tricuspid regurgi- tation (or very rarely stenosis) and right heart dilation, providing a substrate for atrial and ventricular arrhythmias. Associated abnormalities A PFO or ASD is present in most cases, and allows cyanosis to de- velop as the disease progresses and right-to-left shunting occurs. Left-heart abnormalities occur as a consequence of alterations in left ventricular geometry due to leftwards displacement of the interventricular septum (e.g. mitral valve prolapse may occur as re- sult of relatively long chordae in a left ventricle of reduced cavity size). Coexistent Wolfe–Parkinson–White syndrome, with single or multiple right-sided pathways, occurs in 20% of patients. Ebstein anomaly may also form part of other complex congenital le- sions, including pulmonary stenosis and atresia and tetralogy of Fallot. When it coexists with congenitally corrected transposition of the great arteries, the tricuspid valve is the systemic atrioventricular valve. Clinical presentation and course There is a broad spectrum of severity, ranging from intrauterine or neonatal death to presentation in late adulthood. Mortality, both with and without surgery, is influenced by age at presentation, the condition of the tricuspid valve, the cardiac rhythm, and the func- tion and capacity of the right ventricle, including the severity of right ventricular outflow tract obstruction, and the size of the right atrium in relation to the other cardiac chambers. Arrhythmia is the commonest mode of initial presentation in adult life; presentation earlier in life is usually associated with severe disease and additional cardiac lesions. Cyanosis may develop in adulthood if there is an associated ASD or PFO; as the right ventricular filling pressure increases there is a parallel rise in right atrial pressure, and a right-to-left interatrial shunt is established. These patients are at risk of paradoxical em- bolism, but the risk of endocarditis is low because the tricuspid regurgitant jet is of low velocity. Heart failure may intervene as a result of the combination of se- vere tricuspid regurgitation and the onset of atrial fibrillation or flutter. These atrial arrhythmias may be particularly troublesome if a coexistent accessory pathway allows a rapid ventricular response rate. The onset of atrial fibrillation is a predictor of death within 5 years, and may account for the increased death rate in the fifth decade. Physical signs The patient may be acyanotic or cyanosed and clubbed. Even when tricuspid regurgitation is severe the jugular venous pressure may not be particularly high or the ‘v’ wave prominent because of the cap- acity of the right atrium and thin-walled atrialized right ventricle to accommodate the low-pressure regurgitant volume. Once right ventricular failure develops the jugular venous pressure rises further and the ‘a’ and ‘v’ waves become more prominent. In the uncommon situation of tricuspid stenosis, the ‘a’ wave is increased and may be giant. The first heart sound is widely split with a delayed tricuspid component, due to the extra distance that the large anterior leaflet has to travel to reach the limit of its systolic excursion. The second heart sound may be single because low pressure in the right ventricular outflow tract renders the pulmonary component inaudible, or it may be widely split, reflecting right bundle branch block. Third or fourth ventricular filling sounds may be present. The systolic murmur of tricuspid regurgitation varies from inaudible to loud enough to gen- erate a thrill, but is classically decrescendo and scratchy. Once the right ventricle begins to fail and the venous pressure rises, hepato- megaly, ascites, and peripheral oedema are common. Investigations The chest radiograph is characteristic (Fig. 16.12.4). The ECG typ- ically shows a superior axis and right atrial enlargement, with or Fig. 16.12.4 Chest radiograph of a 43-year-old woman with classic cardiac silhouette of Ebstein anomaly due to right atrial enlargement. The aortic knuckle and pulmonary arteries are inconspicuous and the lung fields oligaemic.

 without right bundle branch block. The ‘p’ wave may be peaked and the PR interval prolonged, reflecting the prolonged conduction in the large

right atrium, or there may be evidence of pre-excitation. Right bundle branch block may occur due to abnormal activation and conduction in the atrialized right ventricle. Echocardiography establishes the diagnosis, severity, and asso- ciated abnormalities of Ebstein anomaly. The atrialized and func- tional portions of the right ventricle can be identified, as can the precise attachments and degree of tethering of the anterior leaflet of the tricuspid valve. Echocardiography is the investigation of choice in planning surgical intervention, tethering and restricted mo- tion of the anterior leaflet and a small right ventricle being strong predictors of the need for tricuspid valve replacement rather than repair. Cardiac catheterization is only necessary if specific haemo- dynamic questions remain after noninvasive assessment. Cardiopulmonary exercise testing is invaluable in assessing func- tional capacity when planning timing of surgery. Management Patients should be anticoagulated when atrial arrhythmias develop, particularly if there is an ASD. If re-entry tachycardias cannot be controlled with antiarrhythmic drugs, radiofrequency ablation of accessory pathways may be performed. However, ablation may be made difficult by the size and abnormal shape of the right atrium and abnormal position of the accessory pathway or pathways. Symptomatic patients should be assessed for surgery. In addition, the asymptomatic patient with severe tricuspid regurgitation and normal cardiopulmonary exercise tolerance should be considered for repair if right ventricular function has begun to deteriorate. The timing of surgery may be difficult to decide in the adult patient, even in the few centres with reasonable experience. Once the patient has developed overt right heart failure with a raised venous pressure, hepatomegaly, ascites, and atrial fibrillation, ventricular function may have deteriorated such that repair of the valve is no longer possible and transplantation may need to be considered. Tricuspid valve repair or replacement in this rare condition should only be carried out in experienced congenital cardiac sur- gical centres. Successful repair of the Ebsteinoid valve is difficult, as evidenced by the many techniques described. The aim is to achieve a competent native valve with its insertion at the true annulus and a reduction in right atrial size. Where possible, valve replacement should be avoided, since long-term outcomes are better with repair. If replacement is necessary, the inevitable need for later interven- tion if a bioprosthetic valve is placed should be weighed against the risk of mechanical valve thrombosis, which is much higher than for mechanical valves in other positions. A maze procedure should also be considered to reduce the long-term risk of atrial flutter and fibrillation. For high-risk patients in whom the right ventricle is thought to be unable to support the pulmonary circulation with a competent tri- cuspid valve, techniques to reduce its workload may be considered. The ‘1½’ ventricle repair combines tricuspid valve repair with a cavopulmonary anastomosis so that upper body systemic venous re- turn is directly to the pulmonary arteries, thus offloading the right ventricle. A single-ventricle repair may also be used, resulting in a Fontan circulation (see ‘Fontan operation’). Other right ventricular anomalies Uhl’s anomaly and arrhythmogenic right ventricular cardiomyop- athy (see also Chapter 16.7.2) are rare sporadic or familial conditions affecting the right ventricle. Table 16.12.5 list the key distinguishing features. Early diagnosis and the screening of family members of affected individuals is challenging and requires experience. MRI and high- resolution CT are useful tools, but early abnormalities are subtle and may be overinterpreted. Cor triatriatum and congenital mitral valve anomalies Cor triatriatum This is a very rare defect in which one of the atriums (nearly always the left) is partitioned by a fibromuscular membrane into an upper chamber that receives the pulmonary veins, and a lower chamber connecting with the atrial appendage and mitral valve. This is thought to occur due to a failure of the common pulmonary venous chamber to incorporate into the body of the left atrium early in fetal life. As a result, a persistent membrane inserts into the atrial septum at the fossa ovalis and into the posterolateral wall just above the mouth of the left atrial appendage.

An ASD coexists in about 50% of cases, allowing communication between the right and left atriums. The membrane may be intact, or pierced by one or more holes that are usually restrictive, causing supramitral stenosis. If the membrane obstructs pulmonary venous inflow, presen- tation is early in life, and adult survivors will have undergone sur- gical resection. First presentation in adulthood is unusual unless the membrane is nonrestrictive or coexists with a large ASD. Patients may have signs of an ASD or mitral stenosis. New symptoms in adulthood may be due to fibrosis or calcification of the membrane so that it becomes restrictive, or from progressive mitral regurgitation. The diagnosis is made by echocardiography. The chest radio- graph may also be characteristic, showing signs of pulmonary venous congestion, but not the left atrial appendage enlargement that accompanies valvar mitral stenosis, since the appendage lies Table 16.12.5 Right ventricular cardiomyopathy and Uhl's anomaly Arrhythmogenic right ventricular cardiomyopathy Uhl's anomaly 'Parchment heart' Morphology Patchy, localized fibro-fatty replacement of parietal myocardium mostly affecting outflow tract. Other parts of right and occasionally left ventricle may be involved Congenital absence of parietal ventricular myocardium with direct apposition of endocardium and epicardium. Normal interventricular septum and left ventricle Sex ratio 2:1 male:female Equal Typical presentation As young adult Exercise-induced ventricular tachycardia: palpitation, syncope, sudden death In infancy Congestive cardiac failure

section 16 Cardiovascular disorders 3570 in the low-pressure atrial chamber. The lateral chest radiograph may show enlargement of the pulmonary venous compartment of the left atrium. Treatment is unnecessary if the membrane is unobstructive and there are no significant associated lesions. The results of surgical resection of obstructive membranes and the postoperative prog- nosis are good. Congenital mitral valve anomalies These are rare and frequently coexist with other lesions. A supramitral ring often coexists with congenital mitral stenosis. It differs from cor triatriatum in that the ring is sited inferiorly to the os of the ap- pendage and lies immediately above the mitral valve. Shone syndrome consists of four levels of left heart obstruc- tion: supramitral ring, parachute mitral valve, subaortic stenosis (often with bicuspid aortic valve), and coarctation of the aorta. Parachute mitral valve occurs when the two papillary muscles are fused or there is hypoplasia or absence of one papillary muscle; the valve and its ap- paratus are often additionally dysplastic. Obstruction occurs at the level of the abnormal papillary muscles. The parachute mitral valve may also be regurgitant if the chordae are elongated and not signifi- cantly fused. Shone syndrome forms part of a spectrum of left heart obstruction that has bicuspid aortic valve at one end and hypoplastic left heart syndrome at the other. The recurrence risk is greater than for many forms of congenital heart disease at around 10%. Isolated cleft mitral valve differs from the 'cleft' seen in an AVSD in being in the anterior (aortic) leaflet, directed towards the aortic outflow tract, rather than being in the space between the bridging leaflets and pointing towards the septum. The isolated cleft can be readily repaired to resemble a competent normal mitral valve. Left ventricular outflow tract obstruction Bicuspid aortic valve This is the commonest congenital cardiac anomaly, occurring in 1 to 2% of the population and four times more common in males than in females. Bicuspid aortic valve phenotypes are highly variable and may be associated with aortopathies (bicuspid aortopathy, Loeys– Dietz syndrome), genetic syndromes (e.g. Turner syndrome) and other structural cardiac anomalies such as aortic coarctation, Shone syndrome (serial left-sided obstructive lesions) and hypoplastic left heart syndrome. The families of patients with bicuspid aortic valve associated with aortopathy or with other relatives with structural cardiac anomalies should be offered screening and genetic testing. Lifelong surveillance is necessary, even for patients with appar- ently isolated bicuspid aortic valve, since symptoms occur late in young

people with aortic valve disease and aortic root dilatation may occur in later life. Exercise testing with echocardiography is useful in planning the timing of surgery in those with asymptomatic aortic stenosis and left ventricular hypertrophy: ST segment changes and a failure of blood pressure to rise or cardiac function to improve appropriately in response to stress indicate that intervention should be considered. Aortic stenosis and regurgitation are discussed in Chapter 16.6. Supravalvar aortic stenosis In this least common form of left ventricular outflow tract obstruc- tion there is a localized narrowing of the aorta immediately above the aortic sinuses. Fibromuscular thickening of the aortic wall at the site of obstruction may encroach into the coronary ostia or onto the aortic valve leaflets and adversely influence prognosis. Unlike other forms of left ventricular outflow obstruction, the coronary arteries lie proximal to the obstruction and so are exposed to high left ventricular pressures, resulting in premature atherosclerosis. The condition may be associated with Williams' syndrome, when the prognosis may be worse since there is diffuse arterial involve- ment that may also involve the pulmonary and renal arteries (see Chapter 16.11). Subaortic stenosis Subaortic stenosis may be due to a discrete fibromuscular ridge or ring, or a long muscular tunnel. It may exist in isolation or as part of another lesion such as AVSD, where the 'unwedged' aorta; the elong- ated left ventricular outflow tract, and abnormal insertion of the left atrioventricular valve may all cause obstruction. Whether discrete or tunnel-like, subaortic stenosis tends to progress and may recur following surgical resection. It may result in functional disruption of the aortic valve and secondary aortic regurgitation, which can pro- gress even after resection of subaortic stenosis. Atrial septal defects Interatrial communications are common both in congenital heart disease and in the general population. The different types of ASD are illustrated in Fig. 16.12.5. ASDs account for around 10% of con- genital heart disease. Types of atrial septal defect Patent foramen ovale PFO is a normal variant that occurs in 20–30% of the population. There is no deficiency of atrial septal tissue, but after birth—when left atrial pressure exceeds right atrial pressure and closes the PFO—the valve of the foramen ovale fails to fuse with the septum. Interest has risen in PFO in recent years because of its potential to be a route for paradoxical embolism or for thrombosis in situ, especially if associated with an aneurysmal interatrial septum. PFO is associated with cryptogenic embolic stroke in young adults, with Right ventricle Right atrium SVC Anolmalous right pulmonary vein in sinus venosus ASD Sinus venosus Secundum Primum/ atroventricular Coronary sinus Sinus venosus IVC True atrial septum Fig. 16.12.5 Sites of atrial septal defects. The shaded area delineates the true atrial septum. Sinus venosus and coronary sinus defects are therefore not strictly atrial septal defects although they permit shunting
at atrial level.

 neurological decompression sickness in divers, and with migraine with aura. Device closure of a PFO appears to protect against re- current stroke due to paradoxical embolism and decompression sickness. Whether PFO closure should be considered for secondary provision following cryptogenic stroke is controversial. Careful consideration should be given to all risk factors in as- sessing a patient with an embolic stroke and a PFO for suitability for device closure of the PFO. If there are multiple risk factors for arterial disease, such as advanced age, smoking history, diabetes, hyperlip- idaemia, hypertension, or proven existing atherosclerotic disease, then device closure of a PFO is unlikely to reduce the risk of a fur- ther embolic event. The same is true for patients with risk factors for left-sided intracardiac thrombosis, such as atrial fibrillation, mitral valve disease with a dilated left atrium, or left ventricular aneurysm. In contrast, patients with a PFO and previous embolic stroke who have risk factors for venous thrombosis, such as a thrombophilia or previous venous thromboembolism (i.e.

whose stroke was likely to be due to paradoxical embolism) may be protected against further events by device closure. Ostium secundum atrial septal defect Secundum ASD accounts for 40% of left-to-right shunts in adults aged over 40 years. It is commoner in females, with a sex ratio of 2:1, and may be familial. It may occur as an isolated abnormality with autosomal dominant inheritance, be associated with Holt– Oram syndrome (autosomal dominant skeletal abnormalities and atrioventricular conduction defects due to TBX5 mutation), and is a common association with Down's syndrome. ASD may be an incidental finding in an elderly patient at autopsy, and diagnosis in life may be delayed well into adulthood because of the absence of symptoms and subtlety of clinical signs. However, the natural history of this lesion is not benign: historically only 50% with unoperated nonrestrictive (large) ASD survived to the age of 40 years, and 10% beyond 60 years of age. Presentation in adulthood may be with symptoms of exertional dyspnoea or palpitation, or as a result of incidental clinical or radiographic findings. However, 20% may have developed atrial fibrillation by 40 years, with the figure rising to around 60% by the age of 60 years. Similarly, the volume-loaded right ventricle is well tolerated for many years, but may ultimately fail, usually after the fifth decade. Contributing factors to progression of symptoms with age may be increased left-to-right shunting due to an age-related reduction in left ventricular compliance causing an increase in left ventricular end-diastolic pressure and therefore left atrial pressure, and de- velopment of mitral regurgitation causing an increase in left atrial pressure. In addition, modest pulmonary arterial hypertension in- creases with age, so the right ventricle is exposed to pressure as well as volume overload, precipitating right ventricular failure. A left-to-right shunt at atrial level predisposes to paradoxical em- bolus since simple manoeuvres such as the Valsalva are sufficient to increase right atrial pressure and reverse the shunt. Patients with unoperated ASD are therefore at risk of embolic stroke, and should not dive because of the risk of paradoxical gas embolism. Interactions with coexisting heart disease Acquired disease may coexist and interact with congenital heart dis- ease, especially in the ageing patient. Left ventricular dysfunction due to coronary artery disease and systemic hypertension may in- crease the left-to-right interatrial shunt, resulting in a more rapid clinical deterioration. Similarly, mitral regurgitation increases the effective interatrial shunt and mitral valve abnormalities may be ac- quired secondary to the effects of a secundum ASD. There may be distortion of the anterior mitral valve leaflet with fibrotic shortened chordae due to the abnormal position of the interventricular septum as a result of chronic right ventricular overload. Lutembacher's syn- drome is the association of mitral stenosis with secundum ASD. Mitral valve disease is underestimated in the presence of an ASD because the left atrium is able to decompress through the ASD. If significant mitral stenosis or regurgitation is overlooked at the time of ASD repair, left atrial pressure will rise and the patient may decompensate dramatically. It is therefore vital to ensure thorough assessment of the mitral valve in any patient in whom ASD closure is planned. Since left ventricular dysfunction may also be masked by an ASD, the defect serving to allow the left ventricle to offload, ventricular function must also be assessed carefully prior to ASD closure, particularly in elderly patients. Coexisting pulmonary stenosis may be overestimated in the pres- ence of an ASD, since Doppler velocities are increased in the pres- ence of a left-to-right shunt. Pulmonary vascular disease and atrial septal defect Mild pulmonary hypertension with ASD is a common finding with advancing age, but pulmonary vascular resistance is rarely in ex- cess of 6 Wood units and advanced pulmonary hypertension is rare. Few ASDs develop a right-to-left shunt secondary to pulmonary vascular disease, and a causal relationship between ASD and the Eisenmenger syndrome remains controversial. In ASD, unlike other lesions which may cause the Eisenmenger syndrome such as large VSD, the pulmonary vasculature is not exposed to increased flow at systemic pressure. ASD

with a right-to-left shunt due to pulmonary vascular dis- ease and pulmonary hypertension occurs most commonly in young women, and in some cases may be due to idiopathic pulmonary arterial hypertension with an incidental ASD (see Table 16.12.4, pulmonary hypertension types A–D). In this combination, the prog- nosis may be better than for idiopathic pulmonary arterial hyperten- sion with intact atrial septum, the septal defect protecting the right heart from pressure overload by allowing right-to-left shunting. Persistence of the fetal pulmonary vascular pattern may be impli- cated in the development of pulmonary hypertension in some young patients with ASD. Patients living or born at high altitude have a higher incidence of pulmonary vascular disease because of the ef- fects of relative hypoxia on the pulmonary vasculature. Clinical signs If the defect is nonrestrictive the ‘a’ and ‘v’ waves of the jugular venous pulse tend to be equal. In older patients with reduced left ventricular compliance, the left and therefore right atrial pressure is raised, reflected by an elevated jugular venous pressure. A right ventricular heave may be felt at the left sternal border, and the di- lated pulmonary artery may be palpable in the left second inter- costal space. The first sound is loud because of increased diastolic flow across the tricuspid valve. If the left-to-right shunt is greater than approximately 2:1, the second heart sound is widely split and fixed, and there is loss of normal sinus arrhythmia. There may be a

 pulmonary flow murmur at the upper left sternal edge. Only if the ASD has a high gradient across it will it generate a murmur itself, usually a soft continuous murmur. This is the case if the defect is small and restrictive and the left atrial pressure high (e.g. if there is associated mitral stenosis). If the patient has pulmonary vascular disease, the signs will be the same as for pulmonary hypertension with right-to-left shunt. Investigations The ECG may show sinus node dysfunction, prolongation of the PR interval, right axis deviation, and QRS prolongation with rSr′ in lead V1—which does not represent incomplete right bundle branch block, but occurs since the last part of the myocardium to depolarize is the right ventricular outflow tract that is enlarged and thickened due to volume overload. Postoperatively the ECG may show sinus node dysfunction due to damage when the SVC is cannulated, and the PR interval returning to normal as right atrial size decreases. Macro re-entry circuits at the site of atrial surgery may result in postoperative ectopic atrial tachycardias. The typical chest radiograph shows dilated proximal pulmonary arteries with a small aortic knuckle, plethoric lung fields, and car- diomegaly secondary to dilatation of the right atrium and ventricle. Transthoracic echocardiography demonstrates the volume-loaded right atrium and ventricle. The size of the shunt can be estimated and colour-flow Doppler facilitates the detection of the site of the shunt. If transcatheter device closure is considered, a transoesophageal ap- proach is necessary to define the site and size of the ASD precisely and to identify the pulmonary veins. Cardiac catheterization is indicated only to calculate pulmonary vascular resistance if there is a suspicion of pulmonary hyperten- sion, or to exclude coexisting congenital or acquired cardiac path- ology such as coronary artery disease. Management Indications for closure of atrial septal defect Closure of an ASD is indicated if there is right heart volume over- load, left-to-right shunt is 1.5:1 or more, and the ASD is 10 mm or more in diameter. Prevention of recurrent paradoxical embolism is an additional indication for closure. Contraindications to closure are significant pulmonary hypertension (which may be suggested by a right-to-left shunt on exercise or at rest) and severe left ventricular dysfunction. In addition, merely closing the ASD in the presence of significant mitral valve disease is contraindicated. Irrespective of age, the benefits of device closure should be im- proved functional class, exercise capacity, and breathlessness. Repair of a large isolated secundum ASD by the third decade results in a normal life expectancy. Between the ages of 25 and 41 years it results in a good but shorter than normal

life expectancy, but beyond the age of 41 years morbidity and mortality remain sig- nificantly higher than normal. Nonetheless, functional status and longevity are improved following repair over the age of 40 years, 5- and 10-year survival being estimated as 98% and 95% respect- ively for patients who underwent repair, and 93% and 84% for those treated medically. Before undertaking repair, older patients (>60 years) should be thoroughly assessed for any subclinical left heart disease, in particular diastolic ventricular dysfunction, coronary artery or mitral valve disease, since these may be unmasked by isolated ASD closure. In balancing benefits and risks it must also be recognized that ASD repair in older patients does not reduce the risk of late atrial arrhythmia, particularly if there is right ventricular dysfunc- tion, elevated pulmonary artery pressure, or pre-existing atrial ar- rhythmia. Whether the incorporation of a modified maze procedure or cryoablation into the surgical repair of ASD will reduce the long- term incidence of existing or de novo atrial arrhythmia remains to be determined. Secundum ASDs up to 4 cm stretched diameter may be closed by transcatheter devices so long as the surrounding rim of atrial septal tissue is sufficient. Criteria for device closure of secundum ASD are size less than 4 cm; a situation away from the atrioventricular valves and pulmonary and caval veins; and normal pulmonary venous drainage. The risk of major complication during device closure is 1 to 2%. Following closure, antiplatelet or anticoagulant therapy is recommended for 3 to 6 months. Surgical repair carries also carries a low mortality and morbidity, but perioperative atrial fibrillation is common and recovery time is longer. Other forms of atrial septal defect Sinus venosus atrial septal defect Sinus venosus defects account for 2–3% of ASDs and have an equal sex incidence. They are not truly defects of the atrial septum, but since they allow shunting at atrial level, they are included in the classification of ASDs. The inferior border of the more common SVC type of sinus venosus defect is made by the superior limbus of the fossa ovalis, and the upper border comprises the junction of the SVC with the atrial mass. The superior caval vein overrides the atrial septum, connecting to both atriums, and the right upper pul- monary vein drains anomalously into the SVC. There may be an ec- topic atrial pacemaker because the defect is located in the area of the sinoatrial node. This may be reflected by a leftwards ‘p’ wave axis and an inverted ‘p’ wave in lead III. The sinus venosus defect may not be visualized with transthoracic echocardiography, and a transoesophageal approach is usually ne- cessary to define the defect and is associated anomalous pulmonary venous drainage. They are unsuitable for transcatheter device closure, both because there is no superior rim and because of anomalous drainage of one or more of the right pulmonary veins. The proximity of the sinus node to the SVC type of defect makes it vulnerable to damage during surgical repair; postoperative atrial pacing may be required. Coronary sinus defect The rarest form of ASD, this defect is at the site of entry of the cor- onary sinus to the right atrium. The unroofed coronary sinus is a variation of coronary sinus defect in which the partition between the coronary sinus and the left atrium is absent as the coronary sinus runs posteriorly along the floor of the left atrium. In this condition, a left SVC commonly connects directly to the left atrium, producing a right-to-left shunt and cyanosis. Ostium primum atrial septal defect This is a defect in the true atrial septum that exists as part of an AVSD and is discussed later in the chapter (see ‘Atrioventricular septal defects’).

16.12 Congenital heart disease in the adult 3573 Ventricular septal defects With the exceptions of bicuspid aortic valve and mitral valve prolapse, VSD is the commonest congenital cardiac malforma- tion, occurring in around 3 per 1000 live births. It occurs equally in both sexes. Defects may exist in isolation, in association with other lesions such as coarctation of the aorta, or as an integral part of lesions such as tetralogy of Fallot. This section deals with isolated VSDs. Morphology

and classification An understanding of the basic anatomy of the ventricular septum is necessary to appreciate the various types of VSD. A VSD arises when there is failure of one of the components of the ventricular septum to develop correctly. The septum comprises four parts and is described as viewed from the right ventricle (Fig. 16.12.6): • Inlet septum—separates the mitral and tricuspid valves • Muscular trabeculated septum—extends from the tricuspid valve leaflet attachments to the muscle separating the tricuspid and pul- monary valves (the crista supraventricularis) • Outlet septum—extends from the crista to the pulmonary valve • Perimembranous septum—small fibrous area bordered by the aortic and tricuspid valves VSDs are classified by their location within the septum and by their borders, again viewed from the right ventricle. There are three types: muscular, perimembranous and doubly committed subarterial (Figs. 16.12.6 and 16.12.7). The position of muscular and perimembranous VSDs may be inlet, trabecular, or outlet, depending on which part of the right ventricle they open into. Perimembranous VSD is the commonest type of defect. Only 5 to 7% of VSDs in Europe and North America are doubly committed subarterial defects, whereas they account for up to 30% of defects in Asian patients. Clinical presentation and complications of unoperated ventricular septal defect The presentation of an isolated VSD depends on its size and haemo- dynamic effects (Table 16.12.6). Perimembranous and doubly com- mitted subarterial VSDs may be associated with the development of aortic valve leaflet prolapse and aortic regurgitation, and the con- duction tissue in these types of defects is vulnerable to damage at operation. Adults with isolated unoperated restrictive VSDs are usually asymptomatic and acyanotic, with normal arterial and jugular venous pulses. There may be a thrill at the left sternal border, the left ventricular apex may be thrusting if the defect is large enough to cause volume overload, and a dilated pulmonary artery may be palpable. The second heart sound is usually normally split. There is a loud, harsh pansystolic murmur at the left sternal edge, which is softer and shorter (early systolic) in very small defects. Late complications of unoperated small VSDs include significant risk of endocarditis due to the high-velocity jet from left-to-right ventricles, particularly if the jet is directed onto tricuspid valve tissue; aortic regurgitation if the aortic valve forms part of the border of the VSD; atrial arrhythmia if there is left heart volume overload; and small increased risk of sudden death and ventricular arrhythmia. A moderate-sized restrictive VSD may cause left heart volume overload, and in the long term, atrial arrhythmias and left ventricular dysfunction. A VSD causes left, rather than right, ventricular dilata- tion because the left-to-right shunt reaches the right ventricle during ventricular systole: the right ventricle cannot dilate during contrac- tion, so the additional blood is directed straight into the pulmonary circulation and back into the left heart during diastole. Thus, the left heart is subject to volume overload. Membranous septum Inlet septum Outlet septum Muscular trabecular septum PV AV TV III IIa IIb I Fig. 16.12.6 Schematic representation to show the sites of different types of ventricular septal defects (VSDs). The heart is in cross-section, viewed from the right ventricular aspect. I, muscular VSD; IIa, perimembranous outlet VSD; IIb perimembranous inlet VSD; III doubly committed subarterial VSD. AV, aortic valve, seen through VSD; PV, pulmonary valve; TV, tricuspid valve.

section 16 Cardiovascular disorders 3574 Larger VSDs rarely present for repair in adulthood since the large left-to-right shunt is unlikely to allow unoperated survival unless pulmonary vascular disease has developed. Nonrestrictive defects are not associated with the classical VSD murmur since left and right ventricular pressures are equal. Investigations Investigation should determine the type and number of VSDs, the size of the defect (restrictive or nonrestrictive), an estimation of the size of the shunt (Qp:Qs), pulmonary artery pressure and resistance, and assessment of left

and right ventricular function and volume and pressure overload. Associated lesions that may alter manage- ment should be identified, especially aortic regurgitation, subaortic stenosis, and right ventricular outflow tract obstruction. The chest radiograph is normal if the defect has been small from birth. If the VSD is (or has been) larger, the left ventricle, left atrium, and pulmonary trunk may be dilated and there may be increased pulmonary vascularity. The ECG shows a normal QRS axis unless there are multiple defects, when there may be left axis deviation. In the presence of a large left-to-right shunt the 'p' wave may be broad and there may be evidence of left ventricular hypertrophy. Two-dimensional echocardiography identifies the number and site of defects as well as describing the morphology and associated de- fects. Doppler is used to estimate the size and direction of the shunt, and right ventricle to left ventricle pressure difference, but this may not be accurate if there is an obliquely lying muscular VSD. Cardiac catheterization is important to measure the size of shunt and pul- monary vascular resistance, with reversibility studies if baseline re- sistance is high. Management and prognosis Repair of a VSD is indicated in the presence of symptoms, if Qp:Qs is greater than 2:1, or if there is ventricular dysfunction with right ventricular pressure overload or left ventricular volume overload. Repair should also be undertaken if there are coexisting lesions such as significant right ventricular outflow tract obstruction, or more than mild aortic regurgitation or aortic valve prolapse in the pres- ence of an outlet VSD. An episode of endocarditis may also be con- sidered as an indication for VSD closure. If the pulmonary artery pressure is more than two-thirds systemic pressure, repair should only be considered if Qp:Qs exceeds 1.5:1 or if there is evidence of reversibility in response to pulmonary vasodilators such as oxygen and nitric oxide. The surgical approach aims at avoiding damage to important structures such as the conducting tissues, which are especially vul- nerable in perimembranous defects. Transatrial repair reduces the risk of postoperative ventricular arrhythmias by avoiding a right ventriculotomy. Transient postoperative complete heart block is as- sociated with an increased risk of late high-degree block, and per- manent pacemaker implantation is indicated in the 1–2% of patients in whom complete heart block persists, even if they are asymptom- atic, because there is a significant risk of late sudden death. The prognosis after VSD repair in the early years of life is good, but if repair is delayed into late childhood left ventricular dilatation may persist and systolic function be impaired. Long-term postoperative survival depends on the presence of pulmonary hypertension, left ventricular dysfunction, and complications such as aortic regurgita- tion and endocarditis. Transcatheter device closure of VSDs is possible providing that valvar apparatus can be avoided. Both muscular and selected perimembranous VSDs may be device closed, the latter requiring experienced hands to avoid damage to the aortic valve and heart block. This approach is particularly useful for defects that are diffi- cult to access or close surgically, and a hybrid surgical/interventional technique may be used. Atrioventricular septal defects The key feature of an AVSD (previously termed endocardial cushion defect or atrioventricular canal) is a common atrioventricular Aortic valve RA RV PA TV PV * ** Fig. 16.12.7 Schematic representation of the transthoracic echocardiographic parasternal short-axis view, to demonstrate sites of ventricular septal defects (VSDs).**, site of doubly committed subarterial VSD—the aortic and pulmonary valves are in continuity and form the roof of the VSD.*, site of subaortic perimembranous VSD. PA, pulmonary artery; PV, pulmonary valve; RA, right atrium; RV, right ventricle; TV, tricuspid valve; VSD, ventricular septal defect. Table 16.12.6 Grading of ventricular septal defects by size Small Moderate Large Eisenmenger syndrome Pulmonary artery pressure: systemic pressure ratio <0.3 0.3–0.6 RV = LV pressure RV ≥ LV pressure Qp:Qs <1.4: 1 1.4–2.2: 1

> 2.2:1 <1.5: 1 Clinical grading Negligible haemodynamic changes, normal LV LA and LV enlargement and reversible pulmonary hypertension Pulmonary vascular disease (Eisenmenger syndrome) will develop unless there is RVOTO Restrictive (RV pressure < LV pressure in absence of RVOTO) Nonrestrictive (equal RV and LV pressures in absence of RVOTO) Qp, pulmonary blood flow; Qs, systemic blood flow; RVOTO, right ventricular outflow tract obstruction.

junction and atrioventricular valve ring (Fig. 16.12.8). The atrio- ventricular septum is absent, and the atrioventricular valves share a common junction and fibrous ring, with a five-leaflet atrioven- tricular valve. Since they share common leaflets, the valves are not correctly called mitral and tricuspid valves, but left and right atrio-ventricular valves. As a consequence, the normal offsetting of the right atrioventricular valve towards the right ventricular apex is absent. In addition, the aorta is 'unwedged' from its normal pos- ition between the left and right atrioventricular valves. The left ven- tricular outflow tract is therefore elongated ('gooseneck') and has the propensity to develop obstruction, often due to septal attach- ments of the left atrioventricular valve. 'Cleft mitral valve' refers to the commissure between the anterior and posterior bridging leaflets that renders the left atrioventricular valve potentially regurgitant. The left ventricular papillary muscles are abnormally placed an- teriorly and posteriorly instead of in the normal anterolateral and posteromedial positions. Ostium primum defect describes the atrial component of an AVSD. There are two types of AVSD, partial and complete. Both have a common atrioventricular junction, but in a partial AVSD the right and left atrioventricular valves have separate orifices and the VSD is usually small or absent, and in a complete AVSD there is a common atrioventricular valve and valve orifice, and the VSD is usually large. AVSD occurs with equal sex incidence. The complete form of the defect is most commonly associated with Down's syndrome. A single gene defect may be responsible for AVSD in nonsyndromic patients, when the recurrence risk is about 10% if the mother has an AVSD, less if the father is affected. The physiological consequences of an AVSD are the same as for other conditions with left-to-right shunting at atrial or ventricular level, but may be complicated by left atrioventricular valve regur- gitation or left ventricular outflow tract obstruction. Pulmonary vascular disease may develop if the VSD is large and nonrestrictive. Patients with Down's syndrome are at particular risk of this compli- cation, and coexisting upper airway obstruction and sleep apnoea, and abnormal pulmonary parenchyma, may be contributory factors. Investigations The ECG is distinctive, with a left and superior QRS axis and notching of 'S' waves in the inferior leads. The chest radiograph appearances depend on the degree of interatrial shunting and left atrioventricular valve regurgitation, the former producing cardiomegaly due to left heart dilatation and the latter left atrial enlargement. There may be increased pulmonary vascularity, particularly in young patients with complete AVSD and high pulmonary blood flow. Transthoracic echocardiography reveals the detailed anatomy of the defect and establishes the site and degree of shunting, the pres- ence and nature of left ventricular outflow tract obstruction, and the function and anatomy of the atrioventricular valves. The indications for cardiac catheterization are the same as for secundum ASD, namely to exclude inoperable pulmonary vascular disease. In addition, useful information may be obtained regarding the severity of left atrioventricular valve regurgitation and left ven- tricular outflow tract obstruction. Clinical presentation and course First presentation may occur in adulthood if the left-to-right shunt is small and the left atrioventricular

valve is competent. Physical signs are the same as in other ASDs, and there may also be an apical pansystolic murmur. Paradoxical embolism is less common than in secundum ASD because the position of the primum defect low in the interatrial septum avoids the streaming of blood from the in- ferior vena cava that is most likely to carry emboli and is directed towards the midportion of the septum. Normal heart Partial AVSD Complete AVSD AV AV AV TV MV RAVV RAVV LAVV LAVV Superior bridging leaflet Inferior bridging leaflet Left mural leaflet Right inferior leaflet Right anterosuperior leaflet Fig. 16.12.8 Schematic representation of the atrioventricular junction in atrioventricular septal defect (AVSD). Short-axis view, seen from the atrial aspect. In both forms of AVSD, there is a common atrioventricular valve ring guarded by five valve leaflets. In the partial defect, the superior and inferior bridging leaflets fuse to create two separate valve orifices. This fusion does not occur in complete AVSD, so there is a common valve orifice. AV, aortic valve; LAVV, left atrioventricular valve; RAVV, right atrioventricular valve.

section 16 Cardiovascular disorders 3576 Most adult patients have undergone surgery to repair the defect and left atrioventricular valve: others have survived unoperated and may have developed pulmonary vascular disease. Late complications after repair of AVSD include recurrent atrioven- tricular valve regurgitation, the severity of which may increase with age in response to changes in the left ventricle due to ageing, ischaemia, or systemic hypertension; residual ASD or VSD; residual or recurrent left ventricular outflow tract obstruction, which may be difficult to relieve surgically if it involves left atrioventricular valve tissue; complete heart block, related to the abnormally positioned atrioventricular node that is particularly vulnerable to intraoperative damage; endocarditis, re- lating largely to the left atrioventricular valve; and atrial arrhythmia. It is vital to read the original operation note when planning ablation, since the mouth of the coronary sinus is often left opening into the left atrium, making it inaccessible to the electrophysiologist. Arterial disorders Coarctation of the aorta Aortic coarctation is a narrowing of the aorta, usually sited near the ligamentum arteriosum. It is one of the commonest congenital cardiac lesions, occurring in 1 in 12 000 live births, with a male to female ratio of 3:1. Coarctation is part of a generalized arteriopathy with consider- able variation in anatomy and severity, ranging from a mild obstruction to interruption of the aorta, and from a discrete fibromuscular shelf to hypoplasia of the arch. Coarctation is most strongly associated with bicuspid aortic valve, which coexists in up to 80% of cases. Ascending and descending aortopathy may be present, with medial changes and arterial wall stiffness; aneurysm formation, dissection, and the com- plications of hypertension require lifelong surveillance. Other associ- ations are VSD, patent arterial duct, subaortic ridge, and mitral valve abnormalities. It is a frequent finding in Turner’s syndrome and is also associated with congenital aneurysm of the circle of Willis. Clinical presentation and course Most patients present in infancy, but some survive into adulthood before being diagnosed at routine examination or during investi- gation for hypertension, leg claudication, angina, heart failure, or cerebral haemorrhage. Historically, more than 75% with unoperated coarctation died by age 50 years, from premature coronary disease, stroke, or aortic dissection. Clinical findings include upper body hypertension: the leg blood pressure is lower, as is that in the left arm if the subclavian artery is involved in the coarctation. If there is a good collateral supply, fem- oral arteries may be easily palpable, but they are usually reduced, with radiofemoral delay. Intercostal collaterals may be both visible and palpable over the patient’s back. There is an ejection systolic murmur from the site of coarctation, and systolic collateral murmurs may be heard. Fundoscopy shows a typical corkscrew appearance of the ret- inal vessels and there may be evidence of hypertensive retinopathy. Investigations There may be electrocardiographic evidence of left ventricular hypertrophy. The chest radiograph

(Fig. 16.12.9) has a typical appearance. Transthoracic echocardiography may show left ventricular hyper- trophy, with the coarctation site visualized on two-dimensional imaging and its severity assessed using Doppler mode from the suprasternal notch. A peak gradient of over 20 mm Hg is significant, especially if accompanied by a diastolic tail. MRI provides definitive noninvasive haemodynamic data and two- and three-dimensional images of the coarctation site, collat- erals and related vessels (Fig. 16.12.10). It may obviate the need for angiography unless coronary disease is suspected. In the adult, diagnostic angiography is usually reserved for assessing coronary disease. Management Surgical repair Surgical repair is the conventional approach in neonates and chil- dren, with a risk of less than 1% for those with simple coarctation. Extensive collateral vessels and nonelastic diseased aortic tissue make surgical repair of adult coarctation challenging, and this is as- sociated with significant morbidity. The incidence of perioperative spinal cord ischaemia and paraplegia is up to 0.4%, those patients without an abundant collateral circulation probably being most at risk. Those with well-developed collaterals are at risk of significant intraoperative haemorrhage. Early postoperative hypertension is common and may be difficult to control, and postoperative intes- tinal ileus may persist for several days. Transcatheter balloon dilatation and primary stenting of na- tive coarctation in adults are usually the preferred alternatives to Fig. 16.12.9 Chest radiograph of an 18-year-old man with unoperated coarctation of the aorta and bicuspid aortic valve. There is bilateral rib notching (arrows) and a prominent deformed aortic knuckle. The dilated ascending aorta (*) indicates the associated aortopathy.

surgery. The use of primary stents, particularly covered stents, is likely to support the aorta following dilatation and to reduce the risk of aortic dissection or late aneurysm formation. However, this interventional approach should only be done in specialist centres; careful follow-up is required. Follow-up after coarctation repair Follow-up after repair of coarctation should be lifelong, since late complications are frequent: residual or recoarctation, aneurysm formation, persistent hypertension despite adequate repair, pre- mature atherosclerotic disease, and progression of associated le- sions such as bicuspid aortic valve and aortopathy. Older age at repair is the main risk factor influencing longevity. Late survival is 92% for patients repaired in infancy, 25-year survival is 75% for those repaired between ages and 40 years, but 15-year survival is only 50% for those repaired at age more than 40 years. Recoarctation may be diagnosed when the resting arm–leg sys- tolic blood pressure gradient is 20 mm Hg at rest and 50 mm Hg after exercise. This occurs most commonly following neonatal repair by end-to-end anastomosis, and the diagnosis should be sought when there is new or persisting hypertension. Blood pressure should be recorded in both arms of all such patients; spuriously low readings may be obtained if one of the subclavian arteries (usually the left) is involved in the repair or recoarctation. MRI is the investigation of choice for both recoarctation and aneurysm formation after coarctation repair. High-resolution CT is used following stent repair of coarctation (Fig. 16.12.11), since the artefact produced by the stent renders MRI unhelpful. Balloon angioplasty with or without stent insertion is used to relieve most recoarctations, but reoperation is required for some patients with complex anatomy. The 14-year incidence of aneurysm formation at the site of repair is up to 27%; it occurs most commonly in adults and in those with Dacron patch repair. An aneurysm may rupture into the bronchial tree or oesophagus, hence any patient with a history of coarctation who presents with haemoptysis or haematemesis should undergo emergency noninvasive diagnostic imaging (MRI or CT) and surgical repair. Bronchoscopy and conventional angiography are contraindi- cated since they may cause further damage to the area. Hypertension is a major risk factor for atherosclerotic disease and may persist despite an apparently good result

from surgical repair. Continuing hypertension relates in part to older age at time of sur- gery. Nonetheless, late repair of coarctation or re-coarctation does render systolic hypertension easier to control. Patent arterial duct The pathophysiological consequences of a patent arterial duct in adulthood depend on the size of the shunt. Small ducts are of no haemodynamic significance and are associated with a low risk of infective endarteritis. Moderate-sized ducts may cause left heart volume overload and late atrial fibrillation and ventricular dysfunc- tion. A large nonrestrictive duct may cause pulmonary vascular dis- ease (see 'Eisenmenger syndrome', earlier). Duct closure is usually recommended if a duct is clinically detect- able (i.e. there is a systolic or continuous (machinery) murmur in the left subclavicular area, to avoid long-term haemodynamic com- plications). Ducts up to 14 mm in diameter are usually suitable for transcatheter device closure. Pulmonary vascular disease should be excluded before repair of large ducts is undertaken.
Fig. 16.12.10 MRI of a 20-year-old woman who presented with hypertension. There is a severe discrete coarctation (↓), multiple tortuous collaterals and a dilated ascending aorta (*) associated with a bicuspid aortic valve. Fig. 16.12.11 High-resolution CT scan demonstrating stent deployed at native coarctation site.

 Aortopulmonary window In this rare condition there is a direct communication between adja- cent portions of the proximal ascending aorta and pulmonary artery. The communication is usually large and the physiological conse- quences are the same as for a large patent arterial duct. Rare patients surviving unoperated into adulthood will be cyanosed and have de- veloped the Eisenmenger syndrome. If pulmonary vascular resist- ance is low at the time of childhood repair, long-term postoperative survival is good. Truncus arteriosus/common arterial trunk This condition accounts for 1–4% of all congenital heart disease. It may coexist with interrupted aortic arch, coarctation, coronary anomalies, and DiGeorge syndrome. A single great artery arises from the heart and gives rise to the coronary arteries, aorta, and pul- monary arteries. There is a single semilunar 'truncal' valve that has three or more leaflets, and a subtruncal VSD. Most patients present in infancy with heart failure. If they are left unoperated, pulmonary vascular resistance rises, cyanosis becomes more marked, and the Eisenmenger syndrome becomes established. Repair before pulmonary vascular disease develops involves closure of the VSD, detachment of the pulmonary arteries from the common arterial trunk, and placement of a valved conduit from right ven- tricle to pulmonary artery. The truncal valve then functions as the aortic valve. Late complications following repair include truncal re- gurgitation, truncal (aortic root) dilation, ventricular dysfunction, and the need to replace stenotic conduits. Sinus of Valsalva aneurysm There is dilation of one of the aortic valve sinuses between the aortic valve annulus and sinotubular junction, and the aneurysm progres- sively dilates and may rupture. The right and noncoronary cusps are most often affected; rupture of a noncoronary sinus aneurysm is nearly always into the right atrium and of the right coronary sinus into the right ventricle or atrium. Involvement of the left coronary sinus is rare. Rupture usually occurs in early adulthood and may be precipitated by endocarditis. If sudden, it is accompanied by tearing chest pain, breathlessness, and sudden-onset symptoms suggesting heart failure, with a loud continuous murmur and good systolic ventricular function. Small perforations may remain asymptomatic for many years. The diagnosis and site of the rupture is confirmed echocardiographically and/or angiographically before surgical or transcatheter repair. Coronary artery anomalies The importance of congenital coronary anomalies lies in their poten- tial to impair myocardial blood flow and cause ischaemia and sudden death. Evidence of ischaemia is the main indication for repair. The major types of coronary anomaly are summarized in Box 16.12.3. Anomalous origin of the coronary arteries from an

inappropriate aortic sinus Ischaemia is particularly associated with an anomalous proximal coronary course between the aorta and pulmonary trunk, an intra- mural proximal segment of the coronary artery inside the aortic wall, and acute angulation between the origin of an anomalous cor- onary artery and the aortic wall. Anomalous origin of the left coronary artery from the pulmonary artery This rare condition, known as ALCAPA, usually presents in infancy with myocardial ischaemia and left ventricular failure when pul- monary vascular resistance decreases. However, 10–15% survive into adulthood because an adequate intercoronary collateral circulation is established. Adults may be asymptomatic or present with myocar- dial ischaemia or mitral regurgitation due to papillary muscle dys- function. Survival following surgical repair depends on the amount of ischaemic myocardial damage and degree of mitral regurgitation. Congenital coronary arteriovenous fistulas The coronary arteries arise normally from their aortic sinuses, but a fistulous branch communicates directly with the right ventricle in 40% of cases, the right atrium in 25%, pulmonary artery in 15%, or rarely the SVC or pulmonary vein. Survival to adulthood is usual, but lifespan may be reduced, depending on the size of the fistulous connection and the presence of myocardial ischaemia resulting from any coronary steal phenomenon. Symptoms increase with age and there is a risk of endocarditis, heart failure, arrhythmia, myocar- dial ischaemia and infarction, and sudden death. Surgical repair is recommended unless there is a trivial isolated shunt. Some smaller fistulae are suitable for transcatheter device occlusion. Systemic venous anomalies These anomalies frequently form part a more complex lesion, par- ticularly isomerism. Normal systemic venous drainage is illustrated in Fig. 16.12.12. Superior caval vein anomalies A persistent left-sided SVC occurs in 0.3% of the general popu- lation, approximately 3% of patients with congenital heart dis- ease, and 15% of those with tetralogy of Fallot. The left SVC may be visible on the chest radiograph. It usually drains to the right atrium via the coronary sinus, which is seen to be dilated on two- dimensional echocardiography (Fig. 16.12.13). A right-sided SVC is usually also present, but the two caval veins do not usually com- municate via the brachiocephalic vein. This common anomaly should be sought routinely at cardiac catheterization; although it Box 16.12.3 Major types of coronary anomaly • Anomalous origin from inappropriate aortic sinus or coronary vessel — LAD from right aortic sinus or right coronary artery (RCA) — Absent LMS (separate origins of LAD and Cx) — Cx from right aortic sinus or RCA or absent Cx — RCA from left aortic sinus, posterior sinus, or LAD — Single coronary artery from right or left aortic sinus • Anomalous origin from other systemic artery (rare) — Innominate, subclavian, internal mammary, carotid, bronchial arteries, or descending aorta • Anomalous origin from pulmonary artery • Coronary arteriovenous fistulae Cx, circumflex; LAD, left anterior descending; LMS, left main stem; RCA, right coronary artery.

 does not have any haemodynamic significance, it may cause tech- nical difficulties during transvenous pacemaker insertion and car- diac surgery (Fig. 16.12.14). Other SVC anomalies are rare. An absent right SVC is associated with arrhythmias including atrioventricular block, sinus node dys- function, and atrial fibrillation. The left, or rarely the right, SVC may connect directly to the left atrium, causing an obligatory right-to-left shunt and cyanosis. This may be associated with isomerism of the atrial appendages. Inferior caval vein anomalies Azygos continuation of the inferior vena cava (IVC) occurs in 0.6% of patients with congenital heart disease. The infrahepatic portion of the IVC is absent and continues to the SVC via an azygos vein; the hepatic veins drain directly into the right atrium. This is often associated with complex lesions, particularly left isomerism. The chest radiograph reveals an absence of the IVC at the junction of the diaphragm with the right heart border and a dilated azygos vein (Fig. 16.12.15). Direct connection of the IVC Left internal jugular vein Left subclavian vein Left brachiocephalic vein

Hemiazygos vein Ascending lumbar vein Lumbar azygos veins Azygos veins Right brachiocephalic vein Right subclavian vein Right internal jugular vein IVC SVC Fig. 16.12.12 Schematic diagram of normal systemic venous drainage. CS Ao LV LA RV Fig. 16.12.13 Persistent left superior vena cava. Transthoracic two- dimensional echocardiogram, parasternal long-axis view. The coronary sinus, receiving the persistent left superior vena cava, is dilated. Ao, aorta; CS, coronary sinus; LA, left atrium; LV, left ventricle; RV, right ventricle. Fig. 16.12.14 Chest radiograph of a 56-year-old man with bicuspid aortic valve, aortic regurgitation, and coarctation. A left superior vena cava draining via the coronary sinus to the right atrium is marked by the path taken by the transvenous pacing leads, inserted for complete heart block. Fig. 16.12.15 Chest radiograph of a 50-year-old man with abdominal situs inversus (*) and laevocardia. Left atrial isomerism is inferred from the symmetrical long bronchi (bilateral morphological left lungs). The inferior vena cava is absent at the level of the diaphragm (small arrow), and the azygos vein receiving inferior caval venous blood is prominent (large arrow).

section 16 Cardiovascular disorders 3580 to the left atrium is rare: the patient is cyanosed, as in the SVC–left atrium connection. Pulmonary venous anomalies Total anomalous pulmonary venous drainage Total anomalous pulmonary venous drainage occurs in 1 in 17 000 live births. All four pulmonary veins drain into the right atrium, ei- ther directly or via a common vein into a systemic vein. The anom- alous veins may follow (1) a supracardiac course draining to the SVC, azygos, or brachiocephalic veins; (2) a cardiac course, draining to the right atrium directly or to the coronary sinus directly or via a persistent left SVC connection; or (3) an infradiaphragmatic course, draining to the portal vein or IVC. Since the pulmonary venous confluence is a left atrial struc- ture, total anomalous venous drainage is obligatory in right isom- erism: there are bilateral right atriums and no left atrium for the pulmonary veins to drain to. The presence of pulmonary venous obstruction is the most important predictor of a poor outcome. Associated anomalies include an obligatory right-to-left shunt, nearly always at atrial level. The condition presents in infancy, hence 98% of patients reaching the adolescent or adult clinic will have survived corrective surgery in early life. Unless there is residual pulmonary hypertension most such adults should be asymptomatic, having a normal cardiovas- cular examination and an excellent prognosis. Patients who are still growing may develop obstruction of the redirected pulmonary venous pathway and present with dyspnoea, signs of pulmonary oe- dema, evidence of pulmonary venous congestion on the chest radio- graph, and an obstructive echo Doppler flow signal at the site of the stenosis. The rare patient who reaches adulthood unoperated is likely to have survived because of a large ASD and unobstructed pulmonary venous drainage. They will be cyanosed, have developed pulmonary vascular disease, and be at risk of atrial tachyarrhythmias and right heart failure. The chest radiograph has the appearance of a large ASD with a small aortic knuckle, cardiomegaly, and a dilated main pul- monary artery. In addition, the anomalous veins may cause an ab- normal vascular shadow. Partial anomalous pulmonary venous drainage There is anomalous drainage of some of the pulmonary veins to the right atrium. In 90% of cases the anomalous pulmonary venous con- nection is between the right upper or middle pulmonary vein to the SVC or right atrium, usually in association with an ASD, 10 to 15% of all ASDs and nearly all SVC-type sinus venosus ASDs being asso- ciated with partial anomalous pulmonary venous connection. Partial anomalous pulmonary venous drainage may present in adult life with signs of a left-to-right shunt at atrial level; the patho- physiological consequences are the same as for an ASD with an equivalent shunt. Transthoracic echocardiography may be indicative of a shunt at atrial level, but in adults it may not be possible to image the pul- monary veins and a transoesophageal approach is likely to be ne- cessary. The

identification of all the pulmonary veins is crucial in assessing the suitability of a secundum ASD for transcatheter device closure, this technique being contraindicated in the presence of anomalous pulmonary veins (see ‘Atrial septal defects’, earlier). The indications for surgical repair are the same as those for re- pair of an ASD, but the surgical manoeuvres necessary to commit the anomalous pulmonary vein(s) to the left atrium should be taken into account when deciding whether surgery is appropriate. Surgical repair is straightforward when, for example, the right upper pul- monary vein drains to the superior vena cava in association with a sinus venosus ASD. However, a conduit or tunnelled repair may be required if the anomalous vein(s) drain to the inferior or superior vena cavae more distantly from the atrial mass. The low velocity, low-pressure flow within such a repair is associated with a risk of subsequent obstruction and loss of perfusion to the affected lung tissue, with consequent loss of any benefit to the patient. Scimitar syndrome Partial anomalous pulmonary venous drainage also occurs as part of the rare familial ‘scimitar syndrome’ (OMIM 106700) in which part or all of the right pulmonary venous drainage is to the IVC below the diaphragm. The affected lung lobes are usually hypoplastic (Fig. 16.12.16) and are supplied with arterial blood from the descending aorta. Recurrent infection and bronchiectasis may de- velop in the hypoplastic lobes or lung. MRI demonstrates the ab- normal arterial supply and venous drainage of the affected lung segment, and may obviate the need for diagnostic cardiac cath- eterization. Surgical repair may be complicated by difficulty in maintaining perfusion to the affected lung, and lobectomy may be required. In view of this it should be remembered that patients pre- senting with scimitar syndrome for the first time in adult life have a good unoperated prognosis, similar to that of a small ASD. Fig. 16.12.16 Chest radiograph of a 25-year-old woman with scimitar syndrome. The heart is shifted into the right hemithorax because the right lung is small. The ‘scimitar’ shadow (arrow) is produced by the anomalous descending venous channel which drains into the dilated inferior vena cava (*).

16.12 Congenital heart disease in the adult 3581 Transposition complexes The nomenclature of the transposition complexes may cause confu- sion. There are two types: • Complete transposition of the great arteries (TGA)—this condi- tion is described as concordant atrioventricular connection and discordant ventriculo-arterial connection (Fig. 16.12.15), previ- ously known as D-TGA (Fig 16.12.17). Without intervention it is not compatible with life, since once the arterial duct and foramen ovale have closed, there is complete separation of the systemic and pulmonary circulations such that deoxygenated blood from the systemic veins recirculates to the aorta, and oxygenated blood from the pulmonary veins recirculates to the pulmonary artery. • Congenitally corrected transposition of the great arteries (cTGA)—this condition is described as discordant atrioven- tricular and ventriculo-arterial connections. (Fig. 16.12.18), previously known as L-TGA. cTGA is congenitally physiolo- gically ‘corrected’: deoxygenated systemic venous blood reaches the pulmonary artery, albeit via the morphological left ven- tricle; oxygenated pulmonary venous blood reaches the aorta, but via the morphological right ventricle. Complete transposition of the great arteries (discordant atrioventricular connection, concordant ventriculo-arterial connection) TGA accounts for about 5% of congenital cardiac malforma- tions and is four times more common in males than females. Associated anomalies such as VSD and pulmonary stenosis occur in approximately one-third of patients. As described earlier, unoperated survival after closure of the foramen ovale and arterial duct have closed is dependent upon the presence of other associ- ated lesions, such as a VSD, which allow mixing of the two circula- tions. Without intervention, 30% die within the first week and only 10% survive their first year. If the atrial and ventricular septums are intact, immediate neo- natal management requires a prostaglandin infusion to maintain patency of

the arterial duct until a balloon atrial septostomy is performed. Post-septostomy, the neonate remains cyanosed, but there is usually adequate mixing to allow it to thrive until definitive surgery. There are survivors of four operative approaches in adult clinics: interatrial repair (Mustard or Senning), arterial switch, Rastelli and 'palliative' Mustard/Senning or arterial switch oper- ations. The indications and outcomes of each are described next. Interatrial repair: Mustard or Senning operations This approach was first described in 1957 and can be used for those with TGA or TGA with VSD. Interatrial repair involves excision of the atrial septum and placement of a saddle-shaped patch ('baffle') to direct pulmonary venous blood into the right atrium and right ventricle and thence to the aorta (Fig. 16.12.19). Systemic venous blood is directed into the left atrium, left ventricle, and pulmonary artery. The right ventricle and tricuspid valve therefore support the systemic circulation. The Senning operation uses the patient's own atrial septum to create the baffle, whereas the Mustard operation uses nonautologous material. The Mustard/Senning operations have been superseded by the arterial switch operation, apart from ** * RA LA RV Ao LV PA TV MV Fig. 16.12.17 Schematic representation of complete transposition of the great arteries (discordant ventriculo-arterial connections). The pulmonary and systemic circulations are completely separate once the arterial duct and foramen ovale close. Without intervention, the condition is not compatible with life. Ao, aorta; LA, left atrium; LV, left ventricle; MV, mitral valve; PA, pulmonary artery; RA right atrium; RV right ventricle; TV, tricuspid valve; **patent arterial duct; *patent foramen ovale. RA LA RV Ao LV PA TV MV Fig. 16.12.18 Schematic representation of congenitally corrected transposition of the great arteries (discordant atrioventricular and ventriculo-arterial connections). The circulation is congenitally physiologically 'corrected' in that systemic venous blood reaches the pulmonary artery (via the left ventricle) and pulmonary venous blood reaches the aorta (via the right ventricle). Ao, aorta; LA, left atrium; LV, left ventricle; MV, mitral valve; PA, pulmonary artery; RA, right atrium; RV, right ventricle; TV, tricuspid valve.

section 16 Cardiovascular disorders 3582 some uncommon situations in cTGA in which a Senning operation is part of a more complex procedure. However, there are still signifi- cant numbers of adult survivors of the interatrial repair. Clinical signs and complications after interatrial repair The systemic right ventricle causes a parasternal heave. The aortic component of the second heart sound may be palpable and loud, and the second sound single, due to the anterior-lying aorta. The pres- ence of cyanosis suggests a baffle leak allowing right-to-left shunting between the systemic and pulmonary venous atriums. Systemic venous pathway obstruction may be associated with elevation of the jugular venous pressure and hepatomegaly. Complications after interatrial repair include: • Progressive bradycardias and sinus node disease, due to damage to the sinus node during repair. • Atrial flutter and interatrial re-entry tachycardias, due to extensive atrial surgical scarring—these are often poorly tolerated, are asso- ciated with sudden death, and should be treated with urgent DC cardioversion rather than antiarrhythmic drugs, since the latter can precipitate cardiovascular collapse if there is underlying im- paired ventricular function. After an episode of flutter, ablation should be performed. • Systemic venous pathway obstruction, which usually only causes symptoms if both the IVC and SVC pathways are narrowed—if only one pathway is narrowed, the systemic venous blood flows along the azygos vein and drains to the heart via the unobstructed pathway; obstruction can usually be relieved by balloon dilation or stenting. • Pulmonary venous pathway obstruction such that flow into the atrium and systemic ventricle is obstructed—the patient will be breathless, but clinical signs are few; it is demonstrated by echocardiography or MRI; surgical repair is usually necessary; transcatheter intervention is usually unsatisfactory. • Baffle leak—holes along the baffle suture lines allow shunting which may

be left-to-right, or right-to-left, causing cyanosis; a percutaneous approach sometimes allows successful closure of these interatrial communications. • Systemic atrioventricular valve regurgitation—the tricuspid valve is poorly evolved to support systemic pressures and commonly be- comes regurgitant; if right ventricular function is adequate, valve replacement should be performed because valve repair is rarely successful. • Systemic ventricular failure—the right ventricle may fail because it is inherently unsuitable to support the systemic circulation in the long term, because of long-standing tricuspid regurgitation, and because of poor ventricular filling from the surgically con- structed atrial pathways. There has been much interest in whether placement of a pul- monary artery band to 'retrain' the left ventricle to enable it to sup- port the systemic circulation will allow takedown of the Mustard operation and performance of an arterial switch operation. This approach only appears to be possible in young children, or in older patients with a degree of left ventricular outflow tract obstruc- tion in whom the left ventricle has always retained near-systemic pressures. Arterial switch operation As a result of the late complications of interatrial repair, a different surgical approach was developed that restored the left ventricle to the systemic circulation and avoided extensive atrial surgery: the arterial switch. Since the 1980s anatomical correction by the arterial switch op- eration has superseded interatrial repair as the operation of choice for most patients with TGA. Blood is redirected at arterial level by switching the aorta and pulmonary arteries so that the left ventricle becomes the subaortic ventricle supporting the systemic circulation. The coronary arteries are reimplanted into the neo-aortic root. Late follow-up appears good for these patients, but vigilance is required to detect late problems including neo-aortic or pulmonary valve regurgitation, neo-aortic root dilation, and pulmonary arterial stenosis. Late myocardial ischaemia due to coronary anastomotic stenoses is a theoretical complication, but has not yet become ap- parent as a major problem. Rastelli operation This operation is performed for patients with TGA, VSD, and pul- monary stenosis (Fig. 16.12.20). The VSD is closed so that the left ventricle carrying oxygenated blood empties into the aorta. The stenotic pulmonary artery is ligated and a conduit is placed be- tween the right ventricle and pulmonary artery. The main advan- tage of this operation is that the left ventricle supports the systemic circulation, but it commits the patient to several further conduit replacements—some of which may now be carried out percutan- eously rather than surgically. 'Palliative' Mustard/Senning or arterial switch operations These procedures are performed for patients with TGA, VSD, and pulmonary vascular disease to improve mixing of blood and oxy- genation. The VSD is left open. These patients should be treated in the same way as other patients with Eisenmenger syndrome. SVA PVA RV Ao LV PA MV TV Fig. 16.12.19 Schematic representation of intra-atrial repair for complete transposition of the great arteries (Senning or Mustard operation). Ao, aorta; LV, left ventricle; MV, mitral valve; PA, pulmonary artery; PVA, pulmonary venous atrium; RV, right ventricle; SVA, systemic venous atrium; TV, tricuspid valve.

 Congenitally corrected transposition of the great arteries (discordant atrioventricular and ventriculo-arterial connections) cTGA is a rare condition, accounting for less than 1% of all con- genital heart disease. Both atrial and arterial connections to the vent- ricles are discordant, so pulmonary venous blood passes through the left atrium, through the right ventricle, and into an anteriorly lying aorta (Fig. 16.12.18). Similarly, systemic venous blood reaches the pulmonary trunk via the left ventricle. The circulation is therefore physiologically 'corrected', but the morphological right ventricle and tricuspid valve support the systemic circulation. More than 95% of cases have associated anomalies, most com- monly VSD and pulmonary stenosis, but also Ebstein anomaly of the systemic (tricuspid) atrioventricular valve,

aortic stenosis, AVSD, abnormalities of situs, and coarctation. Congenital complete heart block occurs in around 5% of patients and may develop at any stage of life, particularly following surgery to the atrioventricular valve. Presentation depends on associated lesions. Patients with isolated cTGA may remain asymptomatic and undiagnosed into old age, but failure of the systemic ventricle, systemic atrioventricular valve re- gurgitation, or the onset of complete heart block and atrial arrhyth- mias usually results in presentation with symptoms from the fourth decade onwards. Those with VSD and pulmonary stenosis may be cyanosed, and those with VSD alone may present with pulmonary hypertension. A parasternal heave is usually palpable from the pressure-loaded anteriorly lying systemic right ventricle; this may be especially prominent if it is also volume-loaded by systemic (tricuspid) atrio- ventricular valve regurgitation. There may be a prominent aortic pulsation in the suprasternal notch and the aortic component of the second heart sound may be palpable and loud. The pulmonary component is soft or inaudible due to the posterior position of the pulmonary artery. The ECG may show varying degrees of atrioventricular block or evidence of pre-excitation due to accessory pathways (associ- ated with Ebstein-like anomalies of the systemic atrioventricular valve). There may be left axis deviation. The right and left bundles are inverted, so the initial septal activation is right-to-left, resulting in Q waves in V1–2 and an absent Q in V5–6; this pattern may be wrongly interpreted as a previous anterior myocardial infarction. The chest radiograph has a typical appearance (Fig. 16.12.21). Echocardiography confirms the discordant relations and assesses ventricular and systemic (tricuspid) atrioventricular valve function as well as other associated lesions. Ebstein anomaly may be diag- nosed if the tricuspid valve is apically displaced by more than 8 mm/ m2. Cardiac catheterization is indicated to assess the haemodynamic importance of associated lesions. Angiotensin-converting enzyme (ACE) inhibitors may be useful when there is systemic ventricular dysfunction or atrioventricular valve regurgitation, but there are no trial data to support their use. Transvenous atrioventricular sequential pacing is indicated for complete heart block; active fixation ventricular leads are required because of the absence of coarse apical trabeculations in the mor- phologically left subpulmonary ventricle. If there are associated intracardiac shunts, patients should be formally anticoagulated to reduce the risk of paradoxical embolism, or epicardial pacing should be considered. The conventional surgical approach to systemic atrioventricular valve regurgitation is tricuspid valve replacement (repair is rarely successful), but if systemic ventricular function is poor (ejection RA LA RV Ao LV PA VC Fig. 16.12.20 Schematic representation of Rastelli operation for transposition of the great arteries with ventricular septal defect and pulmonary stenosis. Ao, aorta; LA, left atrium; LV, left ventricle; PA; pulmonary artery; RA, right atrium, RV, right ventricle, VC, valved conduit. Fig. 16.12.21 Chest radiograph of a 23-year-old woman with congenitally corrected transposition of the great vessels. There is a narrow pedicle due to the abnormally related great arteries (small arrow) and the left heart border is straight (large arrow) due to the abnormal position of the left-lying anterior ascending aorta.

section 16 Cardiovascular disorders 3584 fraction <40%) transplantation may be the only option. Replacement of the tricuspid valve before the systemic right ventricle fails improves prognosis. Where there is coexistent VSD and pulmonary stenosis, classical repair involved closure of the VSD and insertion of a valved conduit between the left ventricle and pulmonary artery, with the right ventricle continuing to support the systemic circulation. Anatomical repair, so that the morphological left ventricle supports the systemic ventricle, has had success in children with systemic atrioventricular valve regurgitation and systemic ven- tricular dysfunction. For patients with an associated nonrestrictive VSD the left ventricle is at systemic pressure and therefore

‘pretrained’ to support the systemic circulation. If there is no pul- monary stenosis, a ‘double switch’ may be performed, combining a Senning operation with an arterial switch operation. If there is also pulmonary stenosis, the Senning operation is combined with a Rastelli-type repair. The regurgitant tricuspid valve and right ventricle are therefore placed in the pulmonary circulation. For children with corrected transposition whose left ventricle is at low pressure, a period of left ventricular ‘training’ is required before a double switch operation can be performed, which is achieved by placing a pulmonary artery band to increase left ventricular pres- sure and induce hypertrophy. Pulmonary artery banding per se may improve symptoms, since the increased left ventricular pres- sure causes the interventricular septum to move towards the sys- temic ventricle, reducing systemic atrioventricular regurgitation. The long-term outcome of these anatomical approaches to cor- rected transposition is not yet known; complications relating to the dysfunction of the retrained left ventricle, conduit replacement, neo-aortic valve regurgitation, and arrhythmia may become sig- nificant. There are reports of adults with VSD and pulmonary sten- osis having successfully undergone Senning–Rastelli repair, but it is probably not possible to adequately ‘train’ an adult left ventricle that has been at low pressure for many years. Tetralogy of Fallot Tetralogy of Fallot is the commonest cyanotic defect, occurring in 1 in 3600 live births; it affects males and females equally. Most patients reaching the adult clinics have undergone radical repair, but some natural and palliated survivors may present. The fundamental abnormality in tetralogy of Fallot is anterocephalad deviation of the outlet septum which creates the four key features: subvalvar pulmonary stenosis, VSD, an aortic valve that overrides the VSD, and right ventricular hypertrophy (Fig. 16.12.22). There is great anatomical variation, ranging from minimal aortic override to double-outlet right ventricle (DORV), and from minimal pulmonary stenosis to pulmonary atresia. The VSD is perimembranous and there is usually add- itional pulmonary valvar stenosis. Associations Microdeletions of chromosome 22q11 may occur in associ- ation with tetralogy of Fallot, especially in its most severe form with pulmonary atresia. 22q11 deletions are associated with a broad spectrum of phenotypic abnormalities that form the velocardiofacial syndrome (which includes DiGeorge syndrome; OMIM 601362): (1) other cardiac defects—Fallot with right aortic arch, truncus arteriosus, pulmonary atresia with VSD, interrupted aortic arch; (2) facial abnormalities—cleft palate, hare lip, hypertelorism, narrow eye fissures, puffy eyelids, a small mouth, deformed earlobes; (3) psychiatric disorders and learning difficulties; and (4) neonatal immune deficiency (thymic hypoplasia) and hypocalcaemia (parathyroid hypoplasia). Cardiac defects associated with tetralogy of Fallot include a right- sided aortic arch in 16%, a left SVC in around 15%, additional VSDs in 5%, and a secundum ASD (‘pentalogy’ of Fallot) in 8%. The most important associated coronary anomaly is the crossing of the right ventricular outflow tract by a left anterior descending coronary ar- tery arising anomalously from the right coronary sinus: this is vul- nerable to damage during surgical repair. Unoperated clinical course and management Without surgical intervention, only 2% of patients survive to their fortieth year. Those that do survive may be a selected group in whom subpulmonary stenosis was not severe in early life, but progressed with advancing age. Unoperated patients are at risk of the complications of cyanosis, endocarditis, atrial and ventricular arrhythmias, progressive ascending aortic dilatation (without the high risk of dissection found in Marfan syndrome), aortic regurgitation—causing volume overload of both ventricles and subsequent biventricular failure, and systemic hypertension— adding additional pressure overload to the work of both ventricles and further contributing to the onset of biventricular failure. There is cyanosis and clubbing, a right ventricular heave, and sometimes a thrill over the right ventricular outflow tract. A right- sided aorta may be palpable to the right of the sternum. The second heart sound is usually single, and there is a loud pulmonary ejection murmur.

There may be aortic regurgitation. * RA LA LV RV PA Ao Fig. 16.12.22 Schematic representation of tetralogy of Fallot. *Anterocephalad deviation of outlet septum creates ventricular septal defect, subpulmonary stenosis, aorta overriding crest of interventricular septum, and secondary right ventricular hypertrophy.
Ao, aorta, LA, left atrium, LV, left ventricle, PA, pulmonary artery, RA, right atrium, RV, right ventricle.

16.12 Congenital heart disease in the adult 3585 The ECG shows right axis deviation and right ventricular hyper- trophy, and the QRS duration may be prolonged in older patients. The classical cardiac silhouette is a ‘coeur en sabot’ (i.e. a clog-shaped heart), but this is more likely to be seen in tetralogy with pulmonary atresia (see ‘Pulmonary atresia with VSD’). The heart size is usually normal and pulmonary vascularity reduced. There may be a right- sided aortic arch indenting the right of the trachea, and there may be a prominent dilated ascending aorta. Two-dimensional echocardiography reveals infundibular stenosis with or without pulmonary valve stenosis, right ventricular hyper- trophy, the typical VSD, and varying degrees of aortic override. There may be evidence of left ventricular volume overload, aortic root dilatation, and aortic regurgitation. Cardiac catheterization should be performed prior to surgical repair in adults. The anatomy of the right ventricular outflow tract obstruction and pulmonary arteries is defined, and pulmonary vascular resistance assessed. Selective coronary angiography dem- onstrates any anomalous origin and course as well as acquired cor- onary disease. Aortography shows aortic root dilatation and any aortopulmonary collaterals. MRI may be performed instead of con- ventional cardiac catheterization, except that it does not provide pulmonary vascular resistance data. Palliated history Helen Taussig first suggested palliative surgery in 1943, and the first Blalock–Taussig shunt was performed in 1945 (Fig. 16.12.23 and Table 16.12.7). Nowadays, palliative shunts are usually performed as a staging procedure in small infants; however, occasional patients reach the adult clinic having had palliation without subsequent rad- ical repair. They are cyanosed and clubbed and have a continuous murmur under the clavicle and over the scapula on the side of the shunt. In a classical Blalock–Taussig shunt the ipsilateral radial pulse is diminished or absent and the hand often small. Late complications of systemic to pulmonary artery shunts include infective endarteritis, acquired pulmonary atresia, aortic regurgitation, and biventricular failure, with increasing cyanosis and bronchopulmonary collateral development if the shunt blocks or is outgrown, and pulmonary vas- cular disease if the shunt is too big. Radical repair, late follow-up, and reoperation Radical repair involves patch closure of the VSD with infun- dibular resection with or without pulmonary valvotomy or replace- ment: 86% of patients who underwent such surgery in the 1980s survive to 32 years of age, and survival for those operated in the current era is further improved. However, patients remain at risk of late complications including pulmonary regurgitation and sten- osis, aortic regurgitation, ventricular dysfunction, endocarditis, ar- rhythmia, and sudden death. Those repaired in early childhood and by a transannular approach have a better long-term prognosis than those repaired later or by a transventricular approach. In many patients repair involves placing a patch across the an- nulus of the pulmonary valve in order to create an unobstructed right ventricular outflow. As a result, the pulmonary valve is incom- petent from the time of repair. The pulmonary regurgitant volume is relatively small early after repair, since the stiff hypertrophied right ventricle cannot accommodate much regurgitant blood, the fast heart rate of the small child reduces the time in which regurgitation can occur, and the capacitance of the child’s pulmonary vasculature is low. However, the right ventricle remodels and by the time young adulthood is reached, pulmonary regurgitation is often severe and the right ventricle dilates.

Although pulmonary regurgitation is well tolerated for many years, it results in progressive right ventricular dilation and dys- function, impaired exercise tolerance, and increased risk of atrial and ventricular arrhythmias. A widening of the QRS complex be- yond 180 ms may be a marker for right ventricular dilation and dysfunction, these being risk factors for developing worsening functional class, sustained ventricular tachycardia, and sudden death. Pulmonary valve replacement is indicated if there is impaired Fig. 16.12.23 Chest radiograph of a 36-year-old man with tetralogy of Fallot palliated by a classic left Blalock–Taussig shunt (small arrow). There is secondary dilatation of the left pulmonary artery (large arrow) and a right aortic arch (*).
Table 16.12.7 Systemic to pulmonary arterial shunts Classical Blalock–Taussig shunt Subclavian artery divided distally. Proximal subclavian artery anastomosed end-to-side to pulmonary artery Modified Blalock–Taussig shunt Prosthetic graft between subclavian and pulmonary arteries Central shunts: Waterston shunta Side-to-side anastomosis between ascending aorta and (right) pulmonary artery Potts shunta Side-to-side anastomosis between descending aorta and (left) pulmonary artery Other Prosthetic graft between aorta and pulmonary artery a Now obsolete because not possible to adequately control the size of the shunt.

section 16 Cardiovascular disorders 3586 exercise tolerance, sustained arrhythmia, progressive right ven- tricular dilation, or any evidence of right ventricular dysfunction. Replacing the pulmonary valve before irreversible right ventricular dysfunction occurs is likely to improve long-term outcome. MRI is a valuable tool for assessing right ventricular size and function, and any deterioration. The timing of redo surgery for pulmonary regurgitation remains controversial, although some centres consider that pulmonary valve replacement should be performed before the indexed right ven- tricular end-diastolic volume reaches 150 ml/m2. Pulmonary regurgitation is worsened in the presence of pul- monary arterial stenosis that may occur at the site of a previous shunt. Right ventricular outflow tract obstruction may recur, espe- cially if a valved right ventricular to pulmonary artery conduit was placed, this being due to excessive formation of neointima (peel) in the conduit or to calcification of the valve. Most patients have right bundle branch block after repair (Fig. 16.12.24) due to surgical damage to the right bundle as it runs in the floor of the VSD. Bifascicular block and transient postoperative complete heart block carry a risk of developing late complete heart block. Atrial arrhythmias occur in 30% of long- term survivors and are a major cause of morbidity. Those with left-sided volume overload and left atrial dilatation secondary to residual VSD or previous shunts are at particular risk of atrial flutter and fibrillation. Rapidly conducted atrial flutter is particu- larly poorly tolerated and is likely to be responsible for a proportion of sudden deaths, as are the ventricular arrhythmias that occur in up to 45% of patients. Syncope, poor NYHA functional class, and sustained monomorphic ventricular tachycardia are likely to be a significant risk factor for sudden death, as are atrial arrhythmias and heart block, and ECG parameters such as QRS duration >180 ms nonsustained VT. Adverse right ventricular risk factors include dilatation and dysfunction, outflow tract obstruction, hypertrophy, aneurysm, impaired myocardial blood flow, and pulmonary regurgitation. Surgical risk factors for late sudden death include transventricular versus transatrial repair, large ventriculotomy scar, residual VSD, previous palliative shunt, complex or multiple operations, im- paired left ventricular function, older age at operation, and length of follow-up. (a) (b) Fig. 16.12.24 Electrocardiograms of a 35-year-old woman who underwent radical repair of tetralogy of Fallot. Preoperatively (a) there is right ventricular hypertrophy; postoperatively (b) there is right bundle branch block, due to damage to the right bundle as it runs in the floor of the ventricular septal defect.

16.12 Congenital heart disease in the adult 3587 Tetralogy of Fallot with absent pulmonary valve syndrome This variation accounts for approximately 3% of cases of tetralogy of Fallot. There is a ring-like, usually stenotic malformation, with failure of development of the pulmonary valve cusps. The central pulmonary arteries are usually hugely dilated or aneurysmal. Double-outlet right ventricle In DORV more than one-half of the circumference of both great vessels arises from the morphological right ventricle. A complete or partial muscular infundibulum usually lies beneath each arterial valve. The anatomy and physiology are enormously varied, as are the surgical approaches to repair. The degree of pulmonary sten- osis and the relation of the VSD to the great vessels determine the haemodynamics. Most (80%) subaortic defects have pulmonary stenosis and Fallot- like physiology. The Taussig–Bing anomaly accounts for less than 10% of DORV and describes a subpulmonary defect without pul- monary stenosis. There is transposition-like physiology with cyan- osis and high pulmonary blood flow. As the pulmonary vascular resistance rises, pulmonary blood flow falls, and cyanosis increases. Unoperated survival to adulthood is uncommon, but occurs occa- sionally if the pulmonary vascular resistance establishes adequate but not excessive pulmonary blood flow. If such a survivor also has a patent arterial duct, there will be reversed differential cyanosis. Deoxygenated blood selectively enters the aorta to supply the arch vessels, whereas oxygenated blood enters the pulmonary artery and supplies the descending aorta via the duct; thus, the fingers are more cyanosed and clubbed than the toes. If the VSD is remote from the great vessels, a biventricular repair may not be possible and a single-ventricle repair (Fontan) may be necessary. Pulmonary atresia with ventricular septal defect This is a complex and heterogeneous cyanotic condition. The intracardiac anatomy is the same as tetralogy of Fallot, but the right ventricular outflow tract is blind-ended (atretic). The pulmonary blood supply is derived entirely from three different types of sys- temic vessels: (1) a large muscular duct that resembles a collateral; (2) a diffuse plexus of small ‘bronchial’ arteries arising from medias- tinal and intercostal arteries; and (3) large tortuous systemic arterial collaterals known as MAPCAs (major aortopulmonary collateral arteries), which arise directly from the descending aorta, from its major branches (usually the subclavian artery), or from bronchial arteries, and may connect with central pulmonary arteries or supply whole segments or lobes of lung independently. Prognosis and management depend largely on the pulmonary vasculature, in which there is considerable anatomical variation. Confluent pulmonary arteries with pulmonary vessels having a near normal arborization pattern to all segments of the lungs are associ- ated with the best prognosis. Here radical repair, with recruitment of MAPCAs to the native pulmonary arteries, a conduit from right ventricle to pulmonary artery, and closure of the VSD is likely to be possible, and the pulmonary vascular resistance is likely to be low. The 20-year survival after radical repair is about 75%. The out- look is worse if there are no native pulmonary arteries and multiple tortuous MAPCAs with poor arborization. Radical repair may be extremely challenging or impossible, and pulmonary vascular resist- ance likely to be high. Such patients may be suitable for no or only palliative surgery and will remain cyanosed. Following surgical pal- liation, 20-year survival is around 60%; unoperated survival is very poor, only about 8% reaching 10 years of age, and those that do reach adulthood have a mean age of death of 33 years. Clinical findings Examination findings in the unoperated or palliated patient are similar to those of the unoperated Fallot without pulmonary atresia, except that there are continuous collateral murmurs and often a collapsing pulse. The chest radiograph shows a right aortic arch in 25% of cases and has a typical appearance (Fig. 16.12.25). The pulmonary col- lateral vessels may follow a bizarre pattern. Colour-flow Doppler may identify collateral vessels, but conventional angiography is re- quired to precisely delineate their origin, degree of ostial stenosis, and intrapulmonary course. High-resolution CT and MRI are useful tools in

imaging complex pulmonary vasculature. Outcome Late complications in unoperated or palliated survivors include increasing cyanosis due either to the development of pulmonary vascular disease in lung segments perfused at systemic pressure through nonstenosed collaterals, or to the progressive stenosis Fig. 16.12.25 Chest radiograph of a 21-year-old woman with tetralogy of Fallot and pulmonary atresia, no central pulmonary arteries, and multiple aortopulmonary collaterals which create an abnormal pulmonary vascular pattern. The typical ‘coeur en sabot’ silhouette is due to right ventricular hypertrophy and the pulmonary bay where the pulmonary artery should be (arrow).

section 16 Cardiovascular disorders 3588 of collateral vessels. In the latter, good symptomatic relief may be obtained from stenting. The aortic root may become mark- edly dilated and aortic regurgitation may develop, resulting in biventricular volume overload and failure. Aortic valve endocar- ditis is a particular risk. Late complications after radical repair include those that follow repair of tetralogy of Fallot. In addition, patients face inevitable repeated conduit replacements, and right ventricular failure sec- ondary to high pulmonary vascular resistance. Hearts with univentricular atrioventricular connection Also known as univentricular or single-ventricle hearts, these hearts are defined by the connection of both atriums to one ventricle, or by the absence of one of the atrioventricular connections. There is only one functional ventricle, although there is nearly always a second rudimentary and incomplete ventricle. When the rudimentary ven- tricle is of right morphology, it nearly always lies anteriorly. Less commonly, there is a posteriorly lying morphologically left rudi- mentary ventricle, and rarely, there is solitary ventricle of indeter- minate morphology. The two most common variants are double-inlet left ventricle (DILV) and tricuspid atresia (Figs. 16.12.26 and 16.12.27) which together account for around 4–5% of congenital heart disease. This section considers these two conditions, a discussion of more complex variants being beyond the scope of this text. Clinical course: Unoperated Presentation depends largely on pulmonary blood flow, which in turn is dependent on the degree of pulmonary stenosis. Those with severe obstruction to pulmonary blood flow present as neonates with severe cyanosis. Neonates without pulmonary stenosis have excessively high pulmonary blood flow and present in congestive cardiac failure with breathlessness and only mild cyanosis. The pres- ence of subaortic stenosis or other obstruction to systemic blood flow such as coarctation exacerbates heart failure and results in early decompensation. The outcome is most favourable for patients with left ventricular morphology, moderate pulmonary stenosis, and no subaortic sten- osis, and for those with ‘balanced’ pulmonary and systemic blood flow (i.e. moderately severe pulmonary stenosis and no obstruction to systemic blood flow). Unoperated survival into adulthood is un- common: 50% of patients with DILV die before 14 years, 50% with DORV die by 4 years of age. Nonetheless, rare patients with balanced circulation reach their sixth decade without surgical intervention. In the unoperated patient, there is cyanosis and clubbing. A giant ‘a’ wave may be present in the jugular venous pulse in tricuspid atresia. An absent right ventricular impulse and prominent left ven- tricular impulse are characteristic of DILV and tricuspid atresia. There may be a precordial thrill from pulmonary stenosis, particu- larly if the pulmonary artery lies anteriorly. If there are discordant ventriculo-arterial connections, the aortic pulsation of the anteri- orly lying aorta may be prominent in the suprasternal notch. The second heart sound is usually single. If pulmonary vascular disease has developed there will be add- itional signs of pulmonary hypertension. Signs of congestive heart failure may be present in the ageing patient, particularly with the RA LA LV RV PA Ao Fig. 16.12.26 Schematic representation of double-inlet left ventricle with discordant ventriculo-arterial connections. Both atriums connect to the left ventricle via the

tricuspid and mitral valves, so that systemic and pulmonary venous blood mix in the left ventricle and the patient is cyanosed. The left ventricle supports both the systemic and pulmonary circulations. The aorta arises from the rudimentary right ventricle via the ventricular septal defect (VSD). If the VSD is restrictive, it creates obstruction to systemic blood flow. Ao, aorta; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle; VA, ventriculo-arterial; VSD, ventricular septal defect. RA LA LV RV PA Ao Fig. 16.12.27 Schematic representation of tricuspid atresia. Systemic venous blood leaves the right atrium via an atrial septal defect and mixes with pulmonary venous blood in the left atrium. The left ventricle thus supports both the systemic and pulmonary circulations and the patient is cyanosed. The rudimentary right ventricle does not play a functional role. Ao, aorta; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle.

 onset of atrial arrhythmia, such that the venous pressure is raised, with hepatomegaly and peripheral oedema. The chest radiograph shows cardiomegaly due to chronic ven- tricular volume overload. If ventriculo-arterial connections are dis- cordant, there is a narrow pedicle and the ascending aorta forms a straight edge along the left heart border. Pulmonary vascularity re- flects the pulmonary blood flow, the main pulmonary arteries being small where there is significant pulmonary stenosis, with large main pulmonary arteries indicating high pulmonary blood flow, either past or present. In tricuspid atresia the ECG usually shows right atrial hyper- trophy, normal PR interval, small or absent right ventricular forces, and left axis deviation. There are left axis deviation and large left ventricular forces in DILV. If the rudimentary chamber lies to the right the PR interval is usually normal, but if it lies to the left the PR interval may be prolonged or there may be complete heart block. Two-dimensional echocardiography and colour-flow Doppler allow detailed assessment of the anatomy and physiology, including ventricular morphology and pulmonary and subaortic stenosis. Cardiac catheterization is required to assess pulmonary artery anatomy and resistance. Surgical management of univentricular hearts: The Fontan operation Management requires a staged approach, the ultimate aim of which is to achieve a pink patient in whom the functionally single ventricle supports only the systemic circulation: the Fontan operation. The first stage, in early life, is to obtain control of pulmonary blood flow. In those with excessive flow a pulmonary artery band is placed to create supravalvar pulmonary artery stenosis and limit pulmonary flow. In neonates with severe pulmonary stenosis a systemic artery to pulmonary artery shunt is placed to augment pulmonary blood flow. As the child ‘grows out of the shunt’ they become more cyanosed: the central shunt is replaced with a superior vena cava to pulmonary artery anastomosis (Glenn, or cavopulmonary anas- tomosis), as illustrated in Fig. 16.12.28. This reduces cyanosis, perfuses the pulmonary arteries at low pressure, and reduces the volume load on the single ventricle. However, as the child grows, the relative contribution of the SVC to the circulation diminishes, again resulting in progressive cyanosis. N A T N O F N N E L G L A N O IT C E RI D IB N N E L G L A C IS S A L C BILATERAL BIDIRECTIONAL GLENN in isomerism TOTAL CAVOPULMONARY CONNECTION SVC RA IVC RPA LPA SVC PA RA IVC PA RA PA RSVC LSVC HEPATIC VEINS SVC disconnected from RA. RPA disconnected from PA. SVC to RPA anastomosis created. SVC disconnected from RA. SVC anastomosed to confluent PAs. Proximal PA divided. Anastomosis created between RA and PA. RSVC disconnected from RA. LSVC disconnected, usually from coronary sinus. SVCs anastomosed to confluent PAs. Hepatic veins are the only remaining systemic venous return to RA since IVC drains via azygous continuation to SVC. SVC connected to PA. IVC connected via extra-cardiac conduit to PA, excluding RA from circuit RA PA SVC IVC RA EXTRA- CARDIAC CONDUIT Fig. 16.12.28

Evolution of the Fontan and total cavopulmonary connection operations. IVC, inferior vena cava; PA, pulmonary artery; RPA, right pulmonary artery; SVC, superior vena cava.

section 16 Cardiovascular disorders 3590 The Fontan operation is usually completed by age 4 to 6 years. The principle of this approach is to separate the systemic and pul- monary circulations and abolish cyanosis. This is achieved by using the single functional ventricle to support the systemic cir- culation and leaving the pulmonary circulation without a ventricle (i.e. with phasic rather than pulsatile flow). Since its first descrip- tion in 1972 the atriopulmonary Fontan operation has evolved, so that now several variations exist. The favoured approach nowadays is the total cavopulmonary connection (TCPC), which avoids some of the late complications of the original approach. Nonetheless, all the variations result in the same basic physiology, the 'Fontan circulation'. The Fontan circulation is one of a chronic low cardiac output state, critically dependent upon adequate systemic venous filling pres- sure to drive forward flow across the pulmonary vascular bed. It is a fragile circulation in which small changes in haemodynamics can result in a serious, sometimes catastrophic, fall in cardiac output. Problems that can cause trouble include dehydration, stenosis at the site of connection of the right atrium or systemic veins to the pulmonary artery, pulmonary embolism from in situ right atrial thrombus, a rise in pulmonary vascular resistance, atrial flutter, mi- tral regurgitation, a rise in left ventricular end-diastolic pressure, aortic or subaortic stenosis, drug-induced vasodilatation (e.g. an- aesthetic induction agents, nitrates), and positive pressure ventila- tion that reduces systemic venous return. Clinical features after the Fontan operation Most patients are acyanotic: new or worsening cyanosis is cause for concern. The jugular venous pulse is usually slightly raised and the second heart sound single. No murmur arises from the Fontan connection. There may be a murmur of mitral regurgitation. In pa- tients with discordant ventriculoarterial connections, a loud sys- tolic murmur raises suspicion of subaortic stenosis (which may be at the level of the VSD). The liver edge is often palpable, but new or increasing hepatomegaly is a worrisome finding. Ascites often pre- cedes peripheral oedema in young patients with complications sub- sequent to a Fontan procedure. A combination of echocardiography and MRI provide anatomical and physiological data. Cardiac catheterization is needed to assess pulmonary vascular resistance. Cardiopulmonary exercise testing is a useful indicator of early signs of decompensation. Complications after the Fontan operation Patient selection is important in ensuring a good outcome of Fontan surgery. Survival ranges from 81% at 10 years for 'perfect candidates' to 60 to 70% for all patients. Preoperative risk factors for a poor outcome are pulmonary vascular resistance greater than 4 Wood units, mean pulmonary artery pressure more than 15 mm Hg, ven- tricular hypertrophy, impaired systolic ventricular function, severe atrioventricular valve regurgitation, aortic outflow obstruction, and small or distorted pulmonary arteries. However, even patients with none of these risk factors have limited exercise tolerance and are at risk of a great range of late complications. Complications include intra-atrial re-entry tachycardia (IART)/ atrial flutter, sinus node dysfunction, progressive ventricular dys- function, atrioventricular valve regurgitation, development of subaortic stenosis, pathway obstruction, right lower pulmonary vein compression by dilated right atrium, thromboembolism (most centres anticoagulate adults with a Fontan circulation), recurrent ef- fusions, ascites, peripheral oedema, cyanosis (due to development of venous collaterals to the left atrium or pulmonary arteriovenous fistulas), protein-losing enteropathy, and hepatic dysfunction including fibrosis, cirrhosis, and hepatocellular carcinoma. Careful surveillance is required to detect complications and offer interven- tion and counselling. A detailed discussion of these many complications is beyond the scope of this book, but atrial flutter/IART merits further dis- cussion

because it is an acutely life-threatening complication (Fig. 16.12.29). Flutter is common after a Fontan procedure, and is poorly tolerated, causing a significant fall in cardiac output. Atrial transport is particularly important in the Fontan circulation to fa- cilitate left ventricular filling, so simply controlling the rate of atrial flutter is inadequate: rapid restoration of sinus rhythm is required. Time may be wasted once the patient seeks medical attention, be- cause the ECG appearances are often atypical and may be misin- terpreted as sinus tachycardia. If in doubt, intravenous adenosine will reveal flutter waves and confirm the diagnosis, but will not ter- minate the arrhythmia. Other intravenous antiarrhythmics should be avoided since they may precipitate cardiovascular collapse. The safest approach is DC cardioversion. Intravenous fluids should be given while the patient is nil by mouth to maintain systemic venous filling pressure. Care must be taken to avoid excessive sys- temic vasodilation at induction of anaesthesia, and allowance must be made for the fall in cardiac output that accompanies ventilation. Pregnancy in a woman with a Fontan circulation is possible, but carries a high maternal and fetal risk and requires care in a specialist centre. Women with good functional class and ventricular function who have not yet developed Fontan circulation complications have the best chance of success. Risks include an up to 70% chance of early miscarriage, as well as maternal haemorrhage, arrhythmia, and decompensation with a low output state. Prepregnancy counselling and secure contraception are key. Estrogen-containing preparations are contraindicated; long-acting progestogen-only methods or the desogestrel containing progestogen-only pill are the safest and most reliable options. Most adults with a Fontan circulation undergo functional decline by their fourth decade, with limited life expectancy. They face be- coming a ‘failing Fontan’ with a great range of complications and require a holistic, palliative approach to run in parallel with active interventions, including transplantation. Cardiac transplantation requires particularly careful assessment in an experienced specialist centre, but outcomes are good with prudent patient selection. Hypoplastic left heart syndrome Until recently hypoplastic left heart syndrome (HLHS) was not dis- cussed in adult texts, since there were no survivors to adulthood. With the introduction of the three-stage Norwood operation, re- sulting in a complex Fontan-type circulation, survivors are begin- ning to reach the adult clinic. HLHS is a heterogeneous syndrome in which the left side of the heart is unable to support the systemic circulation because of hypoplasia, stenosis, or atresia at different levels of the left side of the circulation. The three-stage surgical approach to the condi- tion is as follows:

 • Stage I (Norwood operation)—performed in the first few days of life; the right ventricle and main pulmonary artery are used to re- construct the systemic outflow tract; pulmonary blood flow is pro- vided by a systemic–pulmonary artery shunt or right ventricle to pulmonary artery conduit. • Stage II—this operation is performed at around 2 years; the sys- temic shunt or conduit to the pulmonary artery is taken down, and the superior vena cava anastomosed to the pulmonary artery (cavopulmonary or Glenn shunt). • Stage III—Fontan completion is performed at around 5 years, usu- ally with an extracardiac conduit. Fig. 16.12.30 shows a schematic representation of the Fontan cir- culation for HLHS. In early series only about 50% survived the three operations, but survival now approaches 70%. Those who reach the adult clinic will face the complications of any Fontan circulation, and in addition they are at risk of complications from ascending aorta and coarctation repair sites, coronary arteries arising from the hypoplastic remnant of ascending aorta, left pulmonary artery (a) (b) (c) Fig. 16.12.29 Electrocardiograms from a 24-year-old woman with tricuspid atresia and previous Fontan surgery: (a) sinus rhythm; (b, c) interatrial re-entry tachycardias which were poorly tolerated and required urgent DC cardioversion.

section 16 Cardiovascular disorders 3592 stenosis at site of arch repair, and failure of the right ventricle and tricuspid valve as they support the systemic circulation. Other important issues Transition to adult care and lifestyle issues in congenital heart disease The transition from paediatric to adult cardiology services requires a multidisciplinary approach, starting in an age-appropriate way in early teenage years, transferring to an adult transition service between 16 and 18 years, and ending with a young adult who understands their condition and limitations and is ready to take responsibility for their own health. Young adults require education about their condition and an understanding about safe levels of exercise, appro- priate careers, recreational alcohol, and drugs. Young women need to understand what risks a pregnancy may carry, the need for safe and effective contraception, and prepregnancy counselling. Pregnancy and contraception in congenital heart disease Cardiac disease is the leading cause of pregnancy-related death in the United Kingdom. All patients with congenital heart disease should be counselled from adolescence on their risk of pregnancy and their contraceptive options. The risk of pregnancy in congenital heart dis- ease ranges from being the same as that of the general population to a more than 25% risk of maternal death in pulmonary hyperten- sion. Each patient requires specialist individual assessment before embarking on pregnancy. An outline of the risks associated with different conditions is shown in Table 16.12.8: it should be remem- bered that risks are additive, so a repaired septal defect with poor ventricular function moves from a low-risk to high-risk category. Two principles should be remembered when considering contra- ceptive options: the efficacy of the method, and cardiovascular safety of the method. The risk of estrogen-containing preparations (which include the combined oral contraceptive pill) relates to their thrombogenicity. Patients at risk of intracardiac or pulmonary thrombosis and those with right-to-left shunts should not use these preparations. Progestogen-only preparations are safe in cardiac dis- ease, but the mode of delivery may carry risk. For example, insertion of a progestogen-eluting intrauterine device (Mirena® IUS) carries a risk of vasovagal syncope in nulliparous women, a reaction that can provoke cardiovascular collapse in cyanotic, pulmonary hyperten- sive, or post-Fontan patients. In addition, although the progestogen- only ‘minipill’ is safe, its efficacy is poor. The desogestrel containing progestogen-only pill combines cardiovascular safety with an ef- ficacy equal to that of the combined pill. Other safe and effective methods useful for most women with cardiac disease are the subdermal implant Nexplanon® and the injectable DepoProvera®. Heart failure and end-of-life care As with other cardiac conditions, heart failure is the mode of de- cline and death in many patients with congenital heart disease, but in contrast with many forms of acquired heart disease the decline often occurs earlier in life. Regular surveillance may allow the start of deterioration to be detected early, before the patient is aware of a change in symptoms. A fall in cardiopulmonary exercise capacity, a rise in biomarkers, and changes in echocardiographic parameters of ventricular function may all predate symptoms. Evidence for the use of ‘standard’ heart failure medication and resynchronization device therapy is lacking for many with con- genital heart disease, including those with systemic right ventricles, a single-ventricle circulation, and those with subpulmonary right ventricular failure. Vigilance for life-threatening arrhythmia should be maintained, with a low threshold to consider ablation and device therapy. Early holistic engagement with patients and their families is espe- cially important to allow planning for changes in lifestyle and job. Fig. 16.12.30 Hypoplastic left heart syndrome after the third stage Fontan completion. The right heart is used to support the systemic circulation and an ascending aorta is created from the pulmonary valve and pulmonary trunk. The aortic arch is enlarged with homograft tissue. An extracardiac conduit connects the IVC directly to the pulmonary arteries, and the SVC is also connected directly to the pulmonary arteries. Ao, aorta; IVC, inferior vena cava; LA, left atrium;

LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

16.12 Congenital heart disease in the adult 3593 Table 16.12.8 Risk of maternal mortality in different congenital cardiac conditions mWHO 1 mWHO 2 if well and otherwise uncomplicated mWHO 2–3 depending on individual mWHO 3 mWHO 4 Uncomplicated, small, or mild: • pulmonary stenosis • patent arterial duct • mitral valve prolapse Unoperated atrial or ventricular septal defect Mild systemic ventricular dysfunction Mechanical valve Pulmonary arterial hypertension (includes Eisenmenger syndrome) Successfully repaired simple lesions • atrial or ventricular septal defect • patent arterial duct • anomalous pulmonary venous drainage Repaired tetralogy of Fallot Repaired coarctation of the aorta Systemic right ventricle Severe systemic ventricular dysfunction Atrial or ventricular ectopic beats, isolated Most arrhythmias with structurally normal heart Native or bioprosthetic valve disease not considered class 1 or 4; includes most regurgitant valve lesions Fontan circulation Severe mitral stenosis, severe symptomatic aortic stenosis Aortopathies Aortopathies with significant aortic dilatation (Marfan

> 45 mm, bicuspid aortopathy 5 cm) Cyanotic heart disease with no pulmonary vascular disease Native severe coarctation Modified World Health Organization pregnancy risk, adapted from Thorne et al. (2006) and Regitz-Zagrosek et al. (2011). mWHO 1 = no detectable risk of maternal mortality and no/mild increase in morbidity. mWHO 2 = small increased risk of maternal mortality or moderate increase in morbidity. mWHO 3 = significantly increased risk of maternal mortality or severe morbidity. Expert counselling required and specialist cardiac and obstetric monitoring needed throughout pregnancy, childbirth, and the puerperium. mWHO 4 = extremely high risk of maternal mortality or severe morbidity; pregnancy contraindicated. If pregnancy occurs, termination should be discussed. If pregnancy continues, care as for class 3. Table 16.12.9 Risks of infective endocarditis or endarteritis in congenital heart disease Unoperated Operated Low risk: lesions with no or low velocity turbulence and no prosthetic material Anomalous pulmonary venous drainage Anomalous pulmonary venous drainage Secundum ASD Secundum ASD Ebstein anomaly Ebstein anomaly with repaired native valve Mild pulmonary stenosis VSD/tetralogy of Fallot without residual lesions Isolated corrected transposition Patent arterial duct Eisenmenger syndrome without valvar regurgitation Fontan-type procedures Arterial switch for transposition without residual lesions Moderate risk Systemic AV valve regurgitation Residual regurgitation of repaired native aortic or systemic AV valve Subaortic stenosis Nonvalved conduits Moderate—severe pulmonary stenosis Tetralogy of Fallot Double-outlet right ventricle Univentricular heart with pulmonary stenosis Truncus arteriosus Coarctation Restrictive patent arterial duct High risk Bicuspid aortic valve Prosthetic valves Aortic regurgitation secondary to VSD or subaortic stenosis Aortopulmonary shunts, e.g. Gore-Tex, modified Blalock–Taussig Restrictive VSD Valved conduits ASD, atrial septal defect; AV, atrioventricular; VSD, ventricular septal defect.

section 16 Cardiovascular disorders 3594 A particularly successful multidisciplinary model of care is to run a combined active and palliative care approach, which can include interventions such as heart transplantation in parallel with an em- phasis on quality of life and end-of-life planning. Bacterial endocarditis Endocarditis is discussed in Chapter 16.9.2; the risks for specific congenital lesions are outlined in Table 16.12.9. In the United Kingdom, National Institute for Clinical Excellence Guidelines 2016 do not recommend routine use of antibiotic prophylaxis for people with structural heart disease undergoing dental, upper and lower gastrointestinal, urogenital, or respiratory procedures. However, NHS Education for Scotland updated NICE Clinical Guideline 64 in 2018; antibiotic prophylaxis should be considered for high risk groups including those with prosthetic valves and conduits as well as cyanotic patients and those with previous endocarditis. Patients with other intracardiac prosthetic material should receive antibiotic prophylaxis for 6 months after surgery, or lifelong if there remains a residual shunt or regurgitant valve. Healthcare professionals are advised to discuss with patients the rationale behind not using rou- tine antibiotic prophylaxis, and to emphasize the importance of maintaining good oral hygiene. Advice on the risks of body piercing and tattooing should also be given, as should advice on the symp- toms that may indicate endocarditis and when to seek expert advice. It is likely that good oral hygiene and regular dental checks are more important in preventing endocarditis than whether or not antibiotic prophylaxis is given. FURTHER READING Anderson RH, Shirali G (2009). Sequential segmental analysis. Ann Pediatr Cardiol, 2, 24–35. Ávila P, et al. (2017). Sudden cardiac death in adult congenital heart disease. Card Electrophysiol Clin, 9, 225–34. Broberg CS, et al. (2006). Blood viscosity and its relationship to iron deficiency, symptoms and exercise capacity in adults with cyanotic congenital heart disease. J Am Coll Cardiol, 48, 256–65. Cherian G, et al. (1983). Pulmonary hypertension in isolated atrial septal defect. Am Heart J, 105, 952–7. Clapp S, et al. (1990). Down syndrome, complete AV canal and pul- monary vascular obstructive disease. J Thorac Cardiovasc Surg, 100, 115–21. Del Sette M, et al. (1998). Migraine with aura and right-to-left shunt on transcranial Doppler: a case-control study. Cerebrovasc Dis, 8, 327–30. Diller GP, et al. (2006). Presentation, survival prospects and predictors of death in Eisenmenger syndrome: a combined retrospective and case-control study. Eur Heart J, 27, 1737–42. Driscoll DJ, et al. (1992). Five to fifteen year follow-up after Fontan operation. Circulation, 85, 469–96. Dupuis C, et al. (1992). The ‘adult’ form of the scimitar syndrome. Am J Cardiol, 70, 502–7. Fyfe A, et al. (2005). Cyanotic congenital heart disease and coronary artery atherogenesis. Am J Cardiol, 96, 283–90. Galiè N, et al. (2009). Guidelines for the diagnosis and treatment of pulmonary hypertension: the Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT). Eur Heart J, 30, 2493–537. Geva T (2011). Repaired tetralogy of Fallot: the roles of cardiovascular magnetic resonance in evaluating pathophysiology and for pulmonary valve replacement decision support. J Cardiovasc Magn Reson, 13, 9. Hagen PT, Scholz DG, Edwards WD (1984). Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. Mayo Clin Proc, 59, 17–20. Hjortshøj CMS, et al. (2017). Past and current cause-specific mortality in Eisenmenger syndrome. Eur Heart J, 38(26), 2060–7. Ho SY, et al. (1995). Colour atlas of congenital heart disease. Morphological and clinical correlations. Mosby-Wolfe, London. Kirklin JW, Barratt-Boyes BG (1993). Cardiac surgery, 2nd edition. Churchill Livingstone, New York. Knight M, et al. (eds) on behalf of MBRRACE-UK (2014). Saving lives, improving mothers’ care – surveillance of maternal deaths in the UK 2012–14 and lessons learned to inform maternity care from the UK and Ireland confidential enquiries into maternal deaths and mor- bidity 2009–14. Perinatal Epidemiology Unit,

University of Oxford, Oxford, 2016. Koller M, Rothlin M, Senning Å (1987). Coarctation of the aorta: re- view of 362 operated patients. Long term follow up and assessment of prognostic variables. Eur Heart J, 8, 670–9. Konstanides S, et al. (1995). A comparison of surgical and medical therapy for atrial septal defects in adults. New Engl J Med, 333, 469–73. Lumbiganon P, Chaitikpinyo A (2013). Antibiotics for brain abscesses in people with cyanotic congenital heart disease. Cochrane Collaboration/ John Wiley & Sons, London. Mongeon FP, et al. (2008). Congenitally corrected transposition of the great arteries ventricular function at the time of systemic atrioven- tricular valve replacement predicts long-term ventricular function. J Am Coll Cardiol, 57, 8–17. Moodie DS, et al. (1984). Long term follow up in the unoperated univentricular heart. Am J Cardiol, 53, 1124–8. Moon RE, Camporesi EM, Kissolo JA (1989). Patent foramen ovale and decompression sickness in divers. Lancet, i, 513–14. Murphy JG, et al. (1993). Long-term outcome in patients undergoing surgical repair of tetralogy of Fallot. New Engl J Med, 329, 593–9. Murtuza B, et al. (2011). Anatomic repair for congenitally corrected transposition of the great arteries: a single-institution 19-year ex- perience. J Thorac Cardiovasc Surg, 142, 1348–57. Murtuza B, et al. (2017). Impact of mode of failure and end-organ dys- function on the survival of adult Fontan patients undergoing cardiac transplantation. Eur J Cardiothorac Surg, 51(1), 135–41. NICE (2008). Prophylaxis against infective endocarditis: antimicro- bial prophylaxis against infective endocarditis in adults and children undergoing interventional procedures. Clinical guideline. http://guidance.nice.org.uk/CG64/Guidance/pdf/English Perloff JK, Child JS (1998). Congenital heart disease in adults.
W. B. Saunders, Philadelphia, PA. Quinton E, et al. (2015). Prevalence of atrial tachyarrhythmia in adults after Fontan operation. Heart, 101, 1672–7. Redington AN, et al. (1998). The right heart in congenital heart disease. Greenwich Medical Media, London. Regitz-Zagrosek V, et al. (2011). ESC Guidelines on the manage- ment of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). Eur Heart J, 32(24), 3147–97. Regitz-Zagrosek V, et al. (2018). ESC Guidelines for the management of cardiovascular disease in pregnancy. Eur Heart J, 39, 3165–241. Roberts WC (1986). Major anomalies of coronary arterial origin seen in adulthood. Am Heart J, 111, 941–62.

 Sarris GE, et al. (2006). European Congenital Heart Surgeons Association. Results of surgery for Ebstein anomaly: a multicentre study from the European Congenital Heart Surgeons Association. J Thorac Cardiovasc Surg, 32, 50–7. Schamroth CL, et al. (1987). Pulmonary arterial thrombosis in secundum atrial septal defect. Am J Cardiol, 60, 1152–6. Stark J, de Leval MR (ed) (1994). Surgery for congenital heart defects. W. B. Saunders, London. Stout KK et al. (2018). AHA/ACC Guideline for the management of adults with congenital heart disease. Circulation, epub ahead of print. Tay EL, et al. (2011). Replacement therapy for iron deficiency im- proves exercise capacity and quality of life in patients with cyanotic congenital heart disease and/or the Eisenmenger syndrome. Int J Cardiol, 151, 307–12. Thorne S, MacGregor A, Nelson-Piercy C (2006). Risks of contracep- tion and pregnancy in heart disease. Heart, 92, 1520–5. Van Hare GF, et al. (2015). AHA/ACC scientific statement. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: task force 4: congenital heart disease. JACC, 66(21), 735–1097. Villafañe J, et al. (2013). Hot topics in tetralogy of Fallot. J Am Coll Cardiol, 62, 2155–66. Warnes CA (2006). Transposition of the great arteries. Circulation, 114, 2699–709. Warnes CA, et al. (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. Circulation, 118, e714–833. Wilson W, et al. (2007). Prevention of infective endocarditis: guidelines from the American Heart Association

Rheumatic Fever, Endocarditis and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardio vascular Surgery and Anesthesia, and the Quality and Care Outcomes Research Interdisciplinary Working Group. Circulation, 116, 1736–54. Wood P (1958). Eisenmenger syndrome: or pulmonary hypertension with reversed central shunt. Br Med J, ii, 701–9, 755–62.

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