14.6 Heart disease in pregnancy 2597

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ESSENTIALS Pregnancy is a vasodilator state in which plasma volume and car- diac output increase such that many symptoms and signs of cardiac disease can occur physiologically. Disproportionate symptoms or abnormal signs such as a diastolic murmur require investigation as usual; necessary radiological investigations should not be withheld as the risks to the fetus are generally low. Pre-pregnancy risk assessment—this is ideally based on data related to the specific cardiac abnormality, with pre-pregnancy functional status an important predictor of outcome. Issues of particular note are (1) pregnancy is high risk in pulmonary hypertension or severe left ventricular dysfunction—effective contraception and termination should be offered; (2) women at risk of aortic dissection are at in- creased risk during pregnancy—pre-pregnancy elective replacement of the aortic root should be considered if its diameter at its widest point is greater than 4.5–5.0 cm, depending on the underlying aeti- ology; β-blockers and regular echo monitoring should continue through pregnancy. Delivery of the baby—vaginal delivery is recommended, other than in the presence of a dilated aortic root, aneurysm, or dissection, or if the fetal INR is elevated. Low-dose infusions of epidural anaesthesia and oxytocic drugs are safe. Heart conditions arising in pregnancy Peripartum cardiomyopathy—this should be considered in any woman presenting peripartum with dyspnoea or tachycardia. Myocardial infarction—when occurring in pregnancy, this may be due to coronary dissection: immediate angiography with consider- ation of percutaneous coronary intervention is the management of choice, but thrombolysis is not contraindicated. Pregnancy in women with known cardiac disorders Valve diseases and cardiomyopathies—(1) symptomatic mitral stenosis—may be managed medically with diuretics, β-blockade and maintenance of sinus rhythm; failing this, balloon valvuloplasty is usually successful; (2) aortic stenosis—women with satisfactory pre-pregnancy haemodynamics are at low risk of problems in preg- nancy.
(3) Hypertrophic cardiomyopathy—patients generally tolerate pregnancy well. Congenital cardiac lesions—low-risk conditions include atrial septal defect, restrictive ventricular septal defect, and corrected tetralogy of Fallot in the absence of severe pulmonary regurgitation or aortic root dilatation. All cases other than those at low risk should be managed by a multidisciplinary team in a specialist centre. Anticoagulation—the optimal anticoagulation management of a pregnant patient with a mechanical prosthetic valve is not known. Continued warfarin therapy carries the

risk of warfarin embryopathy for the fetus but switching to heparin increases the maternal risk of thromboembolism, although current regimens using low- molecular-weight heparin heparin with monitoring of anti-Xa levels perform better than historical regimens using unfractionated heparin. Introduction Cardiac disease is the commonest cause of maternal death in the United Kingdom. Historically most of these women had rheumatic mitral stenosis, but in the developed world today the leading causes are sudden adult death syndrome, cardiomyopathy, aortic dissec- tion, and myocardial infarction, followed by congenital heart disease and pulmonary hypertension. Maternal death is fortunately rare, but the proportion of pregnant women who have cardiac disease is increasing, reflecting both the improved survival of adults with con- genital heart disease and changes in pregnancy demographics. Cardiovascular changes in pregnancy Early in gestation the up-regulation of nitric oxide synthesis by oestradiol causes arterial vasodilatation and a reduction in both systemic and pulmonary vascular resistance. Simultaneously the normal fall in heart rate at the end of the menstrual cycle fails to occur, and the heart rate increases by 10–20 beats/min for the dur- ation of the pregnancy. The reduction in afterload and blood pres- sure stimulates an increase in plasma volume and hence preload by activation of the renin–angiotensin–aldosterone system. End dia- stolic volume, stroke volume and contractility increase such that 14.6 Heart disease in pregnancy Catherine E.G. Head

Section 14 Medical disorders in pregnancy 2598 cardiac output reaches about 140% of pre-pregnancy level by mid gestation. These changes combined with the development of the low resistance uteroplacental circulation cause blood pressure (systolic and diastolic) to decline by around 10 mm Hg to a nadir at about 20 weeks, before returning to pre-pregnancy levels by term (see Chapters 14.1 and 14.4). Although central venous pressure and pul- monary capillary wedge pressure remain unchanged, serum colloid osmotic pressure is reduced by plasma expansion and the pregnant woman is therefore at increased risk of pulmonary oedema. The 50% increase in plasma volume combined with the 25% increase in red cell mass accounts for a haemoglobin level of around 11 g/dl: the physiological anaemia of pregnancy. Labour, particularly the second stage, is associated with a further increase in cardiac output as pain increases heart rate via the sympa-thetic response and stroke volume is augmented by autotransfusion during contractions and post-partum. This means that the later stages of labour are a period of high risk for pulmonary oedema. Structural changes to the heart and great vessels occur. Orifice areas of all four valves increase, causing a higher incidence of valvular regurgitation. Changes in the extracellular matrix of the aortic media increase compliance but also, in combination with the increased cardiac output, the risk of dissection. Cardiac clinical features of normal pregnancy Fatigue, dizziness, palpitation, oedema, dyspnoea, and reduced exer- cise tolerance may occur in a normal pregnancy. Pressure of the uterus on the inferior vena cava when supine can significantly reduce pre- load and therefore cardiac output, causing presyncope. Symptoms are rapidly relieved by turning on one side. The increased cardiac output of pregnancy, together with the relative sinus tachycardia and the in-creased tendency to ectopy, may be experienced as palpitation, often particularly when at rest lying down. Physiological hyperventilation of pregnancy is perceived as breathlessness, particularly when speaking, by most women at some point during a normal pregnancy. Normal cardiovascular examination findings in pregnancy are: • increased volume ‘bounding’ peripheral pulses • third heart sound • soft ejection systolic murmur at the left sternal edge • peripheral oedema Abnormal findings that require further assessment include: • fourth heart sound • diastolic murmur Cardiovascular investigation in pregnancy Electrocardiogram The rotated position of the heart causes left axis deviation. Common findings also include the presence of a Q wave and T wave

inver- sion in lead III, and inverted T waves in V1 and V2. Changes in autonomic control and ion channel expression result in an increase in corrected QT interval and QT dispersion. Exercise testing Maximal exercise testing is safe for both mother and fetus in a normal pregnancy, with maximal oxygen uptake the same as that of nonpregnant matched controls in nonweight-bearing (static cycle) protocols. European Society of Cardiology guidelines rec- ommend submaximal testing to 80% of target heart rate in asymp- tomatic pregnant patients with suspected cardiovascular disease. Semi-recumbent cycle ergometry is usually the most comfortable modality. There is no specific data on the use of exercise testing to diagnose ischaemic heart disease during pregnancy and so sens- ible extrapolation from the nonpregnant data should be used, remembering that nonspecific T wave changes can be normal in pregnancy. Pre-pregnancy testing is useful in risk stratification. Chest radiograph/Computed tomography The fetal absorbed dose of ionizing radiation is less than 0.01 mGy from a chest radiograph and less than 1 mGy from a chest computed tomography (CT) scan. Maximum recommended total occupational exposure during pregnancy is 1 mGy, the mean annual dose received from background radiation. The threshold dose for fetal malforma- tion is 50–100 mGy, and while there is no threshold associated with an increased rate of later malignancy, the relative risk is modest at ×1.4 for a dose of more than 10 mGy. Thus, a chest radiograph or CT necessary to make a diagnosis should not be withheld from a preg- nant woman, although lung scintigraphy may be preferred to CT pulmonary angiography in the investigation of possible pulmonary embolism if the chest radiograph was normal. Echocardiogram Echocardiography is safe and useful. Views are standard other than for the absence of a subcostal view in later pregnancy. Normal find- ings include a small increase in the size of all cardiac chambers, mild regurgitation of all four valves, and the presence of a small pericar- dial effusion. Cardiac catheterization Diagnostic cardiac catheterization is rarely indicated in pregnancy, but percutaneous intervention may be required for valvular or cor- onary disease. Most interventional cardiac procedures are asso- ciated with a total maternal exposure of less than 50 mGy (usually 1–10 mGy), of which c.20% reaches the fetus. External shielding of the pelvis and abdomen is of limited protective value as most fetal exposure is caused by internally scattered radiation. However, fetal doses can be reduced by use of adjunctive imaging modalities such as transoesophageal echo, use of the transradial route for coronary intervention, and imaging of the woman in the first trimester with an empty bladder. A wedge should be placed under one hip during the procedure to prevent aortocaval compression. Magnetic resonance imaging (MRI) MRI avoids ionizing radiation and yields very high-quality diag- nostic information but is associated with theoretical fetal risk from heat, noise, and electromagnetic fields. If MRI is necessary in

 pregnancy, often for imaging of the aorta, gadolinium contrast is avoided. Pre-pregnancy assessment and risk stratification In all but the most straightforward cases a planned pregnancy is preferable to one that is unplanned. Prior to pregnancy a full clinical assessment should be made, including measurement of oxygen satur- ation, electrocardiogram (ECG), chest radiography, and echocardio- gram. Pre-pregnancy functional capacity is an important predictor of a woman’s ability to tolerate pregnancy, with those in New York Heart Association (NYHA) classes I and II generally having a good outcome. Treadmill exercise testing can be useful to define this: achievement of a level of above 7 METS (multiples of resting oxygen consumption) being used empirically by some centres to predict a good outcome. Invasive investigation may also be necessary. An estimate of maternal and fetal risk can then be given, together with recommendations for any medical, interventional, or surgical treatment before conception (Tables 14.6.1 and 14.6.2). Although it is a difficult issue to discuss, it is also important

that the prospective mother is fully aware of her expected lifespan and capacity. Maternal In parallel with the known lesion-specific risks, generic scoring sys- tems can be used to predict the risk of an adverse maternal event, but these are highly population dependent and tend to overestimate risk. The best overall maternal risk predictor is probably the modified World Health Organization risk classification, which integrates all known ma- ternal cardiovascular risk factors, both lesion-specific and generic. Fetal Maternal baseline NYHA III or IV, cyanosis, left heart obstruction, smoking, anticoagulation, and multiple pregnancy are adverse pre- dictors of fetal and neonatal outcome, especially prematurity and low birth weight. Recurrence risk of any nonmonogenic congenital heart disease is 3–6%, which is up to a 10-fold increase over the gen- eral population. Affected women should be offered fetal echocardi- ography and families with multiple cases of congenital heart disease should be offered referral to a clinical geneticist. Management—general principles Antenatal care Women in WHO class I can generally be managed locally, but in all other cases antenatal care should be multidisciplinary either in, or shared with, a specialist centre. Many cardiac drugs are relatively or ab- solutely contraindicated in pregnancy (see Chapter 14.20), and therapy should be reviewed before conception. In general warfarin should be changed to subcutaneous low-molecular-weight heparin (with anti-Xa level monitoring) for the duration of pregnancy, except in the case of mechanical valve replacements discussed later in this chapter. Cardiac surgery during pregnancy Maternal mortality rates are similar to those reported for emergency procedures in nonpregnant patients, but rates of fetal loss associated with cardiopulmonary bypass are high at 15–33%. Modifications to standard cardiopulmonary bypass may improve fetal outcome, but Table 14.6.1 Classification of maternal risk of pregnancy Risk class Risk of pregnancy by medical conditions I No detectable increased risk of maternal mortality and no/mild increase in morbidity II Small increased risk of maternal mortality or moderate increase in morbidity III Significantly increased risk of maternal mortality or severe morbidity. Expert counselling required. If pregnancy is decided upon, intensive specialist cardiac and obstetric monitoring needed throughout pregnancy, childbirth, and the puerperium IV 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 III Table 14.6.2 Maternal risk of pregnancy for women with various cardiac conditions Conditions in which pregnancy risk is WHO I • Uncomplicated, small, or mild — pulmonary stenosis — patent ductus arteriosus — mitral valve prolapse • Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage) • Atrial or ventricular ectopic beats, isolated Conditions in which pregnancy risk is WHO II or III WHO II (if otherwise well and uncomplicated) • Unoperated atrial or ventricular septal defect • Repaired tetralogy of Fallot • Most arrhythmias WHO II–III (depending on individual) • Mild left ventricular impairment • Hypertrophic cardiomyopathy • Native or tissue valvular heart disease not considered WHO I or IV • Marfan syndrome without aortic dilatation • Aorta <45 mm in aortic disease associated with bicuspid aortic valve • Repaired coarctation WHO III • Mechanical valve • Systemic right ventricle • Fontan circulation • Cyanotic heart disease (unrepaired) • Other complex congential heart disease • Aortic dilatation 40–45 mm in Marfan syndrome • Aortic dilatation 45–50 mm in aortic disease associated with bicuspid aortic valve Conditions in which pregnancy risk is WHO IV (pregnancy contraindicated) • Pulmonary arterial hypertension of any cause • Severe systemic ventricular dysfunction (LVEF <30%, NYHA III–IV) • Previous peripartum cardiomyopathy with any residual impairment of left ventricular function • Severe mitral stenosis, severe symptomatic aortic stenosis • Marfan syndrome with aorta dilated >45 mm • Aortic dilatation >50 mm in aortic disease associated with bicuspid aortic valve • Native severe coarctation

Section 14 Medical disorders in pregnancy 2600 consideration should also be given to early delivery, balancing the risk of fetal loss against those of prematurity. Labour and delivery In women in risk classes WHO III and IV, delivery should occur at the tertiary centre with a written management plan in place. Awaiting spontaneous onset of labour is the norm, with induction indicated for the standard obstetric reasons, maternal cardiac decompensa- tion, or for practical reasons, for example when the mother lives far from the intended site of delivery. Current National Institute for Health and Care Excellence guidelines do not recommend antibiotic prophylaxis for delivery. Vaginal delivery is generally recommended. There is not complete consensus on cardiac indications for caesarean section, but these are generally agreed to be: • aortopathy with aortic root more than 4.5 cm or rapidly dilating • aortic dissection • warfarin therapy within the preceding two weeks (although the maternal INR may be normal, the fetus clears warfarin more slowly and may still be at risk of cerebral haemorrhage) Low-dose epidural anaesthesia does not cause excessive vaso- dilatation, and with adequate volume expansion is the analgesia of choice. Invasive blood pressure monitoring is advisable in women with obstructive lesions (e.g. aortic stenosis), in whom large fluid shifts may be poorly tolerated. Observation and monitoring on a high-dependency unit may be required for up to one week post-partum. Specific cardiac conditions in pregnancy Cardiomyopathy Peripartum cardiomyopathy This is defined as an idiopathic cardiomyopathy presenting with heart failure secondary to left ventricular systolic dysfunction to- wards the end of pregnancy or in the months following delivery, where no other cause of heart failure is found. It is a diagnosis of exclusion. The left ventricle may not be dilated but the ejection fraction is nearly always reduced below 45%. Incidence in Western countries is 1 in 4000. Risk factors include multiple pregnancy, multiparity, hypertension, increased maternal age, and black ethnicity. The cause of peripartum cardiomyopathy is not known but may involve angiogenic imbalance in the heart due to systemic antiangiogenic signals in late pregnancy combined with inadequate local cardiac proangiogenic defences. It may be that activation of cathepsin D by oxidative stress is involved, leading to proteolytic cleavage of prolactin into a potent antiangiogenic, pro-apoptotic, and pro-inflammatory 16 kDa subfragment. Clinical features are those of left ventricular failure; the diagnosis should be suspected in any peripartum woman with dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea, or tachycardia. The differential diagnosis in includes pre-existing cardiomyopathy, valve disease or congenital heart disease, pregnancy associated myocar- dial infarction, pulmonary embolism/amniotic fluid embolism, and myocarditis. Echocardiography is key in the diagnosis, both to establish left ventricular systolic dysfunction and to exclude other cardiac causes (Fig. 14.6.1). Left ventricular failure is managed conventionally, with oxygen, diuretics, vasodilators (angiotensin-converting enzyme (ACE) in- hibitors post-partum only), β-blockers, and (occasionally) digoxin. There is a high risk of thromboembolism, necessitating the add- ition of a prophylactic or, in high-risk cases, treatment dose of low-molecular-weight heparin. There is some evidence to support the use of bromocriptine, an inhibitor of prolactin secretion. Patients with LVEF less than 35% are at increased risk of sudden cardiac death which may be temporarily mitigated by use of a wearable cardioverter-defibrillator device. Patients with haemodynamic instability despite treatment should undergo urgent delivery. Cases refractory to standard medical therapy may require intensive care with inotropic support and con- sideration of a ventricular assist device Extracorporeal membrane oxygenation (ECMO) or cardiac transplantation. Mortality is 9–15%, usually occurring within three months and predicted by poor NYHA class at presentation, larger left ventricle dimensions, lower ejection fraction (LVEF), and lack of contractile reserve on dobutamine stress echocardiography. Up to 60% of patients recover normal resting left ventricular function, which is crucial to the outcome of a future pregnancy (a)

(b) Fig. 14.6.1 Left ventricular dimensions on M mode echocardiogram. (a) Dilated impaired ventricle in peripartum cardiomyopathy. (b) Normal ventricle.

14.6 Heart disease in pregnancy 2601 (Fig. 14.6.2). We counsel against subsequent pregnancy in women whose left ventricular function has not recovered and offer termination of unplanned pregnancy. In those who are NYHA I with a normal resting echocardiogram, we attempt to refine their risk by exercise stress echo- cardiography, judging empirically that women with a normal contractile reserve are less likely to deteriorate during a pregnancy. This, however, will not predict cases of recurrence of the original pathological process and hence a further pregnancy will always involve a degree of risk. Dilated cardiomyopathy DCM is defined by the presence of left ventricular dilatation and systolic dysfunction in the absence of abnormal loading conditions (hypertension, valve disease) or coronary artery disease sufficient to cause global systolic impairment. PPCM is a form of acquired DCM presenting later in pregnancy or postpartum. Women may present with a pre-existing diagnosis or de novo in pregnancy when the haemo- dynamic load unmasks limited cardiac reserve. LVEF less than 40% is a predictor of adverse events in pregnancy and less than 30% or NYHA III/IV clinical status is a contraindication. Management is largely as discussed for peripartum cardiomyopathy, with the important add- ition of consideration of termination of pregnancy for women with worsening symptoms or ventricular function prior to fetal viability. Hypertrophic cardiomyopathy Women with hypertrophic cardiomyopathy generally tolerate preg- nancy well, with outcome predicted by pre-pregnancy functional status. An asymptomatic woman has a better than 90% chance of remaining so throughout her pregnancy. Reported mortality rates are 0–1%, with the two deaths in a recent series both being high- risk cases who had been advised against pregnancy. Pre-pregnancy assessment should include exercise testing, echocardiography, and standard assessment of sudden cardiac death risk. Women with a high outflow tract gradient are at increased risk and those with se- vere systolic or diastolic dysfunction should be advised against preg- nancy. Women with moderate diastolic dysfunction may require diuretic treatment if they do not cope with volume expansion. β- blockers should be continued and atrial fibrillation cardioverted if it occurs. An implantable cardioverter-defibrillator is no bar to preg- nancy. During labour cardiac filling pressures should be maintained by fluid infusion, especially in the event of post-partum haemor- rhage, and any epidural analgesia/anaesthesia should be low dose and slowly titrated to avoid vasodilatation and hypotension. Ischaemic heart disease In the 10 years from 1994, a small decrease in the female prevalence of hypertension and smoking, combined with an increase in dia- betes and obesity, resulted in an unchanged prevalence of cardio- vascular disease in women. However, the proportion of live births occurring to women in their thirties or older has more than doubled over the last 30 years, such that the prevalence of coronary atheroma in pregnant women is increasing. Known ischaemic heart disease pre-pregnancy is rare and should be assessed as if risk-stratifying for noncardiac surgery. Previous per- cutaneous coronary intervention or coronary artery bypass grafting is no bar to pregnancy if functional status is good and ventricular func- tion normal. Angina presenting in pregnancy should be managed with standard medical therapy, other than a statin as these are teratogenic. Percutaneous coronary intervention is feasible, as just described. Drug eluting stents should be avoided as their safety is unknown in pregnancy and their use would require prolonged dual antiplatelet therapy. Troponin I is unaffected by normal pregnancy and delivery. In the United States myocardial infarction occurs in 3–6 in 100 000 deliveries, with mortality 5–7%. Current UK incidence is 0.7/100 000 pregnancies. Most cases occur in the third trimester, largely peripartum. Risk factors include thrombophilia, infection, twin pregnancy, pre-eclampsia, and transfusion in addition to standard coronary risk factors. Coronary

atheroma is present in ap- proximately half of cases (43–60%), with the remainder caused by spontaneous dissection, thrombosis, or embolus. In 29% of cases, angiography is entirely normal and coronary spasm the presumed diagnosis; this has been reported following administration of the vasoconstrictor ergometrine to prevent post-partum haemorrhage (transfusion, listed here as a risk factor, may be a surrogate marker for this). Immediate angiography is the management of choice as it allows percutaneous intervention and appropriate targeting of sec- ondary coronary prevention. Thrombolysis is not contraindicated, but best avoided two weeks peripartum because of the risk of post- partum haemorrhage. Aspirin is safe, but there is only case report evidence about other antiplatelet drugs. Aortopathy Dilated aortic root Aortic root dilatation secondary to cystic medial necrosis occurs in association with Marfan syndrome and related disorders, Turner syndrome, familial thoracic aneurysm, bicuspid aortic valve, and repaired tetralogy of Fallot, but has also been reported in healthy pregnant women. Together with hypertension, atherosclerosis, and infection it confers a risk of type A dissection, most commonly in the third trimester or peripartum—the time of greatest haemodynamic shear stress to the aortic wall. Most of the literature concerns Marfan syndrome, with an overall pregnancy mortality of 1%. It is important to note that although pre-pregnancy aortic root dimensions less than 4 cm tend to remain 50 40 44% 21% 21% 25% 31% 14% 19% 0% 30 20 10 0 HF symptoms Maternal mortality 1 2 1 2 1 Percentage of women 2 1 2

> 20% decreased LVEF 20% decreased LVEF at F/U Fig. 14.6.2 Maternal complications in subsequent pregnancy in patients with previous peripartum cardiomyopathy. Group 1, LVEF more than 50% prior to subsequent pregnancy; group 2, LVEF less than 50%. HF, heart failure. From Elkayam U (2002). Pregnant again after peripartum cardiomyopathy: to be or not to be? European Heart J, 23, 753–6, with permission.

Section 14 Medical disorders in pregnancy 2602 stable during pregnancy, dissection can occur in a nondilated root, especially if there is a family history. Although the number of re- ported cases is small, the risk in Marfan syndrome appears to in- crease significantly if the aortic root diameter is greater than 4.5 cm, in which case elective aortic root replacement before conception should be considered. The risk of dissection is lower in other conditions, such as bicuspid aortic valve and tetralogy of Fallot, and a pre-pregnancy threshold of 5 cm is used for prophylactic surgery. In small women an indexed measurement of 2.7 cm/m2 BSA is more useful. The aorta should be screened by echocardiography and MRI/CT before conception and by echocardiogram every 4–12 weeks during pregnancy and the puerperium (Fig. 14.6.3). It is recommended that, regardless of root diameter, all higher risk women are fully β- blocked throughout pregnancy. If despite these measures the root dilates rapidly or dissects, the management of choice is caesarean delivery of a viable fetus followed by root replacement. If the fetus is nonviable, surgery should proceed, accepting the risk of fetal loss. Low-risk cases should have a normal delivery with consideration of an assisted second stage, but caesarean section should be considered when maximum aortic dimension exceeds 4.5 cm. Other obstetric complications of Marfan syndrome include recur- rent miscarriage, preterm rupture of membranes, and post-partum haemorrhage. Ehlers–Danlos type IV (associated with aortic in- volvement) confers a significant risk of uterine rupture and is there- fore a contraindication to pregnancy. Coarctation of the aorta Pregnancy is low risk in repaired

coarctation as long as there is no aneurysm at the site of repair: MRI or CT should be performed before conception to exclude this. Two recent series reported a single death, by type A dissection, in 104 women (20 unrepaired) under- going 244 pregnancies. The incidence of hypertension is fourfold higher than in the general pregnant population, particularly in those women with a residual or native gradient higher than 20 mm Hg. This should ideally be corrected prior to pregnancy. In the presence of a significant gradient the concerns are dual: maternal hyperten- sion, with risk of aortic dissection and stroke, and hypotension of the fetoplacental unit. Blood pressure should therefore be meas- ured in the right arm and either leg, using β-blockers as the first line antihypertensive agent to achieve systolic pressures of less than 140 mm Hg in the arm and more than 70 mm Hg in the leg. Delivery should usually be vaginal, with consideration of assisted second stage in the presence of a significant gradient or hypertension, un- less an aneurysm is present. Angioplasty and stenting of coarctation during pregnancy and the puerperium is not recommended because of the increased predisposition to dissection during this period, al- though there are no series from which to estimate risk. Pulmonary hypertension Pulmonary hypertension (mPAP >25 mm Hg at rest or 30 mm Hg on exercise) of any cause is high risk for pregnancy, with maternal mor- tality up to 25%. Effective contraception or termination should be advised. Women who elect to continue should be monitored closely in a specialist centre and advised strongly to reconsider termination should they deteriorate in the first or second trimester. Suggested treatments include bed rest, oxygen, anticoagulation, and targeted pulmonary vascular therapies such as sildenafil, nitric oxide, and prostacyclin analogues, but the evidence is scant. Bosentan is not recommended as it has been associated with animal teratogenesis. One small series reported an improved maternal mor- tality with a regimen of oxygen, heparin before delivery, and war- farin after 48 h; 60% of infants were liveborn, with most premature. Early reports of the use of nebulized iloprost, intravenous prosta- cyclin, and oral sildenafil are optimistic, but numbers are small, and deaths still occur. In the presence of a right-to-left shunt (Eisenmenger syndrome), systemic vasodilatation should be avoided as it increases shunting and therefore cyanosis, and thromboembolic prophylaxis should be considered. Admission for bed rest and timing of delivery are determined by the clinical status of the woman. There is no evidence to support the choice of either vaginal or caesarean delivery for cardiac reasons: va- ginal delivery is associated with a lower average blood loss but also increased maternal effort. In practice, early caesarean delivery is often required because of intrauterine growth retardation. In either case regional is preferable to general anaesthesia, as positive pressure ventilation reduces preload. Invasive blood pressure monitoring is required, and oxytocic drugs should be given as a low-dose infusion, rather than a bolus dose. Monitoring should continue for at least a week after delivery because the risk of sudden death post- partum is high. Valvular lesions Mitral stenosis This is generally rheumatic in aetiology, occurring predominantly in those born outside the developed world. The volume expansion and tachycardia of pregnancy can unmask a previously clinically silent lesion. Death rates are low but pulmonary oedema or arrhythmia occur in one-third, particularly those with valve area less than 1.5 cm2 or a history of cardiac events. Medical therapy includes β- blockade to increase time for diastolic filling, diuretics, and consid- eration of anticoagulation, as left atrial thrombus has been reported in pregnancy even in sinus rhythm. New atrial fibrillation should be cardioverted promptly. If NYHA III/IV symptoms develop despite medical therapy, and the valve is morphologically suitable, balloon mitral valvuloplasty is the treatment of choice, being clinically suc- cessful in more than 95% with significantly lower rates of fetal loss than surgery. Aortic stenosis and bicuspid aortic valve Bicuspid aortic valve (Fig. 14.6.3) in the absence of any stenosis or aortic dilatation can be managed as a normal pregnancy. Aortic stenosis is well tolerated if before pregnancy the patient is

asymptomatic, has a normal resting ECG, echocardiography shows normal left ventricle function with peak aortic valve gradient less than 80 mm Hg and mean less than 50 mm Hg, and a treadmill ex- ercise test to target heart rate (220 minus age) reveals no ST seg- ment change or arrhythmia and a normal haemodynamic response. Otherwise aortic stenosis should be relieved before conception using balloon dilatation or a tissue valve (if feasible) to avoid mech- anical valve replacement. A recent series reported a 10% complication rate in pregnant women with peak gradient more than 64 mm Hg or valve area less than 1 cm2, and no complications in those with less severe stenosis. The valve

14.6 Heart disease in pregnancy 2603 gradient increases as pregnancy progresses, and failure to do so is a warning sign of ventricular dysfunction. There is benefit in bed rest and β-blockade if a pregnant woman presents or becomes severely symp- tomatic with dyspnoea, angina, or syncope, but balloon valvuloplasty may need to be considered. Valve replacement during pregnancy car- ries a maternal mortality of 1.5–6%, and fetal mortality of 30%. Delivery should generally be vaginal, avoiding vasodilatation and fluid shifts, with consideration of caesarean under general an- aesthetic in severe symptomatic cases only. It is unknown whether pregnancy accelerates the progression of congenital aortic stenosis. Pulmonary stenosis This is generally well tolerated, although in severe cases may pre- cipitate right heart failure, tricuspid regurgitation, or atrial ar- rhythmia. Women with a pre-pregnancy peak echo gradient of more than 64 mm Hg or symptoms should be considered for balloon valvuloplasty or surgery before conception. Balloon valvuloplasty is also possible during pregnancy if symptoms develop. It has been suggested that women with pulmonary stenosis are at increased risk of hypertensive disorders and preterm delivery, but this requires confirmation. Mitral and aortic regurgitation Left-sided valve regurgitation is generally very well tolerated in pregnancy if ventricular function is normal. The offloading of the left ventricle caused by systemic vasodilatation is beneficial, but diuretics and vasodilators such as nitrates may be necessary in add- ition. ACE inhibitors are contraindicated in pregnancy. Small left-to-right shunts Atrial septal defect In the presence of a normal pulmonary vascular resistance an unre- paired atrial septal defect should be well tolerated. The pre-existing tendency to atrial arrhythmia may increase with the increase in car- diac output. The potential to shunt right to left in combination with the hypercoagulable state of pregnancy increases the risk of para- doxical embolism, especially with increases in intrathoracic pres- sure during labour. There should therefore be a low threshold for the use of compression stockings and prophylactic heparin in the pres- ence of immobility or additional risk factors for venous thrombosis. This also applies to patients known to have a patent foramen ovale. Surgical or device closure of the atrial septal defect removes this risk and if planned should therefore be carried out before pregnancy, al- though there is no evidence to support the same recommendation for patent foramen ovale. Ventricular septal defect or patent ductus arteriosus A small defect with normal right-sided pressures confers no added risk in pregnancy. Because of the large pressure gradient across the defect paradoxical embolism is extremely unlikely. Large defects causing pulmonary vascular disease (Eisenmenger’s syndrome) are high risk as discussed previously. Complex congenital heart disease For full descriptions of these lesions and their sequelae, see Chapter 16.12. Transposition of the great arteries—post Mustard
or Senning atrial repair Successful tolerance of pregnancy depends largely on good function of the systemic right ventricle and its atrioventricular valve. In a total of 195 pregnancies reported in 104 women there were two deaths, one heart transplant, and seven women with a permanent reduction in ventricular function or functional class. Atrial arrhythmia occurs in 10–20%, those with

a previous history being at higher risk. There is an increased incidence of miscarriage, prematurity, and low birth weight. More recently, repair has been by the arterial switch oper- ation, following which pregnancy appears to be well tolerated, but the number reported remains relatively small. Congenitally corrected transposition of the great arteries Outcome of this rare condition (where the circulation is physio- logically ‘corrected’, with blood passing from the pulmonary veins to the left atrium, to the right ventricle, to the aorta) depends on systemic right ventricular function and the presence of associated lesions such as complete heart block, ventricular septal defect, or pulmonary stenosis. Fontan operation for univentricular circulation These patients have two separate circulations in series and are there- fore usually not cyanosed, but they experience a chronic low-output state and are at risk of ventricular failure, atrial arrhythmia, and thrombosis. They are generally anticoagulated with warfarin, which should be converted to full dose low-molecular-weight heparin for (a) (b) Fig. 14.6.3 Bicuspid aortic valve (a) in short axis, (b) showing the aortic root measurements used in monitoring.

Section 14 Medical disorders in pregnancy 2604 the duration of pregnancy. Maternal outcome again depends on functional capacity and ventricular function. If these are satisfac- tory and the woman accepts the two to threefold increase in the rate of first trimester fetal loss, then there is no reason to advise against pregnancy, as any deterioration appears to be reversible. Surgically corrected tetralogy of Fallot Women with good functional capacity and no significant haemo-dynamic abnormality tolerate pregnancy well, although the pres- ence of severe pulmonary regurgitation may confer a 20–30% risk of symptomatic heart failure. If the mother carries del22q11, the re- currence risk is 50%. Cyanotic heart disease without pulmonary hypertension Cyanosis is associated with a poorer outcome for both mother and fetus. The risk of paradoxical embolism should be reduced by appro- priate hydration, mobilization, use of compression stockings, and consideration of thromboprophylaxis. Because cyanosis also con- fers an increased bleeding tendency, full-dose anticoagulation is not used routinely but only if there is an additional indication. Increased right-to-left shunting can occur with the systemic vasodilatation of pregnancy, causing worsening cyanosis. Fetal outcome is dependent on maternal saturation—the chance of a live birth decreases from 92% with pre-pregnancy maternal saturation over 90%, to 12% if maternal saturation is less than 85%, and many of these infants are premature or of low birth weight. Prosthetic valves Bioprosthetic valves do not confer increased risk if haemodynamics are normal, and they do not degenerate more rapidly in pregnancy as previously feared. The management of a mechanical prosthesis is far less straightforward because of a conflict of interest between the mother and fetus. Complication rates associated with the alternative anticoagulation regimens are shown in Table 14.6.3. The increased rate of fetal loss associated with all effective anticoagulation may re- flect retroplacental haemorrhage. A relatively safe option for the mother is to remain on war- farin for the duration of the pregnancy, changing to dose-adjusted unfractionated or low-molecular-weight heparin at 36 weeks (to allow the fetus to clear the warfarin) if vaginal delivery is planned, or at 38 weeks for elective caesarean delivery. This strategy is associated with a risk of warfarin embryopathy, which is significantly reduced if the dose required to achieve target INR is less than 6 mg daily. Heparin does not cross the placenta, hence a strategy of sub- stituting heparin for warfarin during the period of organogenesis (6–12 weeks) abolishes the risk of warfarin embryopathy, but it doubles the maternal thromboembolism rate. Heparin throughout pregnancy has historically been associated with a high risk of thromboembolism but has not always been appropriately dose- adjusted. With twice-daily dosing of low-molecular-weight hep- arin and anti-Xa levels monitored fortnightly, achieving a level of

1–1.2 IU/ml 4–6 h post dose, the thromboembolism rate in one meta-analysis was only 2%. Arrhythmia Ectopy occurs in most pregnancies, but sustained arrhythmia in less than 1%. A pre-existing tachyarrhythmia confers a 50% chance of a recurrence of supraventricular tachycardia and 25% of ventricular tachycardia. The principles of diagnosis and management are the same as in the nonpregnant state—only recurrent symptomatic or life-threatening arrhythmia should be treated and underlying causes such as thyroid disease should be sought and corrected. Vagal manoeuvres are useful as a first line to diagnose or terminate a narrow complex tachycardia. Adenosine is safe in pregnancy, as is DC cardioversion with fetal monitoring. The risk/benefit ratio of all drugs should be assessed: no drug is absolutely contraindicated, as maternal haemodynamic instability may result in worse fetal outcome. Bradyarrhythmia is rare; the presence of a permanent pacemaker or implantable cardioverter-defibrillator is no problem, but the per- manent pacemaker may need to be reprogrammed for delivery. Equipment for temporary pacing during labour is recommended, though not usually needed, for nonpaced women with complete heart block. Contraception Barrier methods These are safe for all cardiac patients and have the added benefit of protection against sexually transmitted infections, but reported failure rates are 2–26 per 100 womanyears. Hormonal methods The oestrogen component of the combined oral contraceptive, whether oral or transdermal, confers an increased risk of thrombosis that is not completely abolished by warfarin. These preparations are therefore contraindicated in women who already have a high thrombotic risk (i.e. pulmonary hypertension, the Fontan circula- tion, older mechanical valves, dilated cardiac chambers with the risk Table 14.6.3 Complication rates (%) of anticoagulation regimens in pregnant women with mechanical heart valves Regimen Maternal thromboembolism Maternal death Fetal abnormality Fetal lossa Source Warfarin to 38/40, then heparin 4 2 6 34 Chan et al. (2000) Heparin 6–12/40, warfarin otherwise 9 4 0b 16 Chan et al. (2000) Heparin throughout 25 7 0 44 Chan et al. (2000) Heparin anti-Xa adjusted throughout 2 0 0 12c Oran et al. (2004) a Refers to miscarriage, stillbirth, or neonatal death. b If heparin instituted at or before 6/40. c Miscarriage and stillbirth only.

 of atrial fibrillation, or in cyanosed patients in whom paradoxical embolism may occur). The standard progesterone-only ‘mini pill’ is safe, but is less reliable than the combined oral contraceptive pill and therefore not the method of choice for women in whom avoidance of pregnancy is critical. Recommended progesterone-only prepar- ations, more reliable as they act by suppression of ovulation, include daily oral desogestrel, 3-monthly depot medroxyprogesterone, and a subcutaneous etonogestrel implant (Nexplanon), which is the method of choice for complex congenital heart disease. Women concurrently taking the endothelin antagonist bosentan require additional protection. Intrauterine devices These are not contraindicated, but insertion of the device can be as- sociated with bacteraemia and also a vasovagal response, which can be life-threatening in a haemodynamically unstable patient such as those with a Fontan circulation or Eisenmenger’s syndrome. Sterilization Sterilization by tubal ligation may be appropriate for women in whom pregnancy would be high risk. However, failure may result in ectopic pregnancy and the surgery is not trivial, especially in women at risk of paradoxical embolism, as it includes a head-down tilt and distension of the abdomen with CO_2. Sterilization of the male partner is not generally advised if he has a much longer potential lifespan than his partner and may therefore wish to father children in a subsequent relationship. See Chapter 14.21 for further discussion of contraception for women with medical diseases. FURTHER READING Bates SM, et al. (2008). Venous thromboembolism, thrombophilia, antithrombotic therapy, and Pregnancy: ACCP Clinical Practice Guideline. Chest, 133, 844S–66S. Bauersachs J, et al. (2016). Current management of patients with se- vere acute peripartum

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Revision #1
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