Congenital Heart Disease in Adolescents and Adults
Series Editors: Massimo Chessa · Helmut Baumgartner
Andreas Eicken · Alessandro Giamberti

Jolien W. Roos-Hesselink
Mark R. Johnson *Editors*

Pregnancy and Congenital Heart Disease

Springer

Congenital Heart Disease in Adolescents and Adults

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The ESC Working Group on Grown-up Congenital Heart Disease
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The aim of this series is to cast light on the most significant aspects – whether still debated or already established – of congenital heart disease in adolescents and adults and its management. Advances in the medical and surgical management of congenital heart disease have revolutionized the prognosis of infants and children with cardiac defects, so that an increasing number of patients, including those with complex problems, can reach adolescence and adult life. The profile of the adult population with congenital heart disease (ACHD) is consequently changing, and in future many adult patients will present different hemodynamic and cardiac problems from those currently seen. A cure is rarely achieved, and provision of optimal care is therefore dependent on ongoing surveillance and management in conjunction with experts in this highly specialized field. Specialists in ACHD management need to have a deep knowledge not only of congenital cardiac malformations and their treatment in infancy and childhood, but of general medicine, too. A training in adult cardiology, including coronary artery disease, is also essential. Similarly, surgeons need to acquire expertise and good training in both adult and pediatric cardiosurgery. Readers will find this series to be a rich source of information highly relevant to daily clinical practice.

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Preface to the Series

In Europe, we are currently faced with an estimated ACHD population of 4.2 million; adults with congenital heart disease now outnumber children (approximately 2.3 million). The vast majority cannot be considered cured but rather having a chronic heart condition that requires further surveillance and timely re-intervention for residual or consequent anatomical and/or functional abnormalities. ACHD patients have very special needs and the physicians taking care of them need expert training. Special health care organization and training programs for those involved in ACHD care are therefore required to meet the needs of this special population.

ACHD problems remain a small part of general cardiology training curricula around the world, and pediatric cardiologists are trained to manage children with CHD and may, out of necessity, continue to look after these patients when they outgrow pediatric age.

There are clearly other health issues concerning the adult with CHD, beyond the scope of pediatric medicine, that our patients now routinely face. Adult physicians with a non-CHD background are therefore increasingly involved in the day-to-day management of patients with CHD.

Experts in congenital heart disease should work to improve the health care system, so that teens and young adults have an easier time making the transition from receiving health care in pediatric cardiology centers to receiving care from specialists in adult cardiology.

The aim of this series is to cast light on the most significant aspects of congenital heart disease in adolescents and adults and its management, such as transition from pediatric to adulthood, pregnancy and contraception, sport and physical activities, pulmonary hypertension, burning issues related to surgery, interventional catheterization, electrophysiology, intensive care management, and heart failure.

This series wishes to attract the interest of cardiologists, anesthesiologists, cardiac surgeons, electrophysiologists, psychologists, GPs, undergraduate and postgraduate students, and residents, and would like to become relevant for courses of cardiology, pediatric cardiology, cardiothoracic surgery, and anesthesiology.

We thank both the wonderful groups of leading cardiovascular experts from around the world, for donating their precious time, producing excellent textbooks and making this book series a reality, and the members of the two Working Groups (ESC and AEPC ACHD/GUCH Working Group) for the invaluable suggestions and support without which this work would not be possible.

San Donato, Italy — Massimo Chessa
Münster, Germany — Helmut Baumgartner
Munich, Germany — Andreas Eicken
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Preface

Advances in diagnostic modalities and treatment options for children born with a congenital heart defect have changed the landscape of patients with congenital heart disease considerably. Advanced cardiac surgery and intensive care have dramatically improved the outcome for these patients: before the introduction of the heart-lung machine, survival was about 15 %; now more than 90 % of patients reach adulthood. Half are women, and most of them want to start a family and raise children. However, pregnancy has a major impact on the cardiovascular system. It not only leads to an increase in cardiac output of up to 50 % but also increases the risk of thromboembolic complications and the development of arrhythmias. Further, pregnancy appears to affect vessel structure, increasing the risk of aortic dissection. Delivery is the period of dramatic fluid shifts predisposing to the development of pulmonary oedema.

Most patients with congenital heart disease are diagnosed when young and have undergone corrective cardiac surgery. However, some still have residual lesions, and, in others, the diagnosis was missed or the condition was found to be inoperable. As a group, women with CHD are at higher risk of developing complications during pregnancy and after delivery. Cardiovascular mortality and morbidity are higher in patients with heart disease; heart failure and arrhythmias are especially common. Therefore, timely counselling and risk stratification are of great importance. In addition, the mother's life expectancy and the impact of the pregnancy on her condition should be discussed openly. Some women may need treatment before embarking on a pregnancy, and others may need to have existing treatment optimized. Follow-up during pregnancy and the timing, place and mode of delivery are also important and sometimes difficult issues.

Specific knowledge is not available from large randomized trials in this field, and therefore, many decisions are made based on "expert knowledge". This book is an extremely valuable resource for all those looking after women with congenital heart disease especially when they are pregnant. It provides up-to-date information on specific topics and gives detailed, lesion-specific information from well-known experts in this field. We hope this book will be the definitive resource for cardiologists, obstetricians, anaesthetists and other members of the team providing care and support to women with congenital heart disease.

Rotterdam, The Netherlands — Jolien W. Roos-Hesselink
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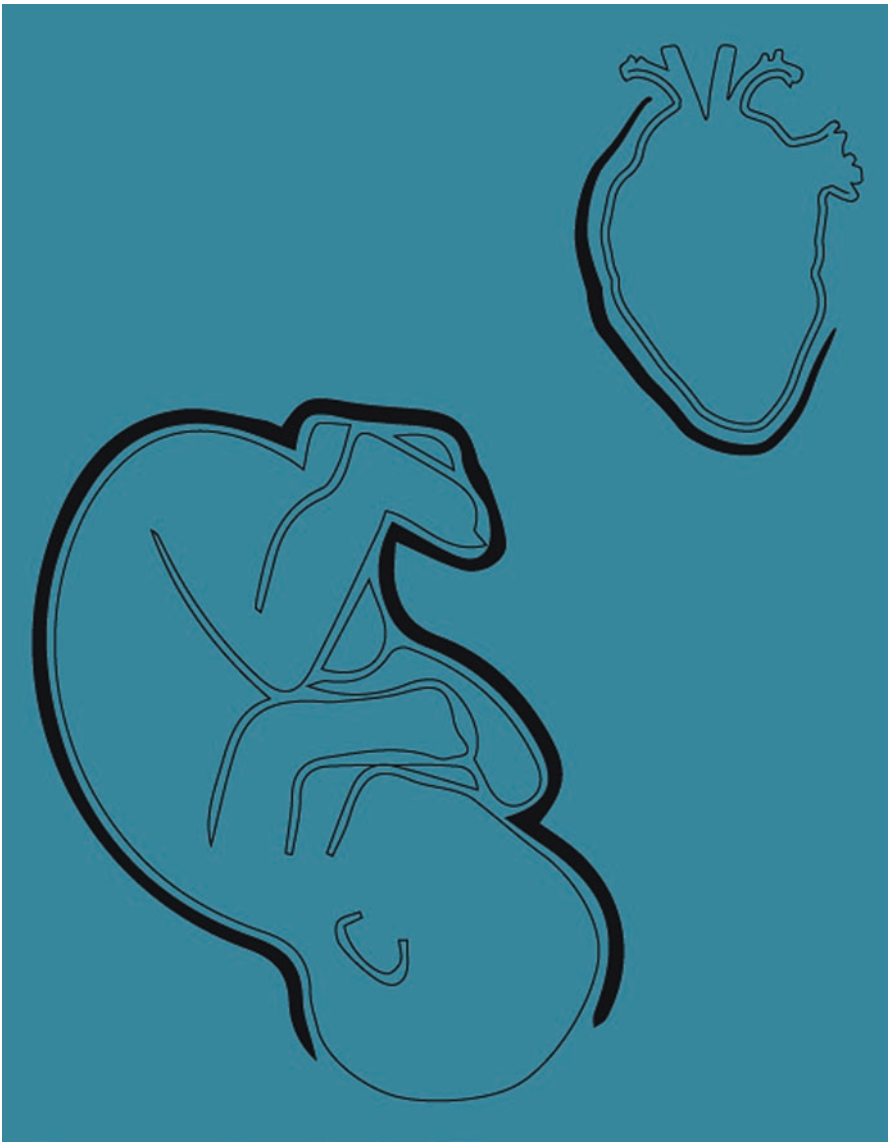

Pregnancy and Congenital Heart Disease

Contents

Part I

General Issues

Fetal Heart Disease

1

Julene S. Carvalho and Olus Api

Abbreviations

3VTV	Three vessels and trachea view
3VV	Three-vessel view
CHD	Congenital heart disease
ISUOG	International Society of Ultrasound in Obstetrics and Gynecology
LA	Left atrium
LV	Left ventricle
NHS FASP	National Health Service Fetal Anomaly Screening Programme
NT	Nuchal translucency
PA	Pulmonary artery
RA	Right atrium
RV	Right ventricle
SSA	Sequential segmental analysis
SVC	Superior vena cava
VMax	Maximal velocity

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1.1 Introduction

Imaging of the fetal heart started in the 1980s but was mainly targeted at high-risk pregnancies [1–3], such as those with previous family history of congenital heart disease (CHD). The introduction of the four-chamber view into routine obstetric scans of low-risk pregnancies was first reported by Fermont et al. in 1985 [4] and initiated the pathway for antenatal screening. However, based on this view alone, antenatal detection remained low, being 23 % in the UK in the mid-1990s [5]. The importance of adding outflow tract views as well as training professionals at the forefront of screening cannot be underestimated, but over the years, improvements in detection rates have been slow. More recently however, dissemination of clinical guidelines and national protocols have had a positive impact on screening.

1.2 Birth Prevalence of CHD

Congenital heart defects are the most common cause of major congenital anomalies. In the EUROCAT study, they accounted for 28 % of major defects [6]. Whilst a birth prevalence of 8 per 1000 live births is generally accepted, there seems to be variation worldwide and over time [7–9]. According to a recent systematic review and meta-analysis, which included eight common types of major CHD, total CHD birth prevalence was found to increase substantially over time. It changed from 0.6 per 1000 live births in 1930 to 1934 to 9.1 per 1000 live births after 1995 but has remained stable over the last 15 years to 2010 [8]. Ventricular septal defects were the most commonly encountered CHD. Significant geographical differences also occurred, being highest in Asia (birth prevalence of 9.3 per 1000 live births) and significantly higher in Europe (8.2 per 1000) than in North America (6.9 per 1000) [8].

Limited access to health care and diagnostic facilities such as echocardiography may be responsible for some of the differences in reported birth prevalence. On the other hand, observed variations may also be of ethnic, genetic and environmental origin. In part, however, some of the differences are due to inclusion of a milder form of CHD such as small ventricular septal defects, mild pulmonary stenosis and bicuspid aortic valves [7, 9]. From the fetal cardiologist's perspective, the more significant forms of CHD are the ones most likely to be suspected on routine screening. These are also more likely to have an impact on fetal and neonatal outcome. Hoffman and Kaplan [9] reported an incidence for moderate to severe forms of CHD of 6 per 1000 live births. In general, approximately half of defects are considered major, i.e. with a prevalence of about 4 per 1000 live births [10].

1.3 Risk Factors for CHD

Inheritance of CHD is multifactorial. Various risk factors, from genetic or genome variations to teratogen exposure, trigger molecular responses during cardiac development that may lead to CHD [11]. However, the vast majority of fetuses with heart defects are

seen in families without a known risk factor, which highlights the importance of having an effective screening programme for the detection of fetal heart disease.

In Chap. 4, inheritance of CHD is discussed at length. Briefly, recurrence is low for most forms of structural defects. In a population-based study, previous history of any CHD in first-degree relatives accounted for 2.2 % of the heart defects [12]. The risk associated with a previous child with a non-syndromic defect is around 2–3 %, rising to 10 % with two previously affected pregnancies [13, 14]. If one of the parents has CHD, the overall risk is increased to about 2–4 % [14, 15] but higher in the presence of maternal CHD (~6 %) [15]. A higher risk is also seen in association with left-sided obstructive lesions [16]. Risks other than family history can be of maternal or fetal origin. They also constitute an indication for fetal echocardiography and are summarized below.

1.3.1 Maternal Risk Factors

1.3.1.1 Autoantibodies

The risk associated with maternal autoantibodies (anti-Ro/SSA, anti-La/SSB) is mainly related to development of fetal heart block rather than structural CHD. With no previously affected child, the risk is around 4 % but significantly higher (19 %) if a previous child has developed heart block [17]. Serial scans are often performed, aiming to capture the development of first- and second-degree block, even though there is no effective evidence-based therapy to prevent progression to complete heart block. Recent evidence also suggests that the individual risk of heart block is affected by the level of maternal antibodies and that serial scans should be restricted to pregnant women with high levels [18]. Currently however, antibody levels are not widely available at the time women are referred for fetal echocardiography.

Autoantibodies have also been linked to myocardial dysfunction and endocardial fibroelastosis [19] and, rarely, rupture of mitral valve subvalvar apparatus leading to important mitral regurgitation [20].

1.3.1.2 Pre-gestational Diabetes

The risk associated with maternal diabetes is five times greater than the general population [21] and up to 8.5 per 100 live births in one study [22]. Common defects include double-outlet right ventricle, truncus arteriosus, transposition of the great arteries and ventricular septal defect [23, 24]. A link with isomerism has also been established [25]. Hyperglycaemia is known to modify multiple biochemical and signal transduction pathways; thus high maternal levels of haemoglobin A1c during early pregnancy are associated with increased risk of malformations [26, 27]. However, maternal diabetes continues to influence the fetal heart through the second and third trimesters. Reversible hypertrophic cardiomyopathy has long been described in infants of the diabetic mothers [28]. It may be observed whether or not there is reasonable metabolic control [26, 29], although there is some evidence that fetal insulin levels are related to myocardial wall thickness [30].

1.3.1.3 Phenylketonuria

Maternal phenylketonuria also increases the risk of CHD significantly, being 15-fold above the general population in untreated pregnancies [31]. High maternal levels of phenylalanine (>30 mg/dL) increase the risk significantly. Preconception or early pregnancy low phenylalanine diet to achieve a basal maternal level <15 mg/dL especially in the first 8 weeks of pregnancy may be effective in preventing CHD. Tetralogy of Fallot, aortic coarctation and hypoplastic left heart syndrome have been reported in the offspring [31, 32].

1.3.1.4 Maternal Obesity

There is some evidence that obese women are at increased risk of having a child with CHD [33, 34]. In a population-based study, the odds ratio of women with BMI >30 having an affected child was 1.15 (95 % CI 1.07–1.23) compared to normal weight women. The risk was even higher for women with BMI >40 compared to BMI >30 (Odds ratio = 1.33 95 % CI 1.15–1.54). A significant trend existed between increasing obesity and the odds ratio of having a child with CHD [33]. There is additional evidence that risks remain high, after excluding women with pregestational diabetes and controlling for oral glucose tolerance test, suggesting that factors other than abnormal glucose metabolism may be involved [34].

1.3.1.5 Folic Acid

There is some evidence that preconceptual folic acid supplementation protects against the development of CHD [35, 36], similar to the known risk reduction for neural tube defects [35–37]. This finding was first identified from a Hungarian randomized trial on birth defects where the use of multivitamins containing folic acid was associated with an approximate 60 % overall reduction in risk for CHD [38, 39]. A similar population-based case-control study done in Atlanta revealed an approximate 25 % overall reduction in risk for CHD [40]. Although folic acid-containing multivitamin supplements seem to have a possible protective effect for CHD, the results are still inconclusive due to the limited number of studies and the multifactorial nature of CHD.

1.3.1.6 Teratogenic Drugs

Exposure to teratogenic drugs during pregnancy may be unavoidable, including anticonvulsants (e.g. phenytoin, carbamazepine and valproic acid) and antidepressants (e.g. lithium carbonate). Other examples include retinoids, ethanol and ACE inhibitors [37].

1.3.2 Fetal Risk Factors

1.3.2.1 Increased Nuchal Translucency

An increased nuchal translucency (NT) thickness measured by ultrasound in the fetus at 10–14 weeks of gestation is a recognized marker for chromosomal abnormalities and is also an independent risk factor for CHD [41]. The reason for this

association is unclear but may be related to the lymphatic system [42]. In chromosomally normal fetuses, the risk of CHD increases with increasing NT measurement [42, 43]. Thus, in a proportion of affected pregnancies, CHD can potentially be identified in the late first/early second trimester. In a pooled analysis of CHD diagnosed in four major centres, increased NT was associated with earlier diagnosis by approximately 6 weeks [44]. However, despite this strong association, the NT measurement alone is only modestly effective as a screening tool as most fetuses with major CHD have normal measurements [45]. It has been shown that NT>95th centile (~2.5 mm but value varies with fetal crown-rump-length) and NT >99th centile (> 3.5 mm) may predict 37 % and 31 % of major CHD, respectively [46]. The presence of increased NT in combination with tricuspid regurgitation and abnormal ductus venosus Doppler flow profile in the first trimester is a stronger marker for CHD [47].

It is currently recommended that all women with a fetal NT measurement greater than 3.5 mm be referred for detailed fetal cardiac assessment. Depending on local resources and expertise, fetuses with NT >4 mm may be evaluated in early pregnancy, at 13–16 weeks of gestation.

1.3.2.2 Extra-Cardiac and Chromosomal Abnormalities

Certain extra-cardiac and chromosomal abnormalities should prompt referral to fetal cardiology. Conversely, in the presence of a major CHD, fetal medicine assessment is also indicated. Important examples include abdominal wall defects (e.g. exomphalos), gastrointestinal obstruction (e.g. duodenal atresia) and diaphragmatic hernia [48–50]. In the latter, the fetal heart may also show features of left heart hypoplasia, even in the absence of a structural defect, which may represent functional alterations due to external compression [51]. Fetal cardiac abnormalities may also occur in association with central nervous, genitourinary and skeletal systems.

The most common examples of chromosomal defects associated with CHD are trisomy 21 (Down syndrome) and micro-deletion of chromosome 22q11 (Di George syndrome), with a high prevalence of atrioventricular septal defects and conotruncal malformations, respectively.

1.3.2.3 Suspected CHD

It is long known that the most important factor to detect fetal CHD is to suspect an abnormality during routine screening. About 80 % of abnormal cases in Alan's series were cases of suspected CHD [1]. Many other reports have echoed these findings and as outflow tract views are gradually incorporated into routine screening, the detection rate of CHD is expected to increase.

1.4 Screening for CHD

Following the French initiative to introduce the four-chamber view to routine obstetric scans and subsequent introduction of outflow tract views, in utero detection of major CHD still remains around 50 % according to most recent studies [52–55]. Cardiac

lesions that require intervention in the first 28 days of life are defined as critical CHD, and without prenatal diagnosis, some may not be identified until after neonatal discharge, leading to increased morbidity and mortality [56–58]. Some reports have shown that prenatal diagnosis of specific types of CHD has a positive impact on outcome [59–61]. Thus, every effort should be made to improve antenatal detection of CHD.

1.4.1 Screening Guidelines and UK Cardiac Protocol

Over the years, the importance of assessing outflow tracts when screening for CHD in pregnancy has been stressed – but with the caveat 'when technically feasible'[62–64]. In 2008, the UK National Institute for Health and Care Excellence [65] also recommended that outflow tracts should be included to screening. However, this was only implemented in 2010 when the National Health Service Fetal Anomaly Screening Programme (NHS FASP), now part of NHS England, published a national cardiac protocol. The FASP protocol included assessment of (1) situs, (2) four-chamber view, (3) left ventricular outflow tract and (4) right ventricular outflow tract or three-vessel view.

In 2013, the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) also published revised guidelines whereby a comprehensive assessment of the fetal heart is recommended and achieved through five axial planes of the fetal chest [66, 67] (Fig. 1.1). The 2010 FASP protocol did not include the fifth plane (three-vessel and trachea view), which is to be incorporated in the UK screening programme in 2016 [68]. Both ISUOG and FASP recommended that fetal laterality and visceral situs be part of screening. This was first suggested in 1997 [69]. Its screening value should not be underestimated as many complex forms of CHD are associated with atrial isomerism/heterotaxy.

In practice, it is difficult to ensure that guidelines are followed at national and international level in order to deliver equal care to all pregnant women worldwide. It is well accepted that the effectiveness of any screening programme is highly dependent on training, so that professionals responsible for screening can deliver such care [70–72]. Data from the UK National Institute for Cardiovascular Outcomes Research [73] shows that the percentage of infants requiring surgery or catheter intervention for CHD has increased over the years since 2003. A steeper increase around 2010 suggests this may be related to introduction of the FASP cardiac protocol.

1.5 Fetal Cardiology Assessment

The role of a fetal cardiologist, beyond making an accurate diagnosis, is to provide the parents with a comprehensive, evidence-based picture of the outcome possibilities, starting with pregnancy, through childhood, and into adult life [74]. This is not an easy task. Surgical results and outcomes are constantly changing and naturally, counselling is lesion specific (e.g. tetralogy of Fallot) and within each lesion, it is further tailored to the scan findings in each individual fetus (e.g. tetralogy of Fallot with pulmonary stenosis versus pulmonary atresia).

Ideally, fetal cardiac assessment happens within a fetal medicine unit or in close collaboration with a fetal medicine specialist to facilitate a multidisciplinary approach. In the fetus with a cardiac abnormality, risk of extra-cardiac, chromosomal or genetic abnormalities and the option of invasive tests (amniocentesis or cordocentesis) need to be discussed. The first step, however, is to establish an accurate diagnosis. Similarly to postnatal cardiology, it is important to adopt a structured approach, often based on a sequential segmental analysis (SSA) of the heart [75–77].

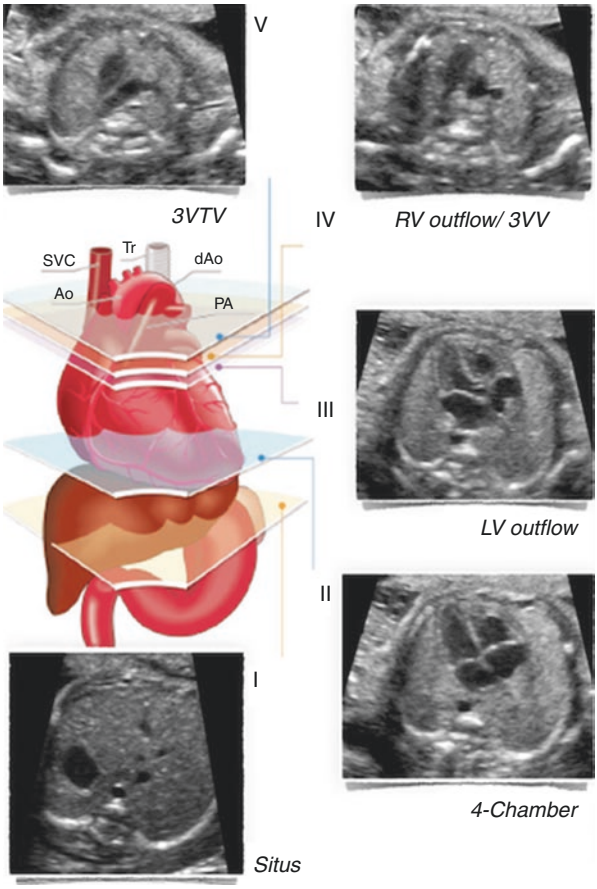

Fig. 1.1 (**a**) The five axial views for optimal fetal heart screening. The colour image shows the trachea, heart and great vessels, liver and stomach, with the five planes of insonation indicated by polygons corresponding to the grey-scale images, as indicated. (*I*) Most caudal plane, showing abdominal situs. (*II*) Four-chamber view. (*III*) Left ventricular (*LV*) outflow tract. (*IV*) Right ventricular (*RV*) outflow tract/three-vessel view (*3VV*). (*V*) Three vessels and trachea view (*3VTV*). *Ao* aorta, *dAo* descending aorta, *PA* pulmonary artery, *SVC* superior vena cava, *Tr* trachea (Modified with permission from Carvalho et al. and Yagel et al. © ISUOG [66, 67]). (**b**) Increase in number referrals for suspected cardiac abnormalities, 2003–2013, Fetal Medicine Unit, St George's Hospital, London, UK

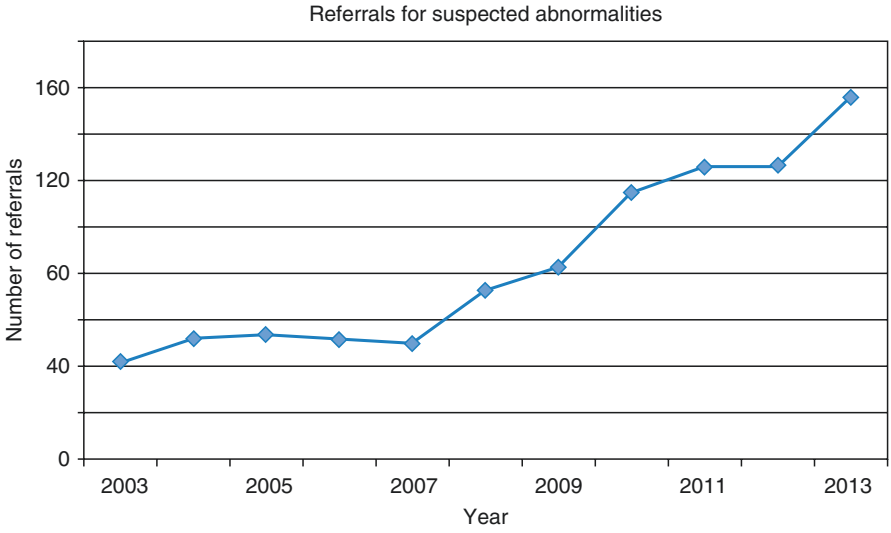

Fig. 1.1 (continued)

1.5.1 Structural Fetal CHD

Being able to confirm normality of the fetal heart is as important as making the diagnosis of CHD, simple or complex. For the pregnant woman who is aware of the increased risk of cardiac malformation in her unborn child, reassurance is of paramount importance. For those referred because of a suspected abnormality, accuracy of diagnosis forms the platform for subsequent pregnancy management. Neither scenario can be underestimated. In both instances, it is important to approach the fetal heart in a logical manner. The SSA offers a step-by-step approach to describing the cardiac anatomy in normal and malformed fetal hearts. Determination of situs, cardiac connections and associated defects facilitates understanding of the pathophysiology of abnormalities, which is essential for counselling families.

When applied to the fetus, the SSA differs, in that prior to ascertaining abdominal situs and by inference, atrial arrangement, it is imperative to determine fetal laterality [69, 77]. This is achieved by assessing fetal lie within the maternal abdomen so that the right and left sides of the fetus can be established. Subsequently, the same 7postnatal rules and definitions used in the SSA apply.

The diagnosis of major CHD involving abnormalities of cardiac connections is often straightforward, such as in tricuspid atresia and complete transposition of the great arteries (Fig. 1.2). More complex lesions, including those seen in the setting of atrial isomerism, can also be identified accurately but are also more challenging.

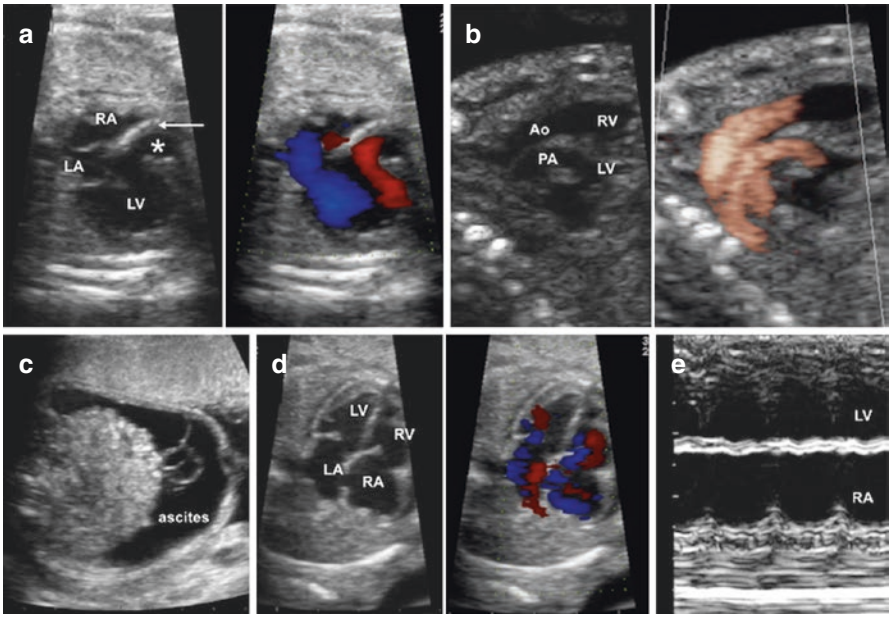

Fig. 1.2 (**a**) Four-chamber view obtained from a fetus with tricuspid atresia, obtained at 32 weeks of gestation. *Left* panel, 2D and *right* panel, with colour Doppler. The *arrow* points to the absent right atrioventricular connection. (**b**) Images obtained from a fetus at 23 weeks of gestation, with complete transposition. *Left* panel (2D) and *right* panel (e-flow mapping) are sagittal views of the fetus showing the parallel arrangement of the two vessels with an anterior aorta and posterior pulmonary artery. (**c**–**e**) Images obtained from a hydropic fetus at 25 weeks of gestation, with supraventricular tachycardia, partially controlled on dual maternal therapy. (**c**) Shows fetal ascites, (**d**) four-chamber view shows cardiomegaly and mitral and tricuspid regurgitation, (**e**) M-mode recoding shows 1:1 atrioventricular conduction with heart rate = 215 bpm. Pretreatment rate was 270 bpm. The rhythm was sinus a few days afterward. *Ao* aorta, *LA* left atrium, *LV* left ventricle, *RA* right atrium, *RV* right ventricle, *PA* pulmonary artery, * rudimentary RV

It can be more difficult to exclude relatively minor defects, e.g. a small to moderate perimembranous ventricular septal defect, than to diagnose a complex abnormality. If images are suboptimal, additional scans may be needed.

An important consideration in fetal heart disease relates to potential progression of obstructive lesions as pregnancy advances [78–80]. A classical example is seen in critical aortic stenosis in mid-pregnancy that is likely to progress to hypoplastic left heart syndrome (Fig. 1.3). Also to be taken into account in predicting postnatal presentation of CHD are the physiological perinatal circulatory changes. In addition to closure of the foramen ovale, ductus arteriosus and ductus venosus, changes in right and left ventricular preload and afterload may alter the appearances of the normal and abnormal heart. This is particularly relevant in cases of borderline left ventricle when trying to predict if it will be able to sustain a biventricular circulation after birth.

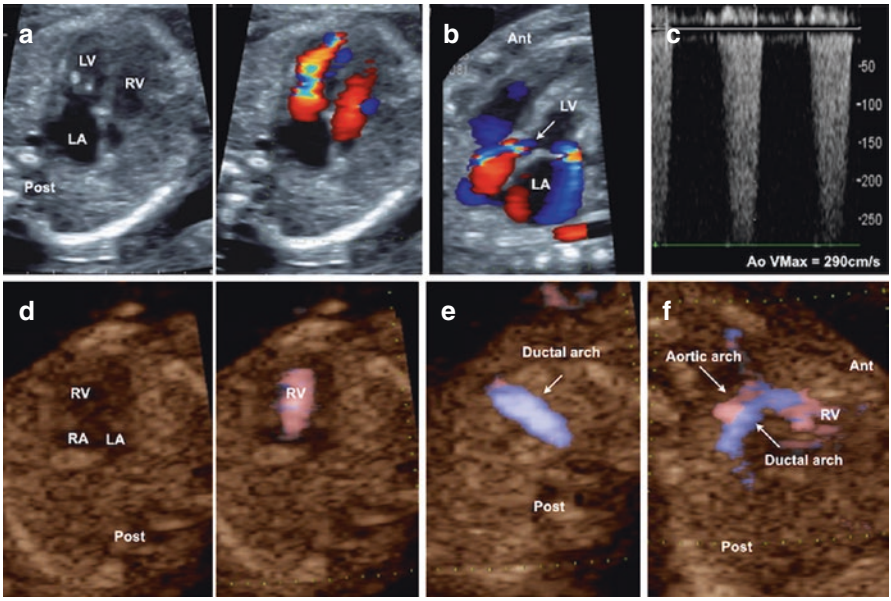

Fig. 1.3 (**a**–**c**) Images obtained from a fetus at 21 weeks of gestation with critical aortic stenosis. (**a**) Four-chamber view in diastole on 2D (*left* panel) and colour flow (*right* panel) shows a dilated left atrium. The left ventricle reaches the cardiac apex and shows areas of hyperechogenicity. (**b**) Left ventricular outflow tract view in systole. Note the presence of important mitral regurgitation and a narrow jet (*arrow*) of forward flow across the aortic valve. (**c**) Pulsed wave Doppler shows high aortic velocity (290 cm/s, normal for gestation ~60–70 cm/s). (**d–f)** Images obtained from a fetus at 14 weeks of gestation with hypoplastic left heart syndrome. (**d**) Four-chamber view in diastole, on 2D (*left* panel) and e-flow mapping (*right* panel). Note filling of the right ventricle only. (**e**) Transverse view through upper mediastinum at the level of the three-vessel view. E-flow mapping shows a large ductal arch only. No aortic flow seen at this level. (**f**) Sagittal view demonstrates forward flow across the ductal arch and reversed flow in the transverse aortic arch. *Ant* anterior, *LA* left atrium, *LV* left ventricle, *Post* posterior, *RA* right atrium, *RV* right ventricle, *VMax* maximal velocity

1.5.2 Fetal Arrhythmias

Fetal cardiac rhythm should be regular and heart rate roughly ranges from 120 to 160 beats per minute (bpm). M-mode echocardiography and pulsed-wave Doppler are the most commonly used methods to assess rhythm in the fetus, based on simultaneous recording of atrial and ventricular activities [81]. The most common rhythm disturbances are intermittent extrasystoles, which are of little clinical relevance. Arrhythmias that potentially affect fetal well-being or have postnatal implications for the newborn and child are relatively uncommon. Less than 10 % of referrals are due to sustained tachy- or bradyarrhythmias [81].

Intermittent extrasystoles are frequently encountered, usually of atrial origin and generally considered to be ‘benign’. They are often described as ‘skipped’ or ‘missed’ beats, which can cause a lot of anxiety, even if the vast majority resolve

spontaneously and require no treatment. In about 2 % of cases, skipped beats may represent incomplete heart block [82] or be associated with intermittent tachycardia. Therefore, it is important that these possibilities be excluded. A scan performed locally by the sonographer or obstetrician usually suffices. If heart rate is within normal range, with no fluid accumulation in any fetal compartment and the cardiac screening views are normal, the pregnant woman can be reassured. Urgent referral to a specialist is only warranted in a few selected cases when either heart rate and/or the scan findings are abnormal [83]. If the ectopic beats occur 'very frequently' (i.e. the rhythm is irregular most of the time), there is a slightly higher risk of fetus developing a tachyarrhythmia [84] and a referral is also warranted, after the initial assessment in the local hospital.

Tachycardia is defined as rate ≥180 bpm. If persistent, it may lead to congestive heart failure and hydrops fetalis (Fig. 1.3). If it is intermittent or not, urgent referral to the fetal cardiologist is required. However, not all cases need treatment as sometimes the arrhythmia resolves spontaneously. Thus, if the fetus is stable, close monitoring of fetal heart rate for 24 h or so to determine if the arrhythmia persists may be appropriate, before initiating therapy. If there is sustained tachycardia or it persists for >50 % of the time, or the fetus is compromised, fetal treatment or delivery of the baby (if gestational age ≥37 weeks) is indicated. Choice of medication varies from centre to centre and with experience. Maternal transplacental transfer is the preferred option to deliver the chosen drug to the fetus. Currently, a randomized controlled trial for treatment of fetal tachyarrhythmia is on its early implementation phase [85].

Traditionally, fetal bradycardia has been defined as rates <100 bpm but current obstetric threshold is 110 bpm [86]. More recently, gestational age-specific heart rates have been developed and centile charts are available [87]. Transient periods of sinus bradycardia during scanning are common and benign. Persistent sinus bradycardia is relatively rare and may be a manifestation of long QT syndrome [87]. More commonly however, fetal bradycardia is due to blocked atrial bigeminy, which typically presents with heart rate around 70–80 bpm. This can be transient or last for days or weeks. Whilst it is well tolerated by the fetus and of no hemodynamic consequence, it is important to differentiate blocked bigeminy from second-degree atrioventricular block with 2:1 conduction [82]. Heart block is often caused by transplacental passage of circulating maternal IgG antibodies (anti-Ro/ SSA and anti-La/SSB), which causes injury to the conduction tissue with subsequent fibrous replacement. Certain forms of CHD can also lead to fetal heart block, notably cases which are associated with left isomerism, but it can also occur in the presence of atrioventricular discordance. The prognosis for autoimmune-mediated complete atrioventricular block is better than if associated with CHD but there still is significant mortality and morbidity. Most survivors require pacemaker implantation in the first year of life [88].

1.5.3 Inherited Cardiac Conditions

Despite recent advances in genetics and better understanding of inherited cardiac conditions that may confer a 50 % risk to the fetus, little has been reported in fetal

life. Inherited cardiomyopathies are relatively uncommon in the fetus [89]. Hypertrophic cardiomyopathy rarely manifests prenatally, but can be associated with Noonan syndrome. Among channelopathies, recent data on prenatal manifestation of long QT syndrome, bradycardia with rates below the 3rd centile for gestational age, has increased interest in identifying affected fetuses [87]. Among aortopathies and related conditions, there are scarce fetal reports, mainly related to the infantile type of Marfan syndrome [90].

1.5.4 Early Fetal Echocardiography

Initial observations of CHD diagnosed in the first trimester of pregnancy were made by obstetricians utilizing a transvaginal approach [91, 92]. Subsequently, it became clear that the transabdominal route could also be used in clinical practice to image the fetal heart at less than 14 weeks gestation [93]. Over the years, this practice has become more common. The number of fetal cardiologists offering a detailed assessment of the fetal heart at 15–16 weeks has increased but it is not yet universally available. Early scans can be challenging due to the small fetal heart size and additional technical limitations sometimes imposed by fetal position and maternal characteristics. Nevertheless, its clinical utility in high-risk pregnancies has been shown by a number of investigators [94–97]. Similarly to mid-gestation, it is very important that the fetus with CHD identified early in pregnancy be assessed by a multidisciplinary team, especially in cases referred because of increased NT measurements. Figure 1.3 illustrates a case of hypoplastic left heart syndrome diagnosed at 14 weeks in a woman referred with family history of CHD.

1.6 Counselling and Pregnancy Options

Counselling a woman who attends for a fetal echocardiogram should start before the scan is performed. For each family, the perceived risks of encountering an abnormality during the scan and/or the likelihood of the scan being normal should be discussed. Limitations posed by early scans (<16 weeks) should be highlighted. This prepares the woman for what to expect, especially when she is referred due to a suspected abnormality.

Following the diagnosis of any form of CHD, the ultrasound findings are explained to the family, often with the help of diagrams to help them understand the anatomy and pathophysiological implications of the defect. An account of the likely postnatal manifestations of the disease, surgical options, risks and need for long-term follow-up is provided. In cases where progression is expected to occur during pregnancy, the need for serial fetal scans is reinforced. Family consultation is often in the presence of a fetal cardiac nurse specialist who provides the family with ongoing support. An obstetric/fetal medicine assessment should also be arranged on the same day or shortly afterwards to exclude or document extra-cardiac abnormalities and review pregnancy risks for chromosomal abnormalities and genetic syndromes.

The option of an invasive procedure (amniocentesis or cordocentesis) to check fetal karyotype is discussed, often jointly between the fetal cardiac and fetal medicine specialists. Depending on the type of CHD, associated abnormalities and gestational age, the option of TOP, if legally possible, is also discussed. Interrupting the pregnancy often involves induction of labour and may require fetocide, depending on gestational age. In the UK, the Royal College of Obstetricians and Gynecologists recommend this be performed at >22 completed weeks of gestation. Spontaneous fetal demise in the absence of heart failure/ hydrops is uncommon, but the risk is increased if there is an associated chromosomal abnormality (e.g. trisomy 21).

There is growing literature – summarized in a recent meta-analysis, indicating that, in the absence of known chromosomal or genetic abnormalities, the child with major CHD is at increased risk of brain abnormalities (detected on neuroimaging) and neurodevelopmental delay [98, 99]. Most of the reported cases are examples of hypoplastic left heart syndrome and complete transposition. In this analysis, the findings were independent of surgical risk, but it did not provide data to indicate if the origin was fetal or postnatal. On a more recent meta-analysis, there is some evidence to suggest that at least in part, some of these changes occur before birth [100]. However, a survey of experts' attitudes towards counselling families regarding risks of development delay in CHD advises caution [101]. Any information provided needs to be accurate but is inevitably based on current knowledge, which is limited by the retrospective nature of the published studies and lack of correlation between individual neuroimaging abnormalities and developmental outcome. Further research is required in this important area.

1.7 Perinatal Plan for the Fetus with CHD

One of the strengths of prenatal diagnosis is optimization of perinatal care. Fetuses expected to have neonatal intervention require delivery in a hospital with facilities to stabilize the neonate. In some instances, this needs to be at or close to a cardiac unit. However, local delivery is also possible, depending on the abnormality and available local human and medical resources [102–105].

Ideally, babies with CHD will be delivered at term. For those with critical defects, retrospective data suggest that mortality is lower if delivery occurs at 39–40 completed weeks. Delivery before 39 weeks is also associated with increased morbidity. However, premature delivery may be unavoidable, for example, if there is spontaneous labour or obstetric concern about fetal growth.

The neonatal team will be aware that a child with major or critical CHD is to be delivered and should be aware of the initial postnatal management.

1.8 Changing Pattern of Fetal CHD

Traditionally, fetal CHD meant complex CHD. The defects were often associated with worse prognosis, with many abnormalities leading to a univentricular circulation. For many years, abnormal hearts showing a normal four-chamber view were

unlikely to be recognized on routine screening. In the mid-1990s only 3 % of infants with complete transposition undergoing surgery were antenatally diagnosed [5]. With improvements in screening and especially the introduction of outflow tract views, fetal diagnosis of less complex abnormalities with potential for biventricular repair has increased. However, there has also been an increase in detection of CHD that may not require intervention or may be considered variants of normal. This new, emerging pattern of fetal CHD will enhance our understanding of natural history. For example, it is clear that many children with an isolated right aortic arch are asymptomatic [106] and would have not been diagnosed had it not been for prenatal screening. It also seems that persistence of a left superior vena draining into the coronary sinus as an isolated finding is not uncommon. Nevertheless, when a pregnant woman is referred for fetal cardiology assessment, the anxiety generated is not insignificant and prompt evaluation is required in order to clarify if fetal CHD is present and the potential impact it may have on the child and family.

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