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Cardiac defects in chromosomally abnormal fetuses

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Introduction

Chromosomal abnormalities are associated with high rates of perinatal death and infant morbidity. Similarly, cardiac abnormalities are the commonest form of severe congenital abnormality, resulting in stillbirth, neonatal and childhood death, and are a major cause of childhood morbidity. It is therefore not surprising that the detection of chromosomal abnormalities and congenital heart defects form two key areas of screening in prenatal diagnosis. Approximately 50% of infants with trisomy 21 are affected by congenital heart disease and the prevalence is even higher in other, more lethal chromosomal abnormalities. Similarly, a high proportion of fetuses with structural cardiac defects have an underlying chromosomal abnormality. This strong association can therefore be used to increase the detection rate of both types of anomaly.

This chapter reviews the data suggesting that structural cardiac defects at the 18–20-week anomaly scan be used to identify pregnancies at high risk of chromosomal abnormality. It examines the association between increased fetal nuchal translucency, a widely used form of screening for chromosomal abnormalities at 10–14 weeks of gestation, and structural cardiac defects. Finally, it examines whether the more recent sonographic finding of intracardiac echogenic foci is significant, particularly in terms of the detection of chromosomal abnormalities.

Cardiac defects and the prediction of chromosomal abnormality

There are considerable data suggesting that pregnancies affected by a cardiac anomaly are also at high risk of chromosomal abnormality, and that parents should be offered fetal karyotyping. The Baltimore–Washington Infant Study found that 12.7% of liveborn infants with congenital cardiovascular malformations had a chromosomal abnormality.[1] This study did not include data for stillbirths or terminations for fetal abnormality. The data were reanalysed, making adjustments for the effect of intrauterine lethality, to determine the risk of aneuploidy in a fetus found to have a cardiac defect at 18–20 weeks' gestation.[2] The authors concluded that, for cardiac anomalies identified at the time of the 18–20-week scan, the risk of a chromosomal abnormality may be as high as 40% and that fetal karyotyping should therefore be performed regardless of maternal age, gestational age or family history.

This mathematical model has subsequently been supported by echocardiographic and pathological data. Two ultrasound-based studies identifying a total of 133 fetuses with a cardiac defect found that 56 (42%) had a chromosomal abnormality, most commonly trisomy 21.[3,4] Both studies concluded that the prenatal diagnosis of a cardiac defect was always an indication for fetal karyotyping. Similarly, in a series of 815 fetuses examined after spontaneous abortion, induced abortion or stillbirth, 43 (34%) of the 126 fetuses with a cardiac defect also had a chromosomal abnormality.[5]

In another series of 160 karyotyped fetuses with a cardiac abnormality, 40 (25%) were chromosomally abnormal, including two cases of DiGeorge syndrome (microdeletion of 22q11), identified by fluorescent in situ hybridization (FISH).[6] The authors noted that trisomy 21, the commonest chromosomal abnormality, was strongly associated with atrioventricular septal defects, Turner syndrome with coarctation of the aorta and DiGeorge syndrome with conotruncal abnormalities. As the risk of chromosomal abnormality was so high, there would be little practical use in calculating the likelihood of a particular defect being associated with a particular chromosomal abnormality. The two exceptions to this were aortic stenosis, where none of the ten cases had a chromosomal abnormality, and conotruncal anomalies, where 10% had

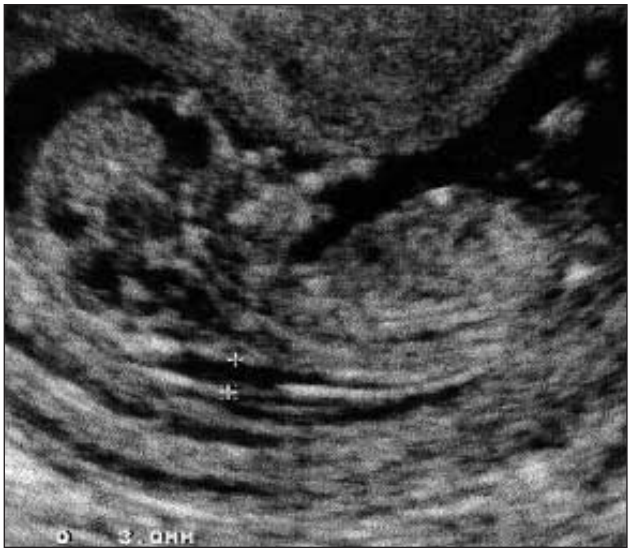

Figure 33.1
An ultrasound image of a fetus of 12 weeks' gestation showing the measurement of fetal nuchal translucency. The measurement of 3.0 mm increases the risk of a chromosomal abnormality above the background risk based upon maternal age.

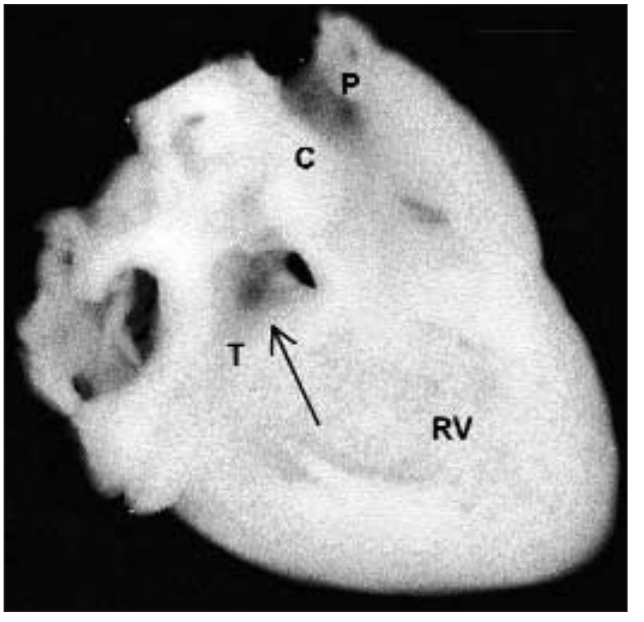

Figure 33.2
Perimembranous ventricular septal defect (arrow) partially guarded by the septal leaflet of the tricuspid valve in a fetal heart from a 13-week trisomy 21 fetus. T, septal leaflet of the tricuspid valve; C, crista supraventricularis; P, pulmonary valve; RV, right ventricle. Scale bar: 1 mm.

a microdeletion of 22q11, which required further cytogenetic evaluation with FISH to make the diagnosis.

Although initial studies in tertiary referral centres suggested that up to 90% of cardiac defects could be determined prenatally,[7] this has not proved to be the case when screening a low-risk population.[8] Examination of the four-chamber view and great arteries at the 18–20-week routine anomaly scan has been shown to detect up to 60% of major cardiac abnormalities in a low-risk population.[9] Of the cardiac defects affecting infants in this study, 42 were not identified prenatally and five (12%) of these infants were also found to have trisomy 21. Whilst the diagnosis of a cardiac defect at 18–20 weeks' gestation provides a strong indication for fetal karyotyping, this is of limited value in screening a low-risk population for chromosomal abnormalities as it is unlikely to detect all those fetuses with a cardiac abnormality, let alone those with normal cardiac anatomy.

The association between increased nuchal translucency and cardiac defects

At 10–14 weeks' gestation many chromosomally abnormal fetuses have an increased accumulation of subcutaneous oedema in the neck, visualized sonographically as nuchal translucency (Figure 33.1).[10] Screening by a combination of maternal age and nuchal translucency thickness can identify about 80% of fetuses with trisomy 21 for a false-positive rate of 5%.[11,12] Similar detection rates are given for other chromosomal abnormalities.

The underlying mechanism for increased nuchal translucency is unknown. During the second trimester of pregnancy, an abnormal collection of fluid behind the fetal neck has been classified as either multiseptated cystic hygroma or nuchal oedema. Cystic hygroma is strongly associated with Turner syndrome and is thought to represent overdistention of the jugular lymphatic sacs as a consequence of failure of communication with the internal jugular vein.[13,14] Histological findings of fetuses with cystic hygroma support this theory and have reported a generalized hypoplasia and partial agenesis of the lymphatic system.[15]

In contrast, nuchal oedema, a soft-tissue thickening in the posterior aspect of the neck, is typically associated with trisomies rather than Turner syndrome.[16] These fetuses have an increased number of lymphatic vessels, suggesting that jugular lymphatic obstruction is not the underlying pathology here.[17] Nuchal oedema is also found with cardiovascular defects, skeletal dysplasias, congenital infection, metabolic and haematological disorders, and it has therefore been suggested that this sonographic feature

Table 33.1. Prevalence of septal defects, valvular abnormalities and narrowing of the aortic isthmus (the denominator is the number of cases examined) in trisomy 21 fetuses in relation to nuchal translucency thickness at diagnosis

Nuchal translucency (mm)	*n*	*Septal defect*		*Valvular abnormalities*	*Aortic isthmus < 5th centile*
		Atrioventricular	*Ventricular*		
1.0–2.4	4	—	—		0/4
2.5–3.4	12	1	1	Bicuspid aortic valve (2) Dysplastic tricuspid valve	0/8
3.5–4.4	9	2	2	Bicuspid pulmonary valve	4/9
4.5–5.4	13	4	3	Bicuspid aortic valve (2)	10/13
5.5–6.4	3	1	—		2/3
6.5–7.4	3	2	—	Bicuspid pulmonary valve	1/3
7.5–8.4	5	2	2		4/5
8.5–9.4	3	—	1		2/3
9.5–10.4	2	1	—		2/2
10.5–14.0	2	—	1		1/2

may represent the mild end of a spectrum of hydrops fetalis and be the consequence of heart failure.[10]

As the chromosomal abnormalities seen in association with increased nuchal translucency appear to be predominantly similar to those seen in association with nuchal oedema, it would be more likely for increased nuchal translucency to share a common aetiology with nuchal oedema rather than with cystic hygroma. The association between increased nuchal translucency thickness and structural cardiac defects has been investigated in a series of 112 fetuses with trisomies 21, 18 and 13 or with Turner syndrome.[18] Chromosomal abnormalities were identified following nuchal translucency screening and chorionic villus sampling at 10–14 weeks' gestation. Pathological examination of the heart and great arteries was then performed in those pregnancies that were terminated for fetal abnormality at 11–16 weeks' gestation. The specimens were fixed in end-diastole using a direct perfusion–inflation technique, divided into three segments using a dissecting microscope and examined either by direct light microscopy or by scanning electron microscopy.[19,20] The great arteries were also measured at eight specific points to allow objective comparison to controls matched for gestational age.[21]

Trisomy 21

In a series of 60 pregnancies affected by trisomy 21, a ventricular or atrioventricular septal defect was detected in 24 of the 54 (44%) hearts available for examination (Table 33.1). Valvular abnormalities were seen in only seven (13%) cases and this was a bicuspid aortic valve in four cases.[18] The prevalence of septal defects in fetuses with trisomy 21 is therefore higher than that which has previously been described in neonatal series (30%).[22–24] There are several possible explanations for this discrepancy. First, there may be spontaneous closure of some septal defects in utero. This appears to be common in infancy where an echocardiographic study of 44 neonates with ventricular septal defects has reported spontaneous closure within 1 year in 20 (45%) of the cases.[25] Similarly, there have been two case reports of prenatal closure of septal defects.[26,27] In this series, two cases were noted to have a perimembranous septal defect partly obliterated by the overlying septal leaflet of the tricuspid valve and this is thought to be the underlying mechanism for subsequent closure (Figure 33.2).

An alternative reason for the higher incidence of intracardiac septal defects in this series of trisomy 21 fetuses may be that there is a higher rate of intrauterine mortality in fetuses with a cardiac defect compared to those without. Snijders et al have reported that 30% of fetuses with trisomy 21 died between 12 and 40 weeks' gestation.[28] There is also some evidence that the rate of intrauterine lethality is higher in those fetuses with a large nuchal translucency thickness.[29] As the prevalence of intracardiac defects increases with nuchal translucency thickness (Table 33.1), affected fetuses will be more likely to die in utero.

The data showing an association between the prevalence of intracardiac septal defects and nuchal translucency may also be useful in counselling parents after prenatal diagnosis. One of the difficulties of counselling after first-trimester diagnosis is the difficulty in providing individualized information about physical abnormalities. Infants with cardiac defects requiring surgical correction

Table 33.2. Incidence of ventricular septal defects and valvular abnormalities in trisomy 18 reported by different modes of investigation

Study	*n*	*Ventricular septal defect*	*Valvular abnormality*			
			Tricuspid	*Mitral*	*Aortic*	*Pulmonary*
Postnatal echocardiography[32,33]	32	25 (78%)	18 (56%)	12 (38%)	19 (59%)	24 (75%)
Postnatal postmortem[34,35]	56	54 (96%)	45 (80%)	38 (68%)	37 (66%)	35 (63%)
Present	17	14 (82%)	11 (65%)	5 (29%)	11 (65%)	13 (76%)

are known to require longer periods of hospitalization, and have higher mortality rates in infancy.[30,31]

Trisomy 18

Trisomy 18 is also associated with increased nuchal translucency, which is found in 80% of fetuses at 10–14 weeks' gestation.[11] The fetal heart was available for examination after first-trimester diagnosis and termination of pregnancy in 23 cases. A cardiac defect was found in all cases, most commonly a ventricular septal defect (in 19 (83%) cases) and valvular abnormalities (in 19 (83%) cases) (Figure 33.3).[18] These findings are similar to those seen in trisomy 18 neonates examined by echocardiography or at postmortem examination (Table 33.2).[32–35]

Scanning electron microscopy has been used to assess the normal process of fetal cardiac development, and these findings suggest that the ventricular septum and semilunar valves are fully developed by 8 weeks' gestation.[19] It is therefore likely that the ventricular septal defects associated with trisomy 18 are due to a form of arrest in cardiac morphogenesis at 6–8 weeks' gestation. The high prevalence of valvular abnormalities at this early gestation suggests that maldevelopment of these valves also occurs during the first trimester of pregnancy. In contrast, Matsuoka et al suggested that many of the tissue abnormalities seen in dysplastic valves represent errors in differentiation occurring as late as the third trimester.[35] Our results do not support this conclusion except perhaps for the mitral valve, where we found a much lower incidence of abnormalities than in trisomy 18 infants.

The two echocardiographic studies of trisomy 18 neonates reported that in the majority of cases valvular abnormalities were of no haemodynamic significance.[32,33] This may offer an explanation for the lack of an obvious association between the overall incidence of valvular abnormalities and the degree of nuchal oedema. However, it is possible that nuchal oedema, reflecting heart failure, may be the consequence of abnormal haemodynamic effects due to the type of pathology affecting certain valves rather than the mere presence of polyvalvular abnormalities. In this respect it is of interest that imperforate valves were observed in four of the nine cases with nuchal translucency thickness of $\geqslant 7$ mm, compared to one of the 14 cases with translucency of < 7 mm.[18]

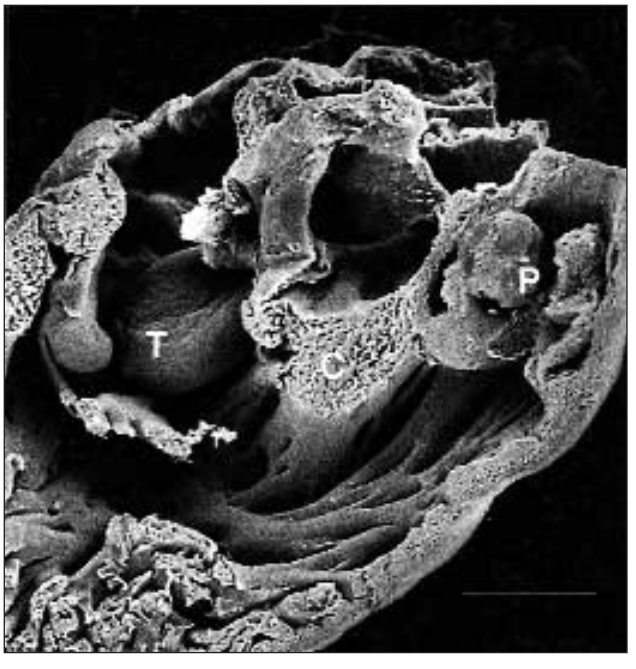

Figure 33.3
Scanning electron micrograph of the parietal aspect of the right ventricle showing marked dysplasia of both the pulmonary (P) and tricuspid (T) valves in a trisomy 18 fetus at 12 weeks of gestation. Scale bar: 500 μm.

In seven cases there was persistence of the left superior vena cava draining into a dilated coronary sinus. This is a rare abnormality more typically associated with transposition of the great vessels and was more prevalent with increasing nuchal translucency. Haemodynamic changes and venous congestion of the head and neck, visualized as increased nuchal translucency, may result in increased flow through the left anterior cardinal vein, leading to

persistence of the left superior vena cava rather than to obliteration of this vessel.

The incidence of trisomy 18 at 11–13 weeks' gestation is seven times higher than in live births because many of the affected fetuses die in utero.[36] Since the incidences and types of cardiac abnormality in our fetuses were similar to those observed in postnatal life, it is unlikely that the high intrauterine lethality of trisomy 18 is the consequence of a specific cardiac abnormality. However, imperforate valves and hypoplastic great arteries may be responsible for haemodynamic changes that can cause venous congestion and the abnormal accumulation of fluid in the head and neck which is visualized as nuchal translucency on an ultrasound scan.

Trisomy 13

The heart was examined in 15 fetuses with trisomy 13.[18] All had cardiac anomalies, often suggestive of cell migration abnormalities. The commonest were atrioventricular and ventricular septal defects and there were also a variety of valvular defects, including agenesis of the pulmonary valve that was not observed in other chromosomal abnormalities (Figure 33.4). The great arteries were also abnormal in all cases. In three cases there was truncus arteriosus—also a finding unique to trisomy 13. Other specimens showed evidence of narrowing of the aortic isthmus.

The prevalence of cardiac defects is higher than that suggested by previous reports. Two studies reviewed the prenatal ultrasound scans from 40 pregnancies affected by trisomy 13 and found cardiac defects in 23 (58%) cases.[32,37] The commonest defects were ventricular septal defects and hypoplastic left heart. The intrauterine lethality of trisomy 13 is 70% between 12 and 40 weeks of gestation, and this may, once again, explain the high prevalence of cardiac anomalies in this first-trimester series.[36] It is difficult to attribute intrauterine lethality solely to cardiac defects. Indeed, echocardiographic examination of trisomy 13 neonates suggested that underlying cardiac defects were not the major cause of neonatal death.[32]

Turner syndrome

Six fetuses affected by Turner syndrome were examined; all had nuchal translucency measurements well above the 99th centile (4.6–9.5 mm) and were found to have a 45XO karyotype at chorionic villus sampling.[18] Five hearts were available for examination; one had a muscular ventricular septal defect and another had a bicuspid aortic valve. All six cases showed tubular hypoplasia of the ascending aorta and aortic isthmus and the narrowing was greater than that seen with the trisomic specimens (Figure 33.5).

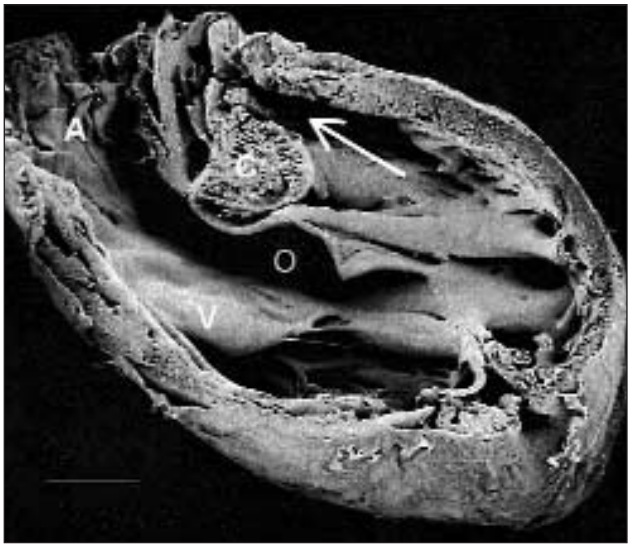

Figure 33.4
The septal aspects of the right ventricle showing a type 1 atrioventricular septal defect (O). The right ventricular outflow tract has collapsed partially during processing of the specimen (arrow). A, right atrium; V, common atrioventricular valve; C, crista supraventricularis. Scale bar: 500 μm.

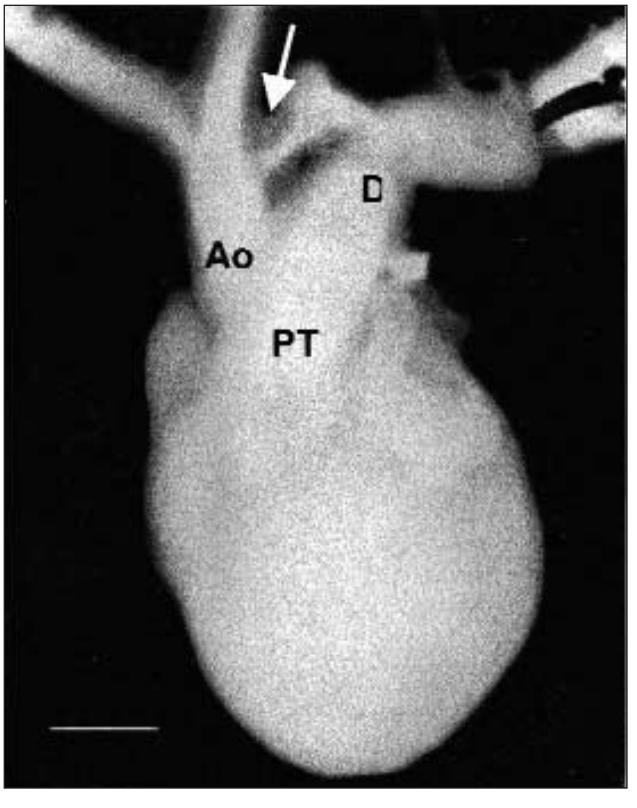

Figure 33.5
The ascending aorta (Ao) is hypoplastic and the aortic arch (arrow) is extremely hypoplastic in this 12-week fetus with Turner syndrome. The ductus arteriosus (D) is dilated. PT, pulmonary trunk. Scale bar: 1 mm.

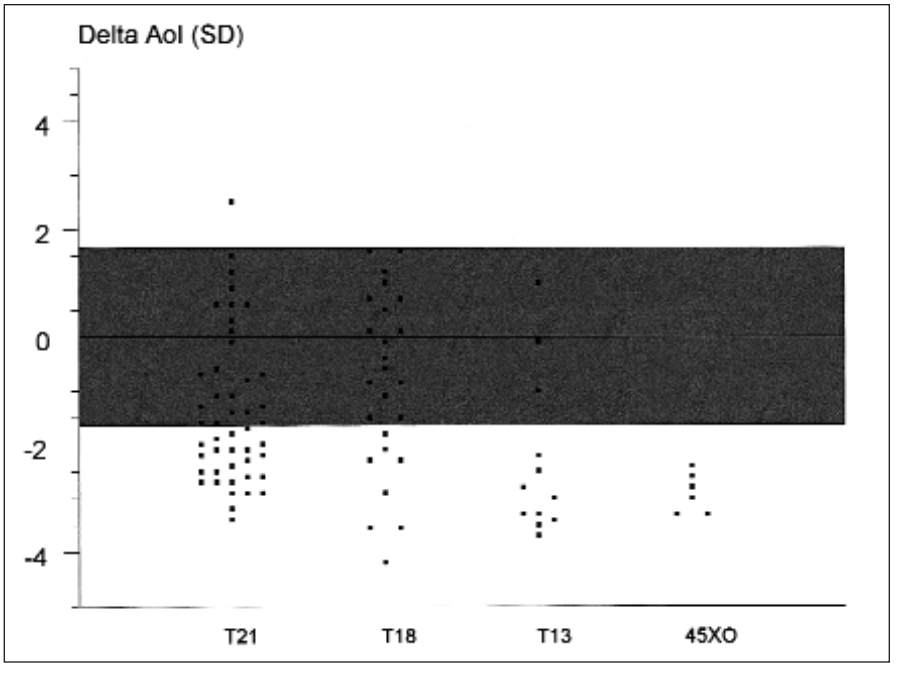

Figure 33.6
Individual delta values for the diameter of the aortic isthmus (AoI) shown for each chromosomal abnormality. T21, trisomy 21; T18, trisomy 18; T13, trisomy 13; 45XO, Turner syndrome.

The prevalence of cardiac defects is much higher than that documented in two large populations of Turner females. The first study, of 179 females affected by Turner syndrome, found that 46 (26%) had cardiac defects, the commonest being abnormalities of the aortic valve (18%) and coarctation of the aorta (10%).[38] Similarly, the second series of 594 patients found that 23% had cardiac abnormalities including a biscuspid aortic valve (12.5%), coarctation of the aorta (6.9%) and aortic valve disease (3.2%).[39] Both series found that cardiac defects, and particularly coarctation of the aorta, were more commonly seen in a subset of Turner patients with a 45XO karyotype, but the prevalence was still far lower than that seen in our limited series of six fetuses.

As this series of fetuses was selected on the basis of increased nuchal translucency thickness, these may represent infants that have a webbed neck and are known to have a higher incidence of congenital heart disease, particularly coarctation of the aorta.[40,41]

Abnormalities of the aortic isthmus

Whilst the nature of intracardiac defects varied between chromosomal abnormalities, the aortic isthmus was consistently significantly narrower than in normal fetuses (Figure 33.6). Combining data from all four groups of chromosomally abnormal fetuses shows that the degree of narrowing was significantly greater in fetuses with high nuchal translucency thickness (Figure 33.7).

In normal fetuses there is differential growth in the diameter of the great arteries with advancing gestation. In particular, the diameter of the aortic isthmus increases more rapidly than the diameters of the ascending aorta and the distal ductus arteriosus.[21] These changes may reflect the differing haemodynamic requirements of the developing fetus. Data for fetuses affected by trisomy 21 can be plotted against gestational age ranges for normal fetuses and show a similar rate of linear growth in the aortic isthmus, although there appears to be a 3-week period of development delay in reaching the same vessel diameter (Figure 33.8). Since blood flow is related to vessel diameter, the findings of narrowing of the aortic isthmus in association with widening of the aortic valve and ascending aorta may result in overperfusion of the tissues of the head and neck and the development of subcutaneous oedema.[42] With advancing gestation and growth, the haemodynamic consequences of narrowing of the isthmus may be overcome.

This hypothesis could offer an explanation for the gestational age-related spontaneous resolution of nuchal translucency; abnormal nuchal fluid was observed in 80% of trisomy 21 fetuses at 11 weeks' gestation, but in only 30% of cases at 20 weeks. It may also explain why narrowing of the aortic isthmus was present in about 50% of this series of trisomy 21 fetuses, whereas the prevalence of coarctation of the aorta in affected neonates is only 2.5%.[22,23]

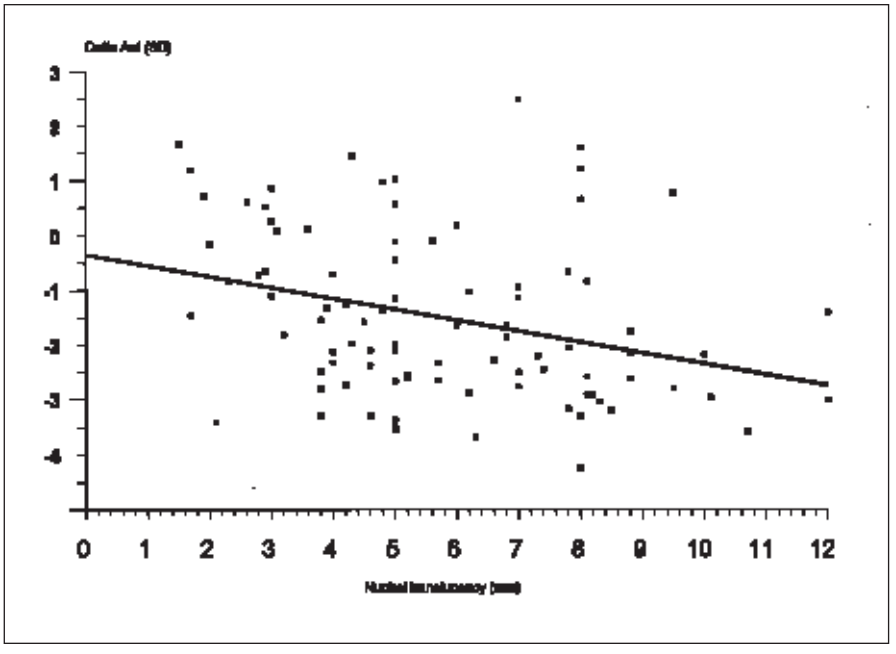

Figure 33.7
Relationship between the degree of narrowing in the aortic isthmus (delta AoI) and nuchal translucency thickness for all chromosomal abnormalities.

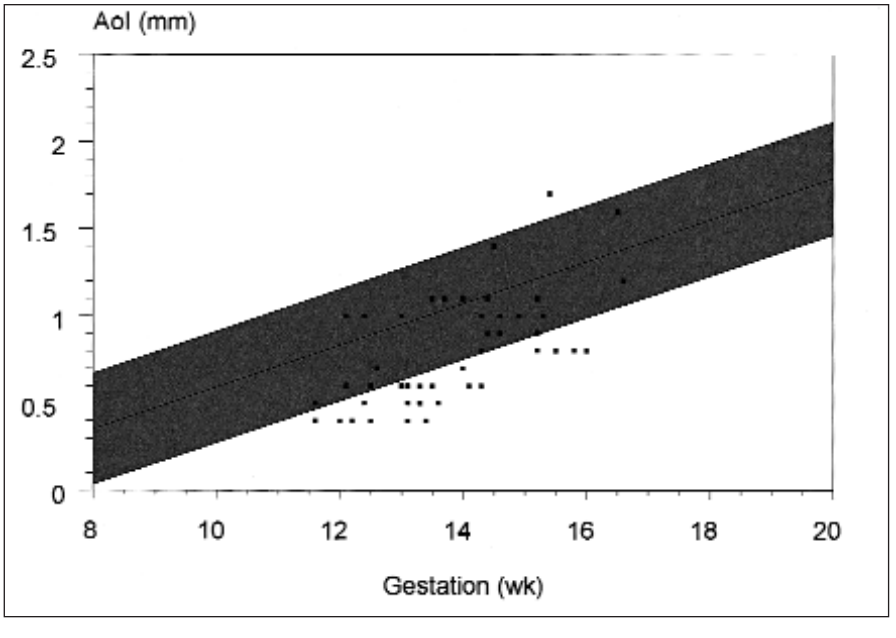

Figure 33.8
Measurements of the diameter of the aortic isthmus (AoI) for a series of fetuses affected by trisomy 21 compared to the normal range for gestational age.

Intracardiac valvular abnormalities made it more difficult to assess changes in the great arteries of trisomy 18 fetuses. There was, however, evidence of narrowing of the aortic isthmus with dilatation of the ascending aorta in this group. The hypothesis that narrowing of the isthmus causes overperfusion of the tissues of the head and neck leading to subcutaneous oedema would also fit this group, but does not appear to work so well in trisomy 13 and Turner fetuses. Although these groups also show narrowing of the aortic isthmus, the proximal aorta is narrowed, rather than dilated, and would not therefore allow increased perfusion to the head and neck.

Table 33.3. Studies examining the prevalence of intracardiac echogenic foci in a low-risk population

First author	*n*	*Echogenic foci*	*Prevalence (%)*
Levy 1988[45]	118	24	20.3
Dildy 1996[46]	506	25	4.9
Merati 1996[47]	1148	37	3.2
Achiron 1997[48]	2214	66	3.0
Whitlow 1998[49]	5385	43	0.8
Bettleheim 1999[50]	6995	150	2.1
Total	16366	345	2.1

Clark has suggested that the primary anomaly in Turner fetuses is obstruction and overdistention of the jugular lymphatic sacs, compressing the ascending aorta and altering the intracardiac blood flow that finally causes coarctation of the aorta.[40] Certainly, recent evidence of altered ductus venosus flow in fetuses with increased nuchal translucency and chromosomal abnormalities suggests that an alteration in intracardiac blood flow and reduction in venous drainage of the head and neck may be as important as increased perfusion.[43,44]

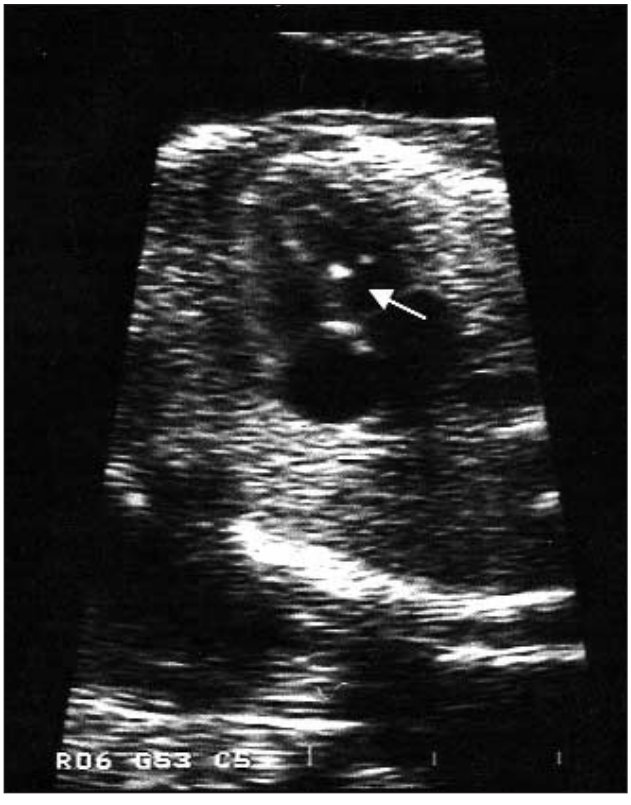

Figure 33.9
Four-chamber view of the fetal heart showing an echogenic intracardiac focus (arrow) within the left ventricle.

Intracardiac echogenic foci: a marker for chromosomal abnormality?

The inclusion of a routine four-chamber view in the 20-week anomaly scan and the improved resolution of modern ultrasound machines have increasingly led to the observation of a bright echogenic focus, or foci, within the fetal cardiac chambers. Combining data from studies reporting intracardiac echogenic foci in low-risk populations suggests a prevalence of 2.1% in the second trimester of pregnancy (Table 33.3).[45–50] The clinical significance of this finding remains controversial. Several studies have suggested that echogenic foci are associated with structural cardiac defects and chromosomal abnormalities,[51–54] whilst others have not shown any significant association.[45–48,55] Analysis of the data is complicated by the identification of single or multiple foci, the location of the foci and the demographics of the population being examined.[56–58]

An intracardiac echogenic focus, also known as a 'golf ball', is defined as a small structure found within the fetal heart that has similar echogenicity to that of surrounding bone (Figure 33.9).[55] Foci measure 1–6 mm in diameter and are closely associated with the papillary muscle and chordae tendinae, moving with the valve leaflets throughout the cardiac cycle. Echogenic foci were first reported in 1987, when 26 of 738 (3.5%) fetuses examined at 16–20 weeks' gestation prior to amniocentesis were found to have an echogenic focus in the left ventricle.[55] One pregnancy was terminated for trisomy 21, whilst the remaining 25 had a successful outcome, with no underlying cardiac dysfunction, although postnatal echocardiography did document thickening of the chordae tendinae in six cases.

Histological studies have also suggested that this sonographic marker may represent microcalcification of the papillary muscle. In a series of three cases examined after termination of pregnancy, a small discrete mineralized area was found in the papillary muscle consistent in size with the sonographic findings.[59] The chordae tendinae were normal and no underlying cause for mineralization could be identified. Roberts et al have also shown that microcalcification of the papillary muscle is strongly associated with both trisomy 21 and trisomy 13.[60] This group therefore hypothesized that intracardiac echogenic

foci would provide another useful marker for the identification of trisomic fetuses at the time of the 20-week anomaly scan.

There is a limited amount of data examining the prevalence of echogenic foci in a population of trisomic fetuses and in each series the population of trisomic fetuses was derived from a preselected high-risk group of pregnancies. Three series reporting a total of 56 fetuses affected by trisomy 21 found echogenic foci at the time of the 16–24-week scan in 10 (18%) cases.[51–53] This would suggest that the incidence of echogenic foci is nine times higher in trisomy 21 fetuses than it is in a low-risk population, and therefore that the probability that an individual is affected by trisomy 21 is nine times higher than that predicted by maternal and gestational age. The prevalence of echogenic foci appears to be even higher in trisomy 13, with 13 (35%) of 37 fetuses being affected, 17 times higher than that of a low-risk population.[38,52]

An alternative method for examining the risk of chromosomal abnormality associated with echogenic foci was described by Vibhakar et al.[54] in a series of 2412 pregnancies karyotyped by amniocentesis, 149 (6.2%) fetuses were found to have echogenic foci and this was associated with other markers in 30 (1.2%) cases. The prevalence of chromosomal abnormalities doubled in fetuses with isolated echogenic foci and tripled in fetuses with other markers. The data for trisomy 21 cannot be examined alone.

The introduction of a comprehensive screening policy for chromosomal abnormality using first-trimester ultrasound examination and/or maternal serum biochemistry changes the characteristics of a population attending for an anomaly scan later in pregnancy. A recent prospective study examined whether the finding of intracardiac echogenic foci maintained significance in this setting.[61] A series of 16 917 pregnancies were scanned at 18–23 weeks' gestation. Previous screening for trisomy 21 with either nuchal translucency measurement at 11–14 weeks' gestation or quadruple maternal serum biochemistry at 16 weeks' gestation had identified 27 of 32 (84%) trisomy 21 fetuses. Of these pregnancies, 22 were terminated before the anomaly scan. Isolated intracardiac foci were found in 144 fetuses (0.9%), but none of these were affected by trisomy 21. The authors concluded that, following a routine screening programme for trisomy 21, the association between intracardiac echogenic foci and trisomy 21 was no longer significant.

Summary

Cardiac defects are a common finding in fetuses with chromosomal abormalities. Whilst each chromosomal abnormality is associated with specific cardiac defects, these associations are not exclusive and cannot be used to make a definitive diagnosis. The identification of a cardiac defect at 20 weeks' gestation is a strong indication for fetal karyotyping, but the poor sensitivity of this sonographic examination in a low-risk population means that this is of limited value in screening for chromosomal abnormalities. Similarly, the finding of intracardiac echogenic foci appears to be of little value in predicting chromosomal abnormality, particularly in a population that has previously been screend for aneuploidy.

Pathological studies of chromosomally abnormal fetuses suggest that the prevalence and type of defect seen in fetal life are broadly similar to those found after birth. The high prevalence of narrowing of the aortic isthmus, seen in fetuses affected by all the common chromosomal abnormalities, may alter fetal haemodynamics and cause increased nuchal translucency, which is known to be a sensitive marker for aneuploidy at 10–14 weeks' gestation.

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