Prenatal Diagnosis of Congenital Heart Disease: Where Are We Now?

Wesley Lee, MD\textsuperscript{a,b,*}, Christine H. Comstock, MD\textsuperscript{a,c}

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The antenatal detection of birth defects is an important public health concern with significant clinical ramifications. In 2002, more than 28,000 infants died within the first year of birth, with an overall rate of 7.0 deaths per 1000 live births in the United States [1]. This mortality rate was largely attributed to birth defects, of which congenital heart disease has been a leading cause of related adverse outcomes [2]. Furthermore, data from the World Health Organization indicates that 42% of infant deaths were attributed to heart defects [3].

Prenatal sonography has played an important role for the timely detection of congenital heart disease (CHD). Despite promising results of early studies, however, the efficacy of fetal cardiac screening programs has been variably successful. This article provides an update regarding various factors affecting the prenatal identification of cardiac defects and summarizes current guidelines for fetal heart screening during the second trimester of pregnancy. The diagnostic imaging characteristics and clinical significance of selected fetal cardiac abnormalities are also reviewed.

Fetal cardiac screening

Cardiac abnormalities occur with an estimated incidence of approximately 4–13 per 1000 live births [4–6]. Most of the affected children will be born to mothers with no identifiable risk factors for CHD. Consequently, standardized approaches are needed to screen low-risk populations for cardiac abnormalities.

Prenatal cardiac screening was introduced in the mid-1980s when the four-chamber view of the heart was incorporated into a routine obstetric scan.
between 18 and 22 weeks, menstrual age [7]. After a training period, several centers in the United Kingdom were able to detect 77% of all cardiac anomalies over a 2.5-year period [8]. Copel and associates [9] also examined fetuses in 1022 pregnancies and found 74 abnormal heart cases using the four-chamber view. They reported 92% sensitivity and 99.7% specificity for the detection of CHD. Unfortunately, others have found a wide range of detection rates for the four-chamber view of the heart in unselected patient populations [10–15]. Additional diagnostic benefit has been subsequently demonstrated for the inclusion of cardiac outflow tracts into routine screening examination of the heart [11,16,17].

One of the most comprehensive studies regarding fetal heart screening in a nonselected population has been recently completed. Tegnander and colleagues [18] analyzed results of a fetal heart screening program over a 10-year period in Norway. Their study population included 29,460 gravidas, representing 98% of their deliveries at a single institution. Routine fetal examinations were performed at approximately 18 weeks, and included the four-chamber view and outflow tracts. Beginning in 1995, patients were also asked to return for another scan if a satisfactory four-chamber view had not been obtained during the initial visit. Heart defects were retrospectively classified after delivery as critical when surgery was likely to be required (eg, transposition of the great arteries, hypoplastic left heart syndrome, atroventricular septal defect, aortic coarctation, and large ventricular septal defects) [19]. This investigation identified 97 critical cases of CHD, of which 55 (57%) had been detected before birth. Forty-four percent of affected fetuses had isolated CHD and 38% had an abnormal karyotype. About one-half (48%) of the abnormal fetuses with ductal-dependent lesions were detected. Only 27% of infants born with critical CHD were alive at 2 years after delivery.

**Factors influencing adequate examination of the heart**

Inadequate examination of the fetal heart can be related to timing of scan, fetal position, image quality, maternal wall thickness, and a history of prior maternal surgical procedures.

**Timing of second trimester fetal heart scans**

Satisfactory views of the fetal heart are typically obtained between 18 and 22 weeks, menstrual age. A prospective and randomized study of 1206 women found an incomplete four-chamber view more frequently between 18 to 18.9 weeks (18.4%) as compared with scans occurring between 20 to 20.9 weeks (2.9%) (P<.001) [21]. Many heart structures can still be satisfactorily visualized beyond this time if the fetal position is favorable. Many patients, however, prefer to know about major cardiac defects at an earlier stage of pregnancy.

**Fetal position**

Optimal views of the fetal heart are often obtained when the cardiac apex is pointing toward the transducer [Fig. 1] [22]. Suboptimal views occur when the spine causes acoustic shadowing over cardiac structures from a prone position. This situation can be worsened in the presence of oligohydramnios.

**Image quality**

Technical specifications of the ultrasound system (eg, beam former, transducer, display screen) can also affect satisfactory visualization of the fetal heart. One should always adjust the lowest acoustic power intensity settings (ie, thermal index and mechanical index) that provide satisfactory diagnostic images from using output display standards and the ALARA (As Low As Reasonably Achievable) principle [23].

Image quality relies on the examiner’s efforts to position the transducer in a manner that is most suitable for acquiring this information. The degree of screen magnification, gain, and acoustic focus should be optimized for the region of interest. The transducer’s field of view should be minimized to improve frame rate (ie, temporal resolution). A color filter can be applied to improve contrast between soft tissue borders. Frame persistence should not be set too high. Images should be zoomed to fill at least one-half the display screen with the fetal heart. Harmonic imaging often improves the image display [24].

Wavelength (sound velocity divided by frequency) is an important concept that is used to explain image resolution [25]. Contemporary ultrasound systems usually produce images with axial resolution between 2 to 4 wavelengths and lateral...
resolution between 3 to 10 wavelengths. Depending on the imaging system, the axial resolution would range between 0.6 and 1.2 mm at 5 MHz. At the same transducer frequency, lateral resolution ranges between 0.9 and 3.0 mm. Therefore, the ultrasound beam resolution and angle of beam insonation can have important ramifications for identifying small structures such as 2-mm ventricular septal defects. The highest transducer frequencies, typically 5 MHz and above, often provide the image resolution necessary to resolve subtle cardiac defects. This has to be balanced as a trade-off between image resolution and acoustic penetration.

**Maternal wall characteristics**

DeVore and colleagues [26] examined technical factors that influence imaging of the fetal heart during the second trimester of pregnancy. More than 700 trimester pregnancies were analyzed to identify independent risk factors that contribute to difficult cardiac screening examinations. Gestational age, maternal adipose tissue thickness, and prior lower abdominal surgery were found as the most significant factors that were associated with poor visualization of the fetal heart.

**Unrecognized abnormalities**

Unrecognized abnormalities are another reason why the prenatal detection rates of CHD have varied so widely. Examiners should be familiar with development of the human heart and how to translate this information to clinical practice. Anatomic and molecular methods are clarifying new aspects of cardiac development. For example, traditional teaching has suggested that the heart initially forms from paired linear tubes that fuse and contain all major cardiac segments. More recent work now indicates that the embryonic heart results from a modular process with initial development of a primary cardiac crescent. Subsequent development of a second, more anterior heart field is responsible for the appearance of the right ventricular outflow tract [27]. Cook and associates [28] have nicely reviewed cardiac development in the human fetus as it relates to the prenatal diagnosis of CHD.

Education and training of health care professionals can improve the prenatal recognition of CHD. As a minimal goal, examiners must understand how to acquire images from standardized cardiac scanning planes to classify them into normal or abnormal categories. Cardiac screening programs can be further improved after continuous training of health care professionals based on feedback, a low threshold for echocardiography referrals, and convenient access to fetal heart specialists [29,30]. As one example, Hunter and colleagues [31] reported a twofold increase in the detection rate (17% to 36%) of major cardiac defects after implementing a targeted training program for fetal heart screening at 16 ultrasound centers in the United Kingdom.

**Evolution of cardiac abnormalities**

Evolution of cardiac lesions is another important reason why these abnormalities are not always detected at the time of an ultrasound scan. An observational investigation of 22,050 pregnant women (77.5% low-risk patients) was undertaken by dividing them into two groups: Group A - 6924 with initial vaginal sonography at 13–16 weeks' gestation that were followed by abdominal scans at 20–22 weeks'; and Group B - 15,126 women who only had initial transabdominal scans at 20–22 weeks' [32]. Both groups were scanned dur-
The third trimester and diagnoses were confirmed after birth. Two experienced examiners conducted all ultrasound examinations.

Congenital heart disease occurred in 168 infants (Group A - 66 infants; Group B - 102 infants). Of the Group A fetuses, 42 (64%) heart anomalies were detected at the first vaginal scan, and 11 (17%) were subsequently identified during the abdominal study. Three additional anomalies (4%) were found during the third trimester exam and 10 more (15%) were only detected after delivery. Group B fetuses had 80 (78%) cardiac malformations identified at the time of their first abdominal scan at 20–22 weeks’ gestation. An additional 7 (7%) and 15 (15%) cases were identified during the third trimester and after delivery, respectively. Ten heart anomalies that were discovered during the third trimester included aortic stenosis (n=2), cardiac rhabdomyoma (n=2), subaortic stenosis (n=1), tetralogy of Fallot (TOF) (n=1), aortic coarctation (n=1), sealed foramen ovale (n=1), ventricular septal defect (n=1), and hypertrophic cardiomyopathy (n=1).

Their results indicated that fetal heart anomalies can vary in appearance throughout pregnancy. In this study, two experienced examiners, using both early vaginal and second-trimester abdominal scans, were unable to identify 20% of CHD cases. Of note, early vaginal scans of the fetal heart were able to detect nearly two-thirds (64%) of abnormal hearts. This observation is consistent with the finding of others who have described early detection of heart anomalies, especially when increased nuchal translucency is present [33–39]. Although second trimester fetal heart screening can often be completed between 18 and 22 weeks’ gestation, many anomalies can still be identified before this stage of pregnancy.

**Standardized images may not demonstrate the anomalous heart**

The inability of specific scanning planes for detecting all forms of CHD can be explained by considering fetal cardiac anatomy. Although the four-chamber view across the fetal thorax can be quite informative, this two-dimensional scanning plane may not provide satisfactory views of a small ventricular septal defect or conotruncal anomalies involving the more anterior ventricular outflow tracts.

**Fetal cardiac screening guidelines**

The primary goal of cardiac screening is to identify which fetuses are likely to have CHD. Current guidelines emphasize a “basic examination” using a satisfactory four-chamber view of the heart. If technically feasible, an “extended basic” examination of the left and right ventricular outflow tracts is also recommended [40–42]. Fetuses with suspected anomalies should be referred for fetal echocardiography to assess the seriousness of the anomaly and the likelihood of a ductal dependent lesion at birth. Common indications for fetal echocardiography are summarized in Box 1 [43].

### Basic examination

#### General considerations

The “basic examination” requires specific sonographic criteria using an adequately visualized four-chamber view of the heart [Table 1; Fig. 2]. This approach must not be mistaken for a simple count of cardiac chambers. Cardiac rate (120 to 160 beats/minute) and regular rhythm should be confirmed, although mild fetal bradycardia can transiently occur during the second trimester. The heart normally fills no more than a third of the thoracic area at the level of the four-chamber view.

A small layer of fluid (<2 mm) can appear around the normal fetal heart, although this finding may

<table>
<thead>
<tr>
<th>Box 1: Common indications for fetal echocardiography</th>
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<tr>
<td><strong>Maternal indications</strong></td>
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<tr>
<td>Family history</td>
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<td>1st degree relative of proband</td>
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<tr>
<td>Pre-existing metabolic diseases</td>
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<td>Maternal infections</td>
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<td>anti-Ro (SSA)</td>
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<td>anti-La (SSB)</td>
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| **Fetal indications**                       |
| Suspected fetal heart anomaly              |
| Abnormal fetal karyotype                   |
| Major extra-cardiac anomaly                |
| Abnormal mucehal translucency              |
| ≥3.5 mm before 14 weeks, menstrual age     |
| Abnormal mucehal fold                      |
| ≥6.0 mm: 15–20 weeks, menstrual age        |
| Abnormal cardiac rate or rhythm            |
| persistent bradycardia                     |
| persistent tachycardia                     |
| persistent irregular heart rhythm          |

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be clinically significant in the presence of cardiac failure, other structural anomalies, or hydrops [44,45].

Cardiac axis and position should be normal [Fig. 3] [46]. The cardiac axis can be shifted as a normal variant, although a detailed examination should be considered for the possibility of associated abnormalities. Abnormal heart deviation into the right chest (dextroposition) may be caused by a chest mass (eg, cystic adenomatoid malformation, pulmonary sequestration, or congenital lobar emphysema), diaphragmatic hernia, or situs anomalies [46–48].

**Cardiac chambers**

Both atrial chambers should appear similar in size with an intact atrial septum primum. The foramen ovale flap should move freely toward the left atrium. In the human fetus, more than one-fifth of combined ventricular output is directed to the lungs and eventually drained back to the heart through the pulmonary veins [49,50]. At least one pulmonary vein should always be seen entering the left atrium.

The ventricular chambers also appear similar in size with an intact intervening septum. Relatively thin ventricular walls usually have no greater than 2 mm of surrounding pericardial fluid. The right ventricle has a moderator band at the cardiac apex and normally resides in the anterior chest on the side opposite the fetal stomach. It usually appears more triangular in shape as compared with the left ventricular chamber.

**Atrioventricular valves**

Both atrioventricular valves should move freely and not appear thickened. The tricuspid valve leaflet normally inserts on the ventricular septum at a position that is closer to the cardiac apex as compared with the mitral valve septal leaflet insertion [51]. This describes the normal “offsetting” of both atrioventricular valves.

**Extended basic examination**

If technically feasible, routine views of the outflow tracts should also be included as part of an “ex-

**Table 1: Basic cardiac screening examination**

<table>
<thead>
<tr>
<th>General</th>
<th>Normal cardiac situs, axis, and position</th>
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<tr>
<td></td>
<td>Heart occupies a third of thoracic area</td>
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<td></td>
<td>Majority of heart in left chest</td>
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<td></td>
<td>Four cardiac chambers present</td>
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<tr>
<td></td>
<td>No pericardial effusion or hypertrophy</td>
</tr>
<tr>
<td>Atria</td>
<td>Atria approximately equal in size</td>
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<tr>
<td></td>
<td>Foramen ovale flap in left atrium</td>
</tr>
<tr>
<td></td>
<td>Atrial septum primum present</td>
</tr>
<tr>
<td>Ventricles</td>
<td>Ventricles about equal in size</td>
</tr>
<tr>
<td></td>
<td>No cardiac wall hypertrophy</td>
</tr>
<tr>
<td></td>
<td>Moderator band at right ventricular apex</td>
</tr>
<tr>
<td></td>
<td>Ventricular septum intact (apex to crux)</td>
</tr>
<tr>
<td>AV Valves</td>
<td>Both atrioventricular valves open and move freely</td>
</tr>
<tr>
<td></td>
<td>Tricuspid valve leaflet inserts on septum closer to the cardiac apex as compared to the mitral valve</td>
</tr>
</tbody>
</table>

Adapted from [22]; with permission.
A four-chamber view of the heart can appear as normal in the presence of a ventricular septal defect or conotruncal anomaly that would otherwise be seen from the extended basic examination. Scanning planes for both the “basic” and “extended basic” examinations are illustrated in Fig. 6 [22]. Both outflow tracts are examined as the transducer is angled from the four-chamber view toward the fetal head. Another method for evaluating the outflow tracts has also been described when the fetal interventricular cardiac septum is perpendicular to the ultrasound beam [52]. This approach begins with a four-chamber view of the heart and involves probe rotation until a left ventricular outflow tract is visualized. The probe can then be rocked cephalad until the pulmonary arterial outflow tract is observed in a plane that appears perpendicular to the aortic outflow tract. Others have reported the use of a “three-vessel view” to describe relative sizes and relationships between the pulmonary artery, ascending aorta, and right superior vena cava [53–55].

Most second trimester cardiac screening examinations will permit satisfactory visualization of the four-chamber view and outflow tracts. Over 18,000 second trimester fetuses underwent cardiac screening of the outflow tracts to evaluate the standardized practice of incorporating a basic fetal cardiac exam into a 30-minute scan [56]. When technically feasible, an extended basic evaluation of the outflow tracts was also attempted. Of the studies that included an adequate four-chamber view, the majority (93%) of scans had satisfactory

**Fig. 3.** Fetal cardiac axis and position The cardiac axis can be measured from a four-chamber view of the fetal heart. A line through the interventricular axis is extended to the posterior border of the heart to produce point P, the location of which can be used to define fetal cardiac position. (Adapted from Comstock CH. Normal fetal heart axis and position. Obstet Gynecol 1987;70:255–9; with permission.)

**Fig. 4.** Left ventricular outflow tract. A left ventricular outflow tract view (LVOT) emphasizes that a great vessel can be seen exiting the left ventricle. The aortic valve leaflets should be freely moving and not thickened. (From Lee W. American Institute of Ultrasound in Medicine. Performance of the basic fetal cardiac ultrasound examination. J Ultrasound Med 1998;17:601–7; with permission.)
views of the outflow tracts. Nonvisualization rates were: left ventricular outflow tract (4.2%); right ventricular outflow tract (1.6%); both outflow tracts (1.3%).

Sonographic detection of selected cardiac anomalies

This section summarizes the clinical significance and sonographic findings associated with selected examples of CHD that may be detected by basic and extended basic cardiac screening exam.

Ventricular septal defects

Ventricular septal defects are the most common type of CHD [Fig. 7]. They are caused by incomplete closure of the ventricular septum during fetal development and can occur at various locations [Fig. 8]. Although isolated lesions may not be clinically significant, their presence should raise the possibility of abnormal karyotype and associated structural findings.

Paladini and colleagues [57] summarized their experience with isolated lesions that are detected using prenatal sonography. Of 26 fetuses that reached the...
1 year of age, 46.1% (12 cases) of all defects closed in utero. Trisomy 21 was found in 50% of fetuses with inlet-type (nine cases) or large (two cases) defects. Trisomy 18 occurred in 56.3% of ventricular septal defects (VSD) lesions (nine cases) that were associated with aortic-septal override. None of the malalignment VSDs closed after birth. By comparison, 69% of the perimembranous and 60% of the muscular defects closed within 1 year of delivery.

In a related pediatric study, Turner and colleagues [58] found that the location of the lesion was relevant to its natural history in 68 infants with VSD. Perimembranous defects accounted for most of the moderate and large defects that required surgical correction. After more than 6 years, almost a third of all perimembranous and just over two-thirds of all muscular defects closed spontaneously.

Tegnander and colleagues [18] studied a nonselected population of 30,149 fetuses: an isolated VSD occurred in 57% (188/333) of noncritical heart defects. Of these, 162 (86%) were muscular and 26 (14%) were perimembranous. During the first year after birth, 77/162 (48%) of the isolated muscular and 3/26 (12%) of the isolated perimembranous VSDs closed spontaneously.

Prenatal detection of a small VSD <2 mm can be particularly difficult and depends on several factors such as the lateral resolution of the ultrasound system, gestational age, fetal size, maternal wall thickness, and a history of prior abdominal or uterine surgeries. Aside from optimizing image settings (e.g., depth, gain, focus), the entire ventricular septum should be systematically examined during both the basic and extended basic cardiac scans.

Other diagnostic tools include the use of digital cineloop technology and Doppler flow studies. Direct measurements of intracardiac pressures in human fetuses indicate that no measurable differences occur between the left and right ventricles [59]. Therefore, color Doppler ultrasonography may not detect flow across a VSD as easily as in the case of adult patients. However, VSD lesions can be identified using frame-by-frame analysis of the ventricular septum (digital cine-loop), sometimes in conjunction with Doppler flow studies as well [Figs. 9 and 10]. Some ultrasound systems provide a “write priority” control that allows the
user to balance the color or power Doppler display so it doesn’t “bleed” over surrounding intra-cardiac structures that are visualized with gray scale. Finally, one should remember to verify suspected VSD lesions from more than one view to avoid diagnostic errors due to sonographic artifacts.

**Atrioventricular septal defects**

Complete atrioventricular septal defects (AVSD) consist of a common atrioventricular junction instead of separate mitral and tricuspid valve orifices [Fig. 11]. In the past, this lesion has also been known as an endocardial cushion defect or AV canal defect. Milder forms of this anomaly (ie, “incomplete AVSD”) have only a defect in the inferior part of the atrial septum, just above the atrioventricular valves. In this case, two separate valve orifices will be visualized.

Allan [60] reviewed the prenatal sonographic findings of 49 fetuses with AVSD. 18 cases appeared to only involve AVSD only, of which 13 were subsequently found to have trisomy 21. Other abnormalities included heterotaxy syndrome (22 cases), left ventricular malformations (8 cases), and TOF (1 case). Increased nuchal translucency has also been found in embryos with AVSD at 10–14 weeks, menstrual age [61].

There were 22 cases of heterotaxy syndrome involving isomerism of the atrial appendages. Sixteen fetuses were suspected to have right atrial isomerism (eg, anomalies of pulmonary venous drainage, double outlet right ventricle with pulmonary valve
atresia, bilateral right bronchi and lung lobation, and asplenia). Six fetuses had sonographic evidence of left atrial isomerism, where typical findings may include an interrupted inferior vena cava with azygous continuation, complete heart block, bilateral left bronchi and lung lobation, and polysplenia. This series emphasized the high rate of intrauterine death for fetuses with left atrial isomerism because only one of six abnormal fetuses survived to delivery, but died soon after birth. Although the prognosis for fetuses with AVSD and right atrial isomerism typically is to survive pregnancy, there is a high postnatal mortality rate found in infancy and early childhood [62].

The sonographic detection of complete AVSD is usually straightforward because the normal offsetting of the atrioventricular valves is not present. Instead, the common atrioventricular valve appears as a straight line [Fig. 12]. Occasionally, a dilated coronary sinus can simulate an AVSD lesion [63]. Incomplete forms of AVSD also may obscure the diagnosis because two separate inlet valves are still seen, in addition to both atrial and ventricular septal defects. As a final consideration, ventricular disproportion may appear as an “unbalanced” form of AVSD. Complete AVSD can be typically repaired with low mortality and good intermediate to long-term results [64].

**Hypoplastic left heart syndrome**

Prenatal identification of hypoplastic left heart syndrome (HLHS), using the basic cardiac screening examination, is extremely important because of improved surgical outcome in fetuses in whom the lesion was detected prenatally [65] [Fig. 13]. Severe ventricular disproportion is the hallmark of this abnormality where the left ventricle can appear very small [Fig. 14]. This condition refers to an underdeveloped left ventricle from abnormal development of the mitral or aortic valve. Valve obstruction causes a shift of blood flow back over the foramen ovale to the right
atrium. The left ventricle stays small due to decreased blood flow. A truly anatomic univentricular heart is very uncommon since a small “slit” can usually be seen to the left of the right ventricle. In severe mitral valve dysplasia, the left ventricle is usually quite small at the time of the screening exam. Milder involvement of the valves causes disparity of the size of the right and left ventricles, but both are still visible. Another presentation is that of an enlarged left atrium with a large noncontracting left ventricle. Although the ventricle is large, blood does not flow into or out of it. The enlarged ventricle can shrink with advancing pregnancy. Associated findings may include aortic valve atresia, coarctation of the aorta, and echogenic thickening of the ventricular walls due to endocardial fibroelastosis.

Hypoplastic left ventricle can also occur with other defects such as atrioventricular septal defect. It is rare that chromosomes are abnormal, but if they are, trisomy 18 is the most frequent aneuploidy. Hypoplastic left ventricle can also occur in left-sided diaphragmatic hernia due to pressure on the left ventricle. The pregnancy course is usually uneventful in the absence of heart failure (eg, atrioventricular valve insufficiency, pericardial effusion, cardiomegaly).

After birth the newborn will depend on a patent foramen ovale and ductus arteriosus to get blood to the aorta and neck vessels. Prostaglandin infusion will keep these fetal shunts open temporarily, but eventually surgery will be necessary. The conventional surgical repair is a three-stage procedure, the first of which is a Norwood procedure that involves connecting the aorta to the proximal pulmonary artery, thus allowing the right ventricle to pump blood to the body. Two lower risk operations, the hemi-Fontan (4 to 6 months of age) and Fontan (18 months to 2 years of age) are subsequently required. Although these children are now reaching young adulthood and are doing remarkably well, recent studies suggest increased risk for cognitive, neuromotor, and psychosocial problems.

Tricuspid valve abnormalities

Tricuspid valve atresia is caused by marked dysplasia of the leaflets and cords where a connection fails to develop between the right atrium and ventricle. Therefore, systemic venous blood return bypasses the right heart and traverses a patent foramen ovale (secundum atrial septal defect, ASD) into the left atrium and ventricle. An inlet VSD typically allows some blood flow from the left ventricle into an underdeveloped right ventricle.

Tongsong and colleagues published prenatal sonographic findings for isolated tricuspid valve atresia. The four chamber view fails to demonstrate a patent tricuspid valve and this area appears echogenic.

Fig. 13. Hypoplastic left heart syndrome Hypoplastic left heart syndrome consists of a small left ventricle (LV) with abnormal mitral or aortic valve development. The LV will initially appear slightly small during early pregnancy, with subsequent development as a rudimentary slit-like cavity as the pregnancy progresses. The dominant chamber is the right ventricle (RV). Blood flow across the foramen ovale is reversed from the right (RA) to left (LA) atrium. (Adapted from Fetal ultrasound simulator [CD-ROM]. Washington, D.C: American College of Obstetricians and Gynecologists; 1998; with permission.)

Fig. 14. Hypoplastic left heart syndrome. Sonographic findings demonstrate marked underdevelopment of the left ventricular cavity that gives it a “slit-like” appearance. This degree of ventricular disproportion may not be as obvious at an earlier stage of pregnancy.
pending on size of the VSD. Right ventricular outflow tract obstruction may occur as subvalvular pulmonary stenosis or pulmonary valve stenosis—a potential cause of ductal dependency. Approximately 20% of cases will be associated with transposition of the great arteries. Aortic arch abnormalities have also been reported. Chromosomes are usually normal and it is rare to have extracardiac defects. Increased nuchal translucency, however, has been reported in embryos with tricuspid atresia as early as 11 weeks, menstrual age [61].

The surgical outcome of infants born with this lesion depends on the presence of associated anomalies and relies on use of the Fontan procedure. The Hospital for Sick Children recently summarized a total of 137 infants who underwent a Fontan procedure [71]. Cohort survival was 90% at the age of 1 month, 81% at 1 year, 70% at 10 years, and 60% at 20 years.

The tricuspid valve septal leaflet is normally not formed before 12 weeks, menstrual age [28]. However, Ebstein’s malformation is another tricuspid valve anomaly that is caused by failure of the inferior atrioventricular cushion to properly develop this leaflet from the right side of the ventricular septum. This anomaly is characterized by increased offsetting of the atrioventricular valves and tricuspid valve insufficiency that leads to an enlarged right atrium. A nomogram of the mitral to tricuspid valve distance is helpful for confirming this diagnosis [51]. Melendres and colleagues [72] recently reported a missed case of Ebstein’s anomaly that was obscured by misinterpretation of an atrioventricular groove. Ebstein’s anomaly has a poor perinatal prognosis with a mortality rate as high as 85% [73].

**Conotruncal abnormalities**

A primitive endocardial heart tube, superior to the primitive ventricles, becomes divided in half by a spiral septum to form great arteries early in gestation. This process may be interrupted for unknown reasons, leading to a spectrum of developmental cardiac anomalies such as truncus arteriosus, transposition of the great arteries, double-outlet right ventricle, and TOF. The fundamental lesion depends on where formation of the spiral septum is disrupted and where the great arteries are positioned in relation to each other at that time. Sonographic distinction between these specific abnormalities may be very difficult before birth [74,75].

Some conotruncal abnormalities, such as TOF and double outlet right ventricle, are also at increased risk for chromosomal abnormalities [76]. In a recent population-based study of 255,849 births, 43 children were found to have 22q11.2 deletion with an overall prevalence of 1 in 5950 births (95% CI, 1 in 4417 – 1 in 8224 births) [77]. Most affected children (81%) had a heart defect that included conotruncal anomalies (46%), interrupted aortic arch (19%), ventricular septal defects (16%), and other assorted extra-cardiac vascular anomalies (51%). Conotruncal aberrations are more frequent in diabetics and in those women who have a congenital abnormality themselves or have had a child with a genetic disorder.

The basic cardiac examination, using a four-chamber view alone, is notoriously unreliable for detecting these anomalies. However, an extended basic examination of the outflow tracts is the key for their effective prenatal detection. The cardiac axis may provide an initial sonographic indication of a conotruncal anomaly during the basic examination [78,79]. DeVore [80] has also described the use of color Doppler sonography to visualize great vessel relationships for second and third trimester pregnancies.

**Truncus arteriosus**

Truncus arteriosus occurs when one great artery arises from the base of the heart and gives rise to the coronary, pulmonary, and aortic circulations. The truncus usually overrides a VSD. The pulmonary arteries arise from the truncal root as a common trunk (Type I, most frequent) [Fig. 16A, B], close but separate (Type II), or widely separate (Type III) [81]. Fortunately, they are not ductal-dependent lesions.

Fetal echocardiography should focus on the ventricular origin of the truncus, truncal valve annular
diameter, and evidence for valvular dysplasia. Doppler studies may reveal truncal valve stenosis or insufficiency [82]. In a pathology study of 28 Type I and Type II cases, other cardiovascular lesions included anomalous position of the left coronary artery (18.5%), right aortic arch (36%), and interrupted aortic arch (11%) [83]. The distinction between truncus arteriosus and pulmonary valve atresia with VSD can be very difficult [84]. An investigation from the University of Michigan described 46 infants with truncus arteriosus undergoing early primary repair and found an actuarial survival rate of 81 ± 6% at 90 days and beyond [85]. More recently, an observational study of 23 affected fetuses indicates the following outcomes: termination of pregnancies (34.8%); intrauterine death (8.7%); postnatal deaths (21.7%) [84]. The eight remaining neonates (34.8%) were alive and doing well after surgery (n=6) or awaiting repair (n=2). Major cardiac surgical centers currently favor a primary repair of truncus arteriosus during the neonatal period.

**Transposition of the great arteries**

Transposition of the great arteries (TGA) occurs when the aorta arises from the right ventricle and the pulmonary artery arises from the left ventricle. The usual spiral relationship of the great arteries is lost so that the outflow tracts are parallel to each other [Fig. 17] [86]. In about half of cases there is no VSD. Affected newborns without a large VSD may not have adequate mixing of oxygenated blood and can experience rapid hemodynamic decompensation as the ductus arteriosus closes. This abnormality can be easily missed from the four-chamber view unless a very large VSD is present. In this case, an extended basic examination of the outflow tracts is likely to identify TGA. Congenitally corrected transposition of the great arteries can also rarely occur where parallel vessels are also seen exiting the heart. In this situation, the atria connect with anatomically discordant ventricles and the ventricles connect with discordant and transposed great arteries [87]. Careful attention to the chamber morphology, presence of moderator band, and papillary muscle relationships can pro-

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**Fig. 16.** Truncus arteriosus. (A) Axial view of the fetal thorax reveals a small pulmonary artery (arrow) that directly originates from a large truncal root (Tr). The fetal spine (Sp) is seen as a point of reference. (B) Oblique coronal view of the left hemithorax demonstrates a large truncal vessel, with ventricular septal defect, that exits the right (RV) and left (LV) ventricles. This truncal vessel overrides the ventricular septum and gives off a small pulmonary vessel (arrow).

**Fig. 17.** Transposition of the great arteries. The main-diagnostic findings is the manner by which the great arteries exit the ventricles in a parallel manner. Fetal echocardiography would demonstrate that the aortic root originates from the right ventricle (RV), whereas the pulmonary artery would exit the left ventricle (LV). A small ventricular septal defect is also present (arrow).
vide important clues to help the examiner accurately distinguish between right and left ventricles.

The potential impact of early prenatal diagnosis is illustrated by a study that examined clinical outcome in 68 affected neonates in whom a prenatal diagnosis of TGA was suspected [88]. Results were compared with 250 affected neonates who were first identified with TGA after delivery. Newborns with late diagnosis had increased delay between birth and admission for special care and were more likely to present with metabolic acidosis and multi-organ failure. Preoperative mortality was 6% for the neonatal group as compared with no deaths in the prenatal group. Postoperative morbidity was not different between groups, although the hospital stay was slightly longer in babies diagnosed after birth. Postoperative death was significantly higher in the neonatal group (20 of 235 versus 0 of 68, \(P < .01\)). Their results suggest that prenatal diagnosis of TGA reduces mortality and morbidity. Timely detection of TGA before delivery provides adequate planning for monitoring and antepartum care. This information also facilitates in utero transfer of fetuses to a tertiary care facility that can appropriately treat newborns with ductal dependent lesions.

**Double-outlet right ventricle**

Double-outlet right ventricle (DORV) describes a condition in which most of the aorta and pulmonary artery arise from the right ventricle [89]. The sonographic findings may closely resemble TOF or transposition of the great arteries with VSD [Fig. 18]. The outcome of infants with DORV depends largely on the associated anomalies.

As in TOF there is always an accompanying VSD but, unlike TOF the relationship of the great vessels is often abnormal; the aorta is commonly transposed anterior and to the right of the pulmonary artery. Other defects are not infrequent such as pulmonary valve stenosis, right cardiac axis deviation, right aortic arch, atrial septal defect, and total anomalous pulmonary venous return. DORV with transposition is known as a Taussig-Bing defect and is commonly associated with coarctation. The combination of DORV and AVSD is difficult to repair surgically.

**Tetralogy of Fallot**

TOF is the only conotruncal anomaly in which the usual spiral relationship of the great vessels is maintained. The aorta overrides a ventricular septal defect [Fig. 19]. The pulmonary artery may be small due to uneven division of the primitive truncus. In the fetus, unlike in children, the right ventricle is not hypertrophied because of shunting across the foramen ovale and the VSD reduces the load on the right heart.

Early fetal TOF may simply present as a VSD with aortic septal override. This anomaly can be missed on a screening four-chamber view if the VSD is small [Fig. 20]. Left cardiac axis deviation may provide an initial diagnostic clue for this lesion [79]. However, the extended basic cardiac examination is most likely to demonstrate a VSD with aortic override. The aortic root itself can also be enlarged, although pulmonary valve stenosis may be become
apparent until later pregnancy [90,91]. The aortic to pulmonary size ratio will be high despite normal valve diameter measurements. In TOF, this ratio increases as gestational age advances because there is less than the usual growth of the pulmonary diameter [92]. The 90% confidence interval for the pulmonary artery to aortic diameter (Pa/Ao) ratio ranges from 0.84 to 1.41 and remains constant throughout pregnancy [93]. The right ventricular outflow tract should be re-evaluated before delivery to identify affected fetuses at greatest risk for ductal dependency.

These newborns may experience hemodynamic decompensation if the pulmonary valve diameter is small (≤ 5 mm at term) or if there is retrograde flow across the ductus arteriosus. Immediate surgery may not be required for affected infants with sufficient pulmonary valve flow and absence of ductal dependency.

One variation, in which the pulmonary valve is atretic and the pulmonary artery is not visible, is known as “pseudotruncus” as only a solitary large vessel is seen straddling the VSD. Another variation of TOF involves absence of the pulmonary valve so that there is regurgitation back and forth. The pulmonary artery may enlarge to massive proportions and hydrops may occur.

**Aortic coarctation**

Cardiac ventricular disproportion can occur as a normal variant, a consequence of fetal growth restriction, or an indirect sign of aortic coarctation [Fig. 21]. Aortic coarctation is usually difficult to directly visualize, especially in the context of a cardiac screening examination. However, the prenatal diagnosis of aortic coarctation has been reported to improve survival and reduce morbidity [94].

Allan and colleagues [95] found that 24 fetuses had dilatation of the right heart as compared with the left side. In 18 of these cases, the diagnosis of aortic coarctation or interruption was correctly inferred from indirect sonographic findings. Hornberger and associates [96] summarized a multicenter investigation for 20 infants with coarctation. They found quantitative hypoplasia of the aortic isthmus and transverse arch as the best predictors...
for coarctation and emphasized the importance of conducting serial studies for suspected cases. Ventricular disproportion has only a moderate degree of sensitivity (62%) for the detection of coarctation that occurs with a high false-positive rate after 34 weeks [97]. The 90% confidence interval for the right ventricular to left ventricular diameter ratio is constant throughout pregnancy and ranges from 0.79 to 1.24 [93].

Total anomalous pulmonary venous return

The left atrium is normally positioned near the descending aorta. In the space between these two structures are the main left and right pulmonary veins. They can be followed to their drainage point in the back of the left atrium. In total anomalous pulmonary venous return (TAPVR), both main pulmonary veins drain into the right atrium via a vertical vein which then drains into a coronary sinus, persistent left superior vena cava, innominate vein, the hepatic veins, or even below the diaphragm (20%) into the inferior vena cava. Thus oxygenated blood from the lungs never reaches the body and brain but rather circulates around and around in the lungs with the only mixing available across a patent foramen ovale. TAPVR can lead to cardiorespiratory decompensation of the newborn that is unresponsive to prostaglandin infusion. This circulatory abnormality should be considered when a dilated coronary sinus, cardiac chamber disproportion, or size disparity between the great arteries is seen. It is particularly common in fetuses with heterotaxic abnormalities. Direct documentation of pulmonary venous flow into the left atrium is the most reliable way to exclude TAPVR [98] [Fig. 22].

A nonlethal variation is partial anomalous venous return in which the right vein drains to the right atrium but the left still drains to the left atrium. As long as some return goes to the left atrium, oxygenated blood is available to the body and brain.

Summary

CHD is a leading cause of infant morbidity and mortality that results from birth defects. Diagnosticians who use ultrasonography to evaluate the fetal heart must be familiar with key factors that can impact the success of their cardiac screening programs. A good understanding of practice guidelines for the “basic” and “extended basic” cardiac examination is essential. Efforts should also be made to standardize diagnostic training of these who perform these examinations in an ongoing manner. The primary goal is for these individuals to accurately identify who should be referred for a more detailed evaluation of the fetus.

References


