



Chapter 4

Cardiovascular system

INTRODUCTION TO CONGENITAL HEART DISEASE

Abnormalities of the heart and great arteries are the most common congenital abnormalities. In general, about half are either lethal or require surgery and half are asymptomatic. The first two groups are referred to as major.

Prevalence

Cardiovascular abnormalities are found in 5-10 per 1,000 live births and in about 30 per 1,000 stillbirths.

Etiology

The etiology of heart defects is heterogeneous and probably depends on the interplay of multiple genetic and environmental factors, including maternal diabetes mellitus or collagen disease, exposure to drugs such as lithium, and viral infections such as rubella. Specific mutant gene defects and chromosomal abnormalities account for less than 5% of the patients. Heart defects are found in more than 90% of fetuses with trisomy 18 or 13, 50% of trisomy 21, and 40% of those with Turner syndrome, deletions or partial trisomies involving a variety of chromosomes.

Recurrence

When a previous sibling has had a congenital heart defect, in the absence of a known genetic syndrome, the risk of recurrence is about 2%, and with two affected siblings the risk is 10%. When the father is affected, the risk for the offspring is about 2% and if the mother is affected the risk is about 10%.

Reliability of prenatal diagnosis

Echocardiography has been successfully applied to the prenatal assessment of the fetal cardiac function and structure, and has led to the diagnosis of most cardiac abnormalities. Studies from specialist centers report the diagnosis of about 90% of defects. However, the majority of such studies refer to the prenatal diagnosis of moderate to major defects in high-risk populations.

Screening for cardiac abnormalities

The main challenge in prenatal diagnosis is to identify the high-risk group for referral to specialist centers. The indications include congenital cardiac defects in one of the parents or previous pregnancies, maternal diabetes mellitus or ingestion of teratogenic drugs. However, more than 90% of fetuses with cardiac defects are from families without such risk factors. A higher sensitivity is achieved by examination of the four-chamber view of the heart at the routine 20-week scan; screening studies have reported the detection of about 30% of major cardiac defects. Recent evidence suggests that a higher sensitivity (more than 50%) can be achieved by referral for specialist echocardiography of patients with increased nuchal translucency at 10-14 weeks.

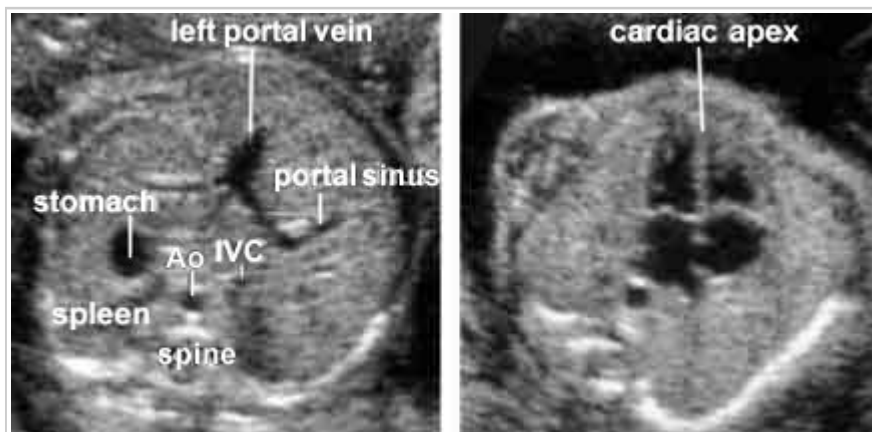
ASSESSMENT OF THE FETAL HEART

Real-time 2-dimensional evaluation

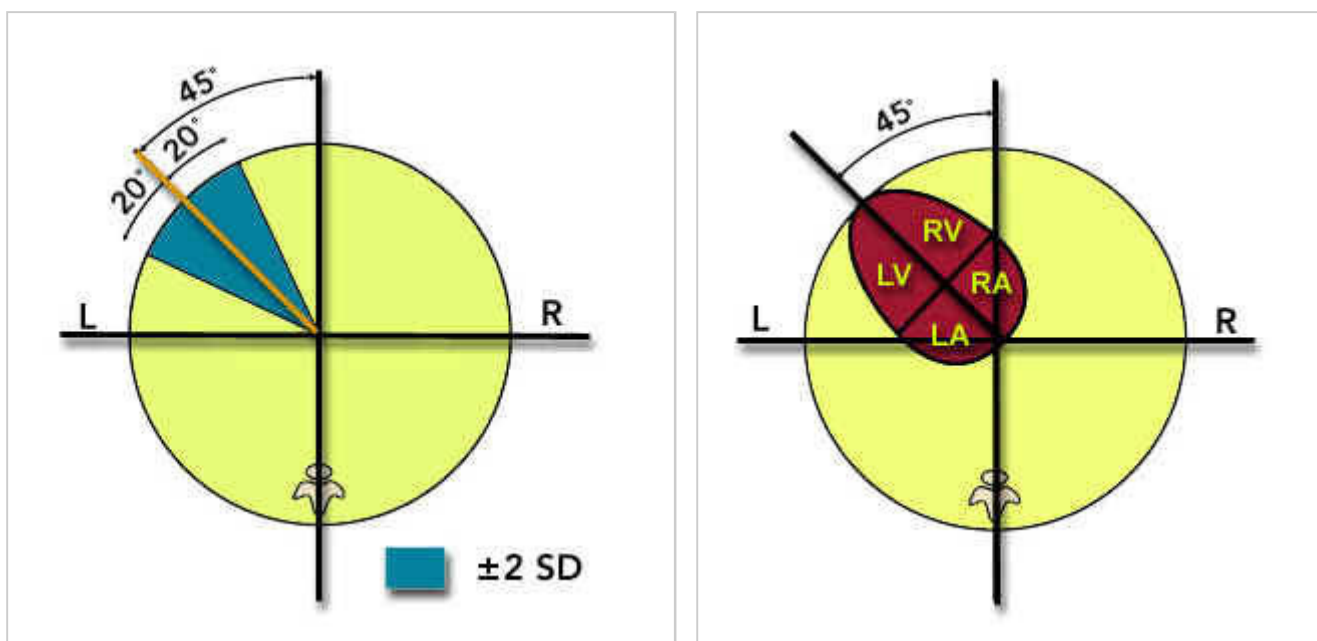
The heart can be observed in an infinity of planes, but a few sections are the basis on which most of the diagnoses are made. These planes include the four-chamber, left and right chambers and great vessel views. Although it is convenient to refer to these standardized views for descriptive purposes, in practice it may be difficult to reproduce these exact sections, and the operator should be familiar with small variations of these planes.

Complex cardiac anomalies are frequently associated with an abnormal disposition of the heart and extra-cardiac viscera. Fetal echocardiography should always include an assessment of topographic anatomy of the abdomen and chest. The left and right sides are assessed by determining the relative position of the head and spine. The visceral situs is then assessed by demonstrating the relative position of the stomach, hepatic vessels, abdominal aorta and inferior vena cava.

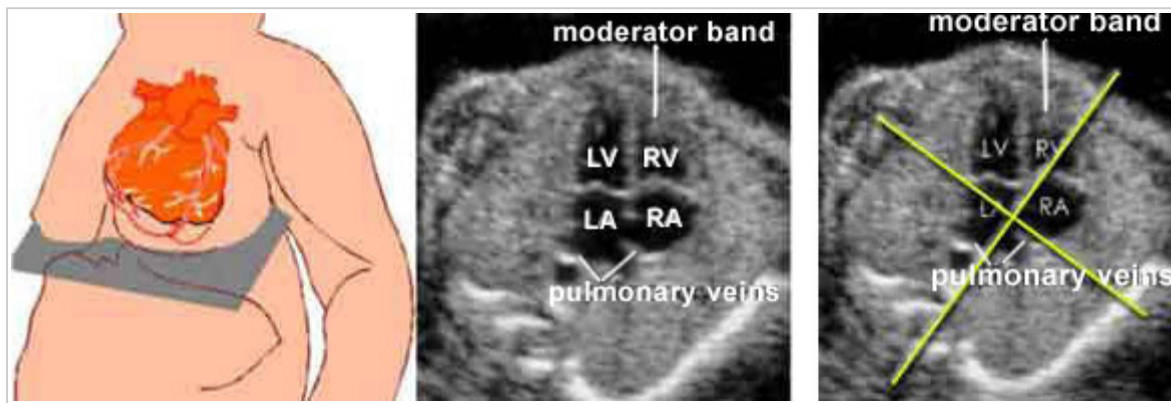
The examination of the fetal heart begins with the assessment of the disposition of abdominal and thoracic organs, as an abnormal disposition is frequently associated with complex cardiac anomalies. A transverse section of the upper abdomen, the same used for the measurement of the abdominal circumference, allows to identify the position of the liver, stomach and great abdominal vessels. A transverse section of the thorax reveals the four-chamber view of the fetal heart. The heart occupies approximately one third of the thorax. The heart is not mid-line but shifted to the left side of the chest, with the apex pointing to the left. The axis of the interventricular septum is about 45° to 20° to the left of the anteroposterior axis of the fetus.



The examination of the fetal heart begins with the assessment of the disposition of abdominal and thoracic organs

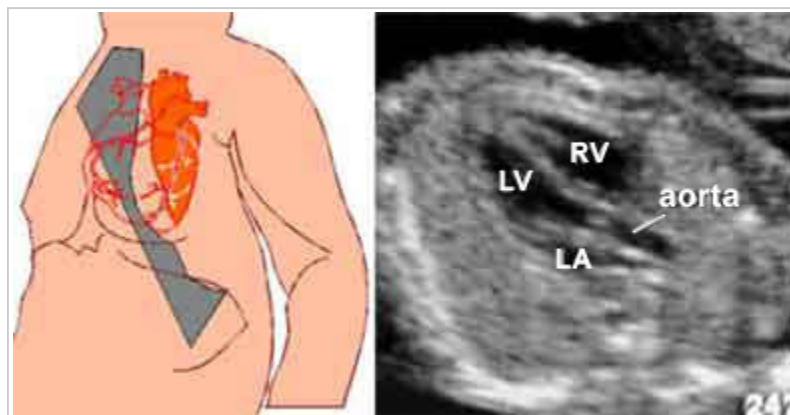


In the four chamber view the normal ventricles, atria, atrio-ventricular valves, ventricular and atrial septae, foramen ovale flap, and pulmonary venous connections can be identified. The thickness of the interventricular septum and of the free ventricular walls is the same. The interatrial septum is open at the level of the foramen ovale. The foramen ovale flap is visible in the left atrium, beating toward the left side. The insertion of the tricuspid valve along the interventricular septum is more apical than the insertion of the mitral valve. The confluence of the pulmonary veins into the left atrium serves to identify it as such. Probably, about 90% of ultrasonographically detectable fetal cardiac defects demonstrate some abnormalities in this view.

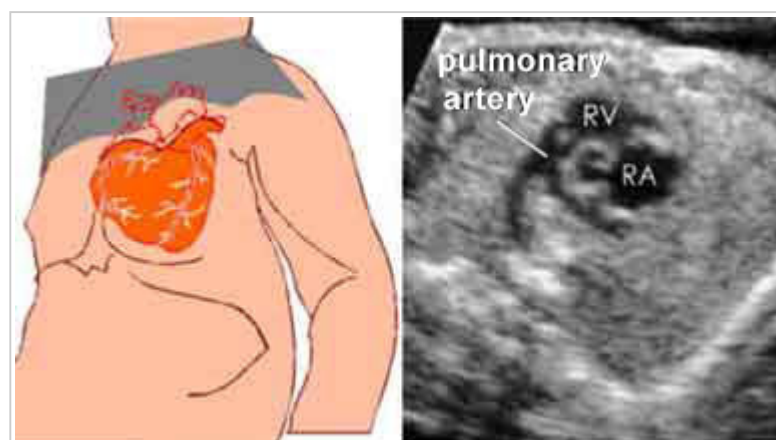


Normal Cardiac Axis

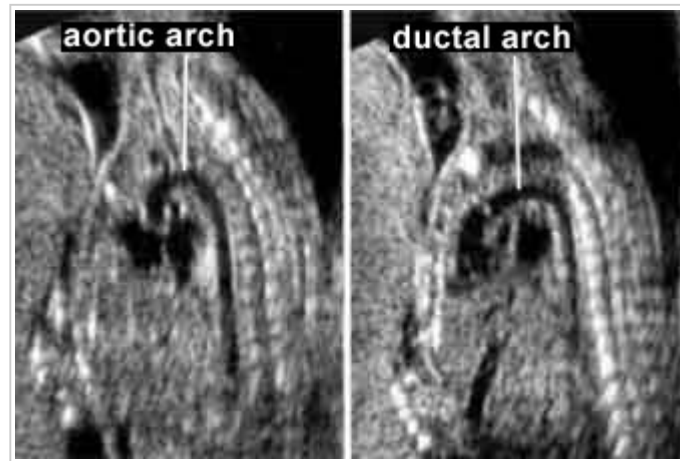
Evaluation of the cardiac outflow tracts can be difficult, and at present it is not considered a part of the standard examination of fetal anatomy. However, we believe that it is important to attempt such an examination because this improves the detection of many abnormalities of the heart and great arteries. The outflow tracts and great arteries can be demonstrated by slight angulations of the transducer from the four-chamber view. By turning the transducer while keeping the left ventricle and the aorta in the same plane, one can obtain the left heart views, while the right heart views are obtained by moving the transducer cranially and tilting slightly in the direction of the left shoulder. The left heart views demonstrate the left ventricle and aortic outflow tract. The anterior wall of the aorta is in continuity with the interventricular septum.



The right heart views demonstrate the right ventricle and the right ventricular outflow tract. The main pulmonary artery originates from the anterior ventricle and trifurcates into a large vessel, the ductus going into the descending aorta, and two small vessels, the pulmonary arteries

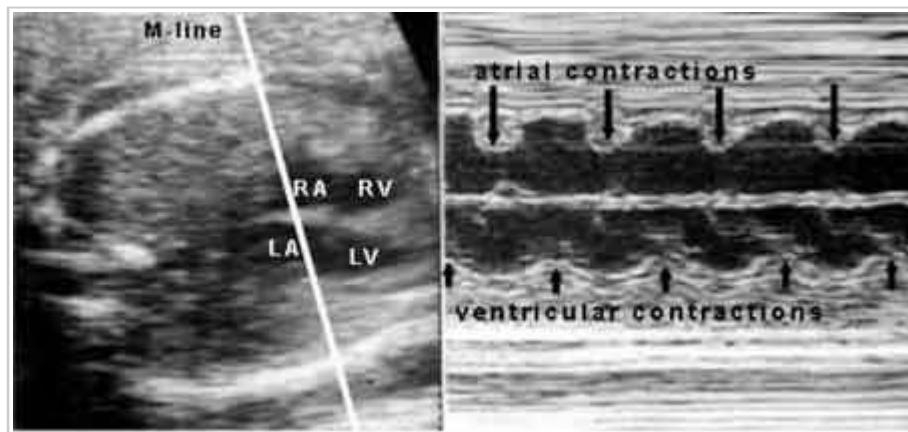


There are two arches in the fetus (aortic arch and curve of the ductus) and they should be distinguished. The brachiocephalic vessels originate from the aortic arch, while no vessels emanate from the ductus. Furthermore, the curve of the aortic arch is gentler than that of the ductus, which is slightly more angular. The caevae can be seen in a longitudinal view as they both enter the right atrium.

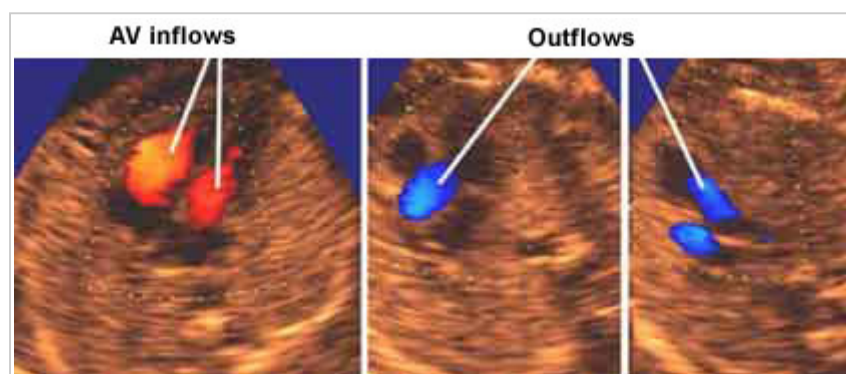


M-Mode

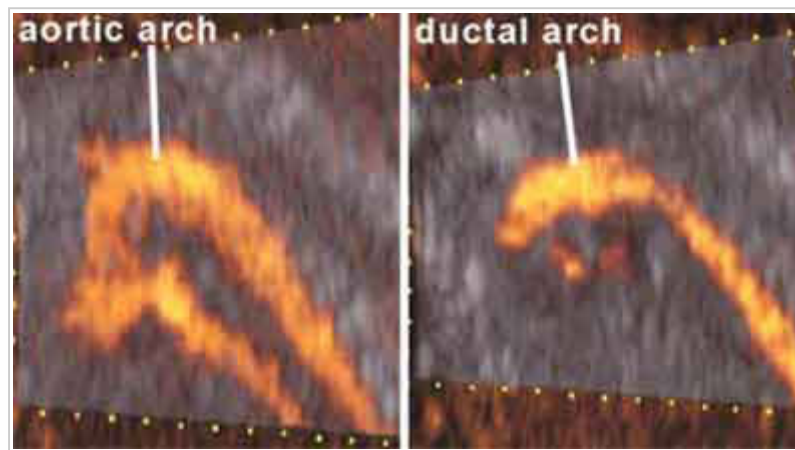
Heart rate and rhythm are assessed subjectively. M-mode, which is not used routinely, is useful for the evaluation of abnormal cases. In M-mode ultrasound, one line of information only is continuously displayed: instead of a two-dimensional scan of the heart, a recording of the variations of echoes along a single line is produced. Thus, M-mode is of little help in the analysis of the morphology of the heart but is useful in assessing motions and rhythms. One simply “drops” an M-mode line over one atrial and ventricular wall and is able to quantify cardiac frequency, and to infer the atrioventricular sequence of contractions.



Pulsed wave and color Doppler



Color Doppler overlays a representation of flow velocity over a conventional gray scale image. This allows a rapid recognition of the flow pattern. Color Doppler is useful to assess normal anatomy and physiology, valvular regurgitation or stenosis, shunting and the orientation of flows. Pulsed wave Doppler is used to analyze the spectral shift (to assess the resistance in a vessel), to obtain flow velocities (how the resistance affects the flow), and flow predictions (to estimate the perfusion). Pulsed Doppler ultrasound, in combination with two-dimensional and M-mode sonography, has proved useful in the evaluation of both fetal dysrhythmias and structural anomalies. Pulsed Doppler can be useful in the detection and assessment of severity of valvar abnormalities (stenosis, insufficiency). Analysis of atrioventricular inflows, hepatic veins and inferior vena cava can also be used to assess cardiac rhythm.



ATRIAL SEPTAL DEFECTS

Most atrial septal defects involve either the septum primum (the portion of the atrial septum below the foramen ovale) or the septum secundum (the portion above the foramen ovale). Primum atrial septal defect is the simplest form of the atrioventricular septal defects (see below). Secundum atrial septal defect, which are the most common, are usually isolated, but may be related to other cardiac lesions (such as mitral, pulmonary, tricuspid or aortic atresia) and are occasionally found as part of syndromes (including Holt-Oram syndrome in which there is hypoplasia of the thumb and radius, triphalangeal thumb, abrachia, and phocomelia).

Prevalence

Secundum atrial septal defects, which represent about 10% of congenital heart defects, are found in about 1 per 3,000 births.

Diagnosis

Although the in utero identification of secundum atrial septal defect has been reported, the diagnosis remains difficult because of the physiological presence of the foramen ovale and only unusually large defects can be recognized with certainty.

Prognosis

Atrial septal defects are not a cause of impairment of cardiac function in utero, as a large right-to-left shunt at the level of the atria is a physiological condition in the fetus. Most affected infants are asymptomatic even in the neonatal period.

VENTRICULAR SEPTAL DEFECTS

Defects in the ventricular septum are either isolated (about 50%) or they are part of a complex heart defect. They are classified into perimembranous, inlet, trabecular or outlet defects depending on their location on the septum.

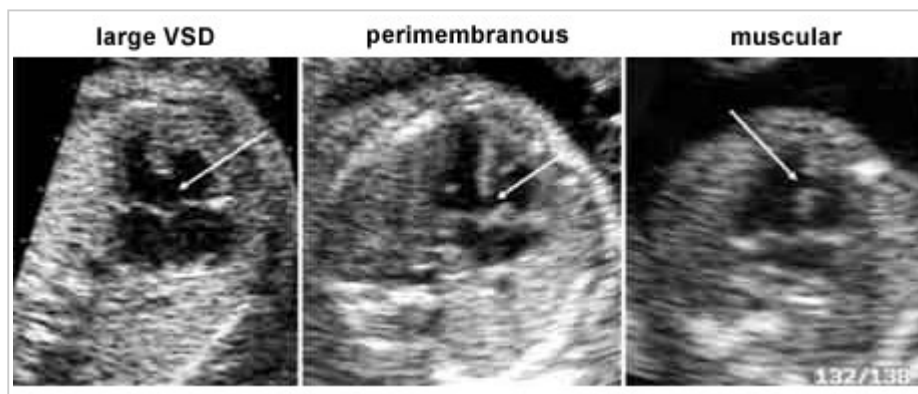
Perimembranous defects (80%) involve the membranous septum below the aortic valve, but also extend to variable degrees into the adjacent portion of the septum. The inlet defects are on the inflow tract of the right ventricle and thus affect the implantation of the septal chordae of the tricuspid valve. The trabecular defects occur in the muscular portion of the septum, and the outlet defects are in the infundibular portion of the right ventricle.

Prevalence

Ventricular septal defects, which represent 30% of all congenital heart defects, are found in about 2 per 1,000 births.

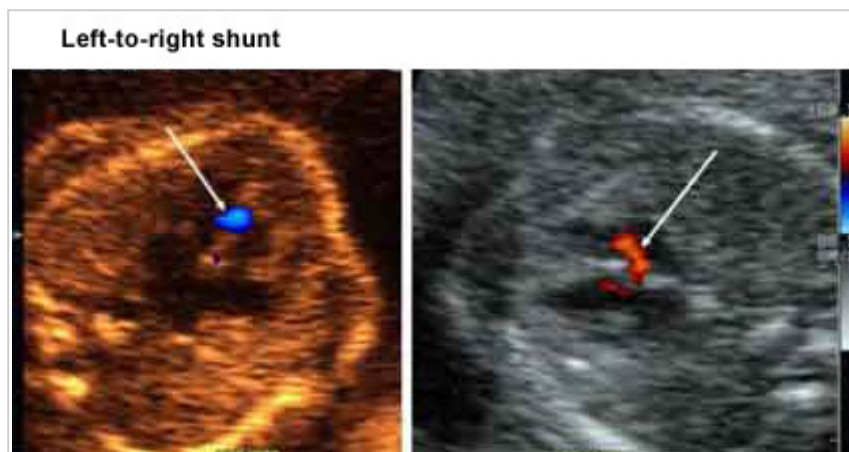
Diagnosis

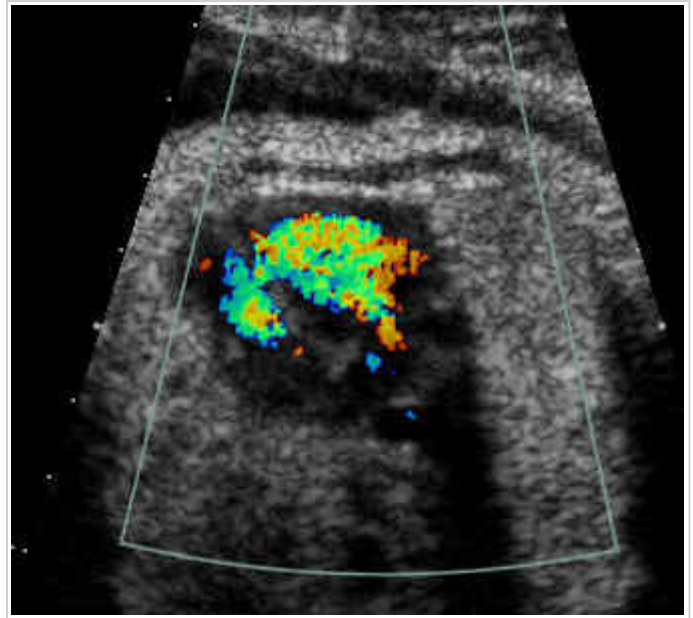
Echocardiographic diagnosis depends on the demonstration of a dropout of echoes in the ventricular septum. Since most ventricular septal defects are perimembranous and subaortic, a detailed view of the left outflow tract is the best picture to image them. While evaluating the ventricular septum in search of defects, multiple views should be used. Overall, small isolated ventricular septal defects are difficult to detect prenatally, and both false positive and false negative diagnoses have been made.



Ventricular Septal Defects

In dubious cases, Color Doppler may be useful, in that many ventricular septal defects are associated with a demonstrable left to right shunt.



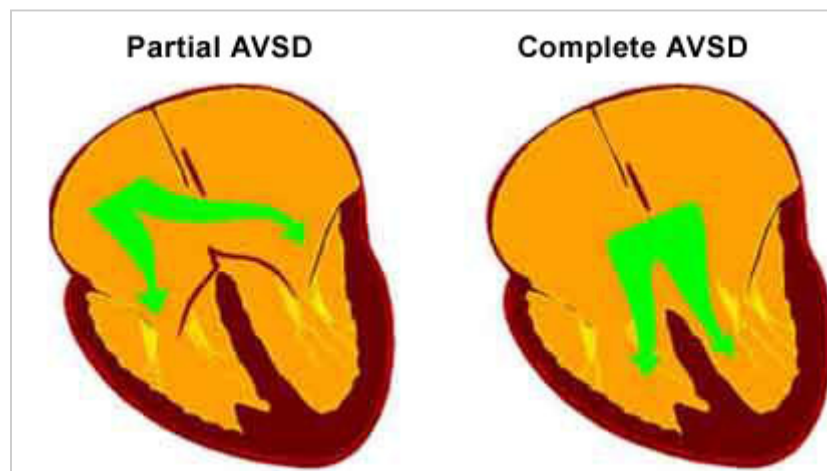


Prognosis

Ventricular septal defects are not associated with hemodynamic compromise in utero because the right and left ventricular pressures are very similar and the degree of shunting should be minimal. More than 90% of small defects close spontaneously within the first year of life. Large defects present with congestive heart failure at 2-8 weeks of life and require medical treatment (digoxin and diuretics). Rarely very large defects, associated with massive left to right shunt, can be associated with congestive heart failure soon after birth. If medical treatment fails surgical closure is undertaken; survival from surgery is more than 90% and survivors have a normal life expectancy and normal exercise tolerance.

ATRIOVENTRICULAR SEPTAL DEFECTS

The ontogenesis of the apical portion of the atrial septum, of the basal portion of the interventricular septum and of the atrioventricular valves depends on development of mesenchymal masses (endocardial cushions). Abnormal development of these structures is commonly referred to as endocardial cushion defects, atrioventricular canal or atrioventricular septal defects. In the complete form, persistent common atrioventricular canal, the tricuspid and mitral valve are fused in a large single atrioventricular valve that opens above and bridges the two ventricles. In the complete form of atrioventricular canal, the common atrioventricular valve may be incompetent, and systolic blood regurgitation from the ventricles to the atria may give rise to congestive heart failure.

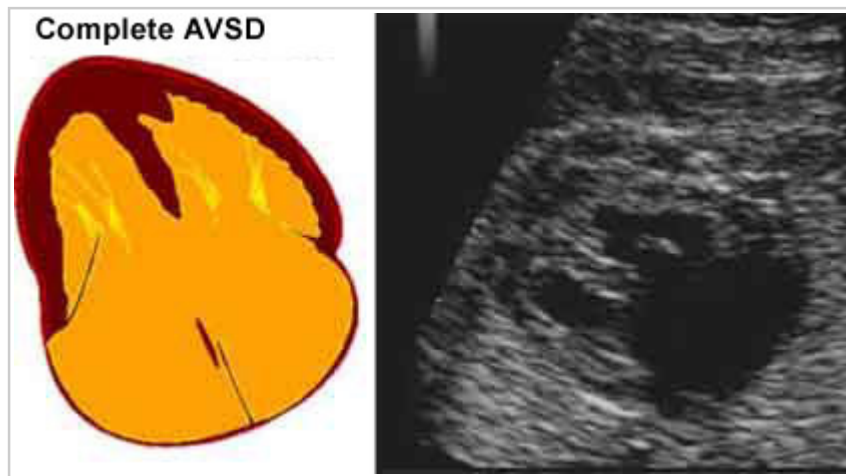


Prevalence

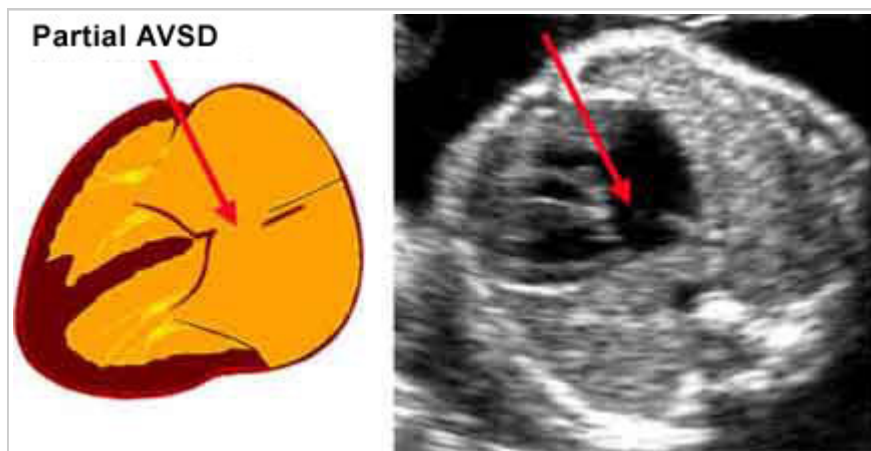
Atrioventricular septal defects, which represent about 7% of all congenital heart defects, are found in about 1 per 3,000 births.

Diagnosis

Antenatal echocardiographic diagnosis of complete atrioventricular septal defects is usually easy. An obvious deficiency of the central core structures of the heart is present. Color Doppler ultrasound can be useful, in that it facilitates the visualization of the central opening of the single atrioventricular valve. The atria may be dilated as a consequence of atrioventricular insufficiency. In such cases, Color and pulsed Doppler ultrasound allow one to identify the regurgitant jet.



The incomplete forms are more difficult to recognize. The main clue is the absence of the atrial septum below the level of the foramen ovalis. Another useful hint is the demonstration that the tricuspid and mitral valves attach at the same level at the crest of the septum. This apical displacement of the mitral valve elongates the left ventricular outflow tract. The atrial septal defect is of the ostium primum type (since the septum secundum is not affected) and thus is close to the crest of the interventricular septum.



Prognosis

Atrioventricular septal defects will usually be encountered either in fetuses with chromosomal aberrations (50% of cases are associated with aneuploidy, 60% being trisomy 21, 25% trisomy 18) or in fetuses with cardiosplenic syndromes. In the former cases, an atrioventricular septal defect is frequently found in association with extra-cardiac anomalies. In the latter cases, multiple cardiac anomalies and abnormal disposition of the abdominal organs are almost the rule.

Atrioventricular septal defects do not impair the fetal circulation per se. However, the presence of atrioventricular valve insufficiency may lead to intrauterine heart failure. The prognosis of atrioventricular septal defects is poor when detected in utero, probably because of the high frequency of associated anomalies in antenatal series. About 50% of untreated infants die within the first year of life from heart failure, arrhythmias and pulmonary hypertension due to right-to-left shunting (Eisenmenger syndrome). Survival after surgical closure (which is usually carried out in the sixth month of life) is more than 90% but in about 10% of patients a second operation for atrioventricular valve repair or replacement is necessary. Long-term prognosis is good.

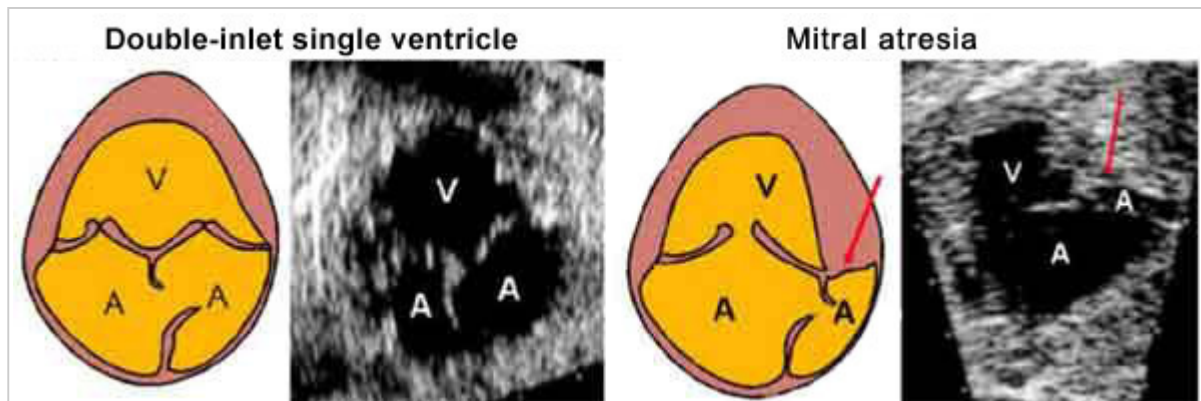
UNIVENTRICULAR HEART

This term defines a group of anomalies characterized by the presence of an atrioventricular junction that is entirely connected to only one chamber in the ventricular mass. Therefore, univentricular heart includes both those cases in which two atrial chambers are connected, by either two distinct atrioventricular valves or by a common one, to a main ventricular chamber (double-inlet single ventricle) as well as those cases in which, because of the absence of one atrioventricular connection (tricuspid or mitral atresia), one of the ventricular chambers is either rudimentary or absent.

Prevalence

Univentricular heart is rare; it represents about 1.5% of all congenital cardiac defects.

Diagnosis



In double-inlet single ventricle, two separate atrioventricular valves are seen opening into a single ventricular cavity without evidence of the interventricular septum. In mitral / tricuspid atresia, there is only one atrioventricular valve connected to a main ventricular chamber. A small rudimentary ventricular chamber lacking of atrioventricular connection is a frequent but not constant finding. Demonstration of two patent great arteries arising from the ventricle allows a differential diagnosis from hypoplastic ventricles (hypoplastic left heart syndrome, pulmonary atresia with intact ventricular septum).

Prognosis

Surgical treatment (the Fontan procedure) involves separation of the systemic circulations by anastomosing the superior and inferior vena cava directly to the pulmonary artery. The survivors from this procedure often have long-term complications including arrhythmias, thrombus formation and protein-losing enteropathy. The 5-year survival is about 70%.

AORTIC STENOSIS

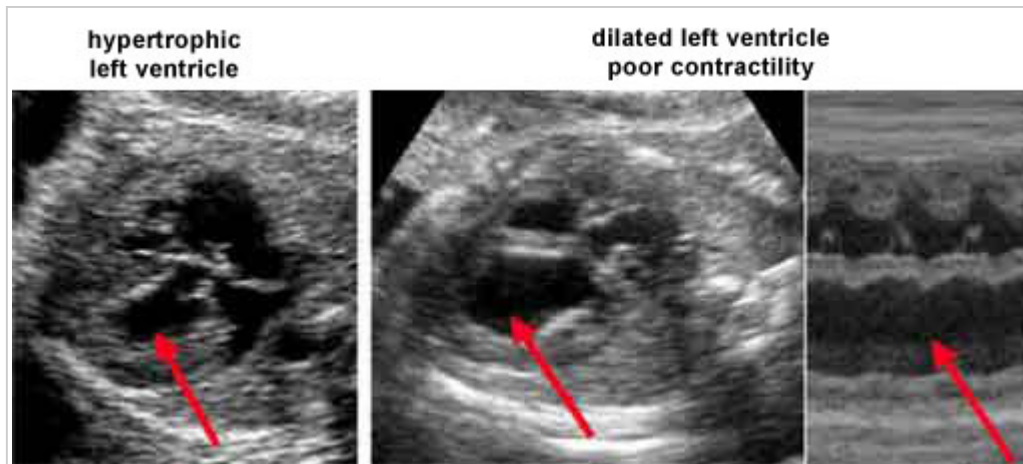
Aortic stenosis is commonly divided in supravalvar, valvar and subaortic forms. Supravalvar aortic stenosis can be due to one of three anatomic defects: a membrane (usually placed above the sinuses of Valsalva), a localized narrowing of the ascending aorta (hourglass deformity) or a diffuse narrowing involving the aortic arch and branching arteries (tubular variety). The valvar form of aortic stenosis can be due to dysplastic, thickened aortic cusps or fusion of the commissure between the cusps. The subaortic forms include a fixed type, representing the consequence of a fibrous or fibromuscular obstruction, and a dynamic type, which is due to a thickened ventricular septum obstructing the outflow tract of the left ventricle. The latter is also known as asymmetric septal hypertrophy or idiopathic hypertrophic subaortic stenosis. A transient form of dynamic obstruction of the left outflow tract is seen in infants of diabetic mothers, and is probably the consequence of fetal hyperglycemia and hyperinsulinemia.

Prevalence

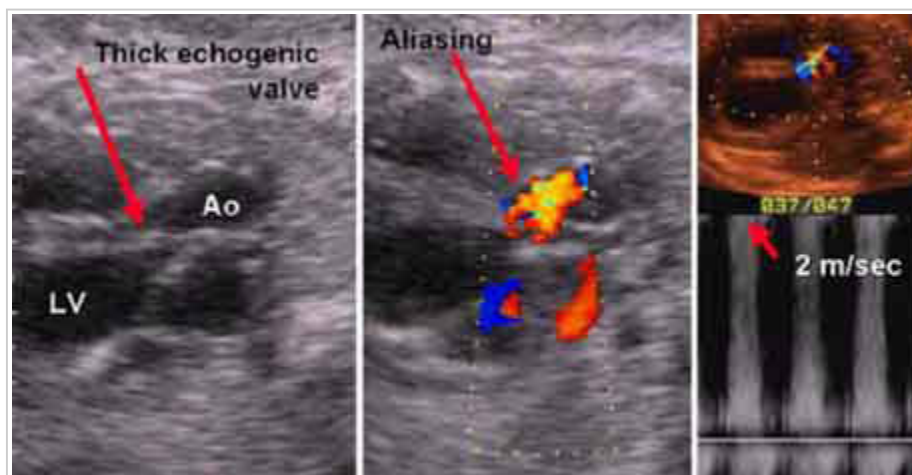
Aortic stenosis, which represents 3% of all congenital heart defects, is found in about 1 per 7,000 births.

Diagnosis

Most cases of mild to moderate aortic stenosis are probably not amenable to early prenatal diagnosis. Severe valvar aortic stenosis of the fetus is usually associated with a hypertrophic left ventricle. Less frequently, a dilated and poorly contracting left ventricle is found.



Within the ascending aorta (that can be small or enlarged) pulsed Doppler demonstrates increased peak velocity (usually in excess of 1 m/sec). At the Color Doppler examination, high velocity and turbulence results in aliasing, with a mosaic of colors.



Severe aortic stenosis may result in atrioventricular valve insufficiency and intrauterine heart failure. Asymmetric septal hypertrophy and hypertrophic cardiomyopathy of fetuses of diabetic mothers resulting in subaortic stenosis has been occasionally diagnosed by demonstrating an unusual thickness of the ventricular septum. We are not aware of cases of supralvalvular aortic stenosis detected in utero.

Prognosis

Depending upon the severity of the aortic stenosis, the association of left ventricular pressure overload and subendocardial ischemia, due to decrease in coronary perfusion, may lead to intrauterine impairment of cardiac function. Subvalvular and subaortic forms are not generally manifested in the neonatal period. Conversely, the valvar type can be a cause of congestive heart failure in the newborn and fetus as well. Although there is concern that cases seen in early gestation may progress in severity, the lesion usually remains stable. The neonatal outcome depends on the severity of obstruction. If the left ventricular function is adequate balloon valvuloplasty is carried out in the neonatal period and in about 50% of cases surgery is necessary within the first 10 years of life because of aortic insufficiency or residual stenosis. If left ventricular function is inadequate a Norwood-type of repair is necessary (see hypoplastic left heart).

Fetal therapy

Antenatal transventricular balloon valvuloplasty has been attempted in a handful of cases but the results are uncertain.

COARCTATION AND TUBULAR HYPOPLASIA OF THE AORTA

Coarctation is a localized narrowing of the juxtaductal arch, most commonly between the left subclavian artery and the ductus. Cardiac anomalies are present in 90% of the cases and include aortic stenosis and insufficiency, ventricular septal defect, atrial septal defect, transposition of the great arteries, truncus and double outlet right ventricle. Non-cardiac anomalies include diaphragmatic hernia, Turner syndrome but not Noonan syndrome.

Diagnosis

Coarctation may be a postnatal event, and this limits prenatal diagnosis in many cases. It should be suspected when the right ventricle is enlarged (right ventricle to left ventricle ratio of more than 1.3). Narrowing of the isthmus, or the presence of a shelf are often difficult to demonstrate because in the fetus aortic arch and ductal arch are close and are difficult to distinguish. In most cases, coarctation can only be suspected in utero and a certain diagnosis must be delayed until after birth.



Prognosis

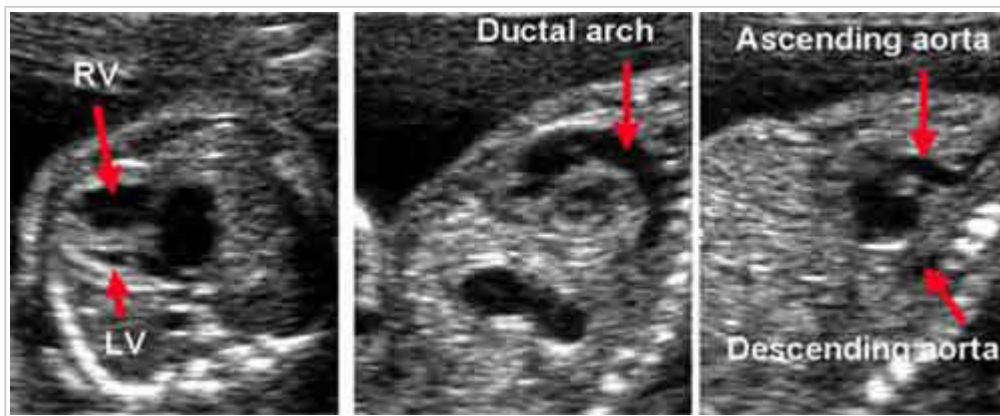
Critical coarctation is fatal in the neonatal period after closure of the ductus and therefore prostaglandin therapy is necessary to maintain a patent ductus. Surgery (which involves excision of the narrowed segment and end-to-end anastomosis) is associated with a mortality of about 10% and the incidence of restenosis in survivors (requiring further surgical repair) is about 15%.

INTERRUPTED AORTIC ARCH

The interruption of the aortic arch can be complete or there may be an atretic fibrous segment between the arch and the descending aorta. It may be isolated or associated with intracardiac lesions that cause obstruction to the blood flow from the left heart (aortic stenosis, aortic atresia, malaligned ventricular septal defects). Associated extracardiac anomalies are frequent and include DiGeorge syndrome (association of thymic aplasia, type B interruption and hypoplastic mandible), holoprosencephaly, cleft lip/palate, esophageal atresia, duplicated stomach, diaphragmatic hernia, horseshoe kidneys, bilateral renal agenesis, oligodactyly, claw hand and syrenomelia.

Diagnosis

Interrupted aortic arch should always be considered when intracardiac lesions diverting blood flow from the left to the right heart are encountered (aortic stenosis and atresia in particular). Isolated interruption of the aortic arch is often encountered with enlargement of the right ventricle (right ventricle to left ventricle ratio of more than 1.3). As the sonographic access to the arch is difficult, the diagnosis is not always possible. The characteristic finding of an ascending aorta more vertical than usually, and the impossibility to demonstrate a connection with the descending aorta suggest the diagnosis.

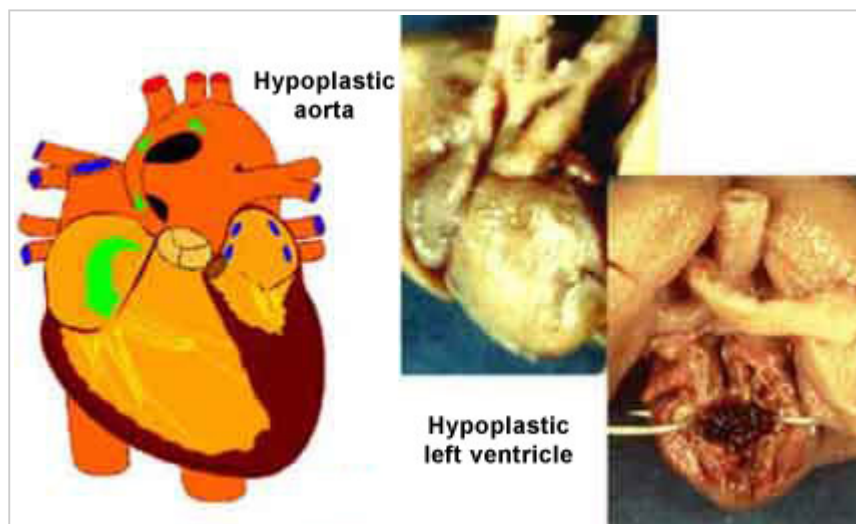


Prognosis

The median age at death for unoperated infants is four days. The initial treatment is the same as for any anomalies in which the perfusion is ductus dependent: prostaglandin E_1 . Recent reports suggest an overall late survival of more than 70% after surgery.

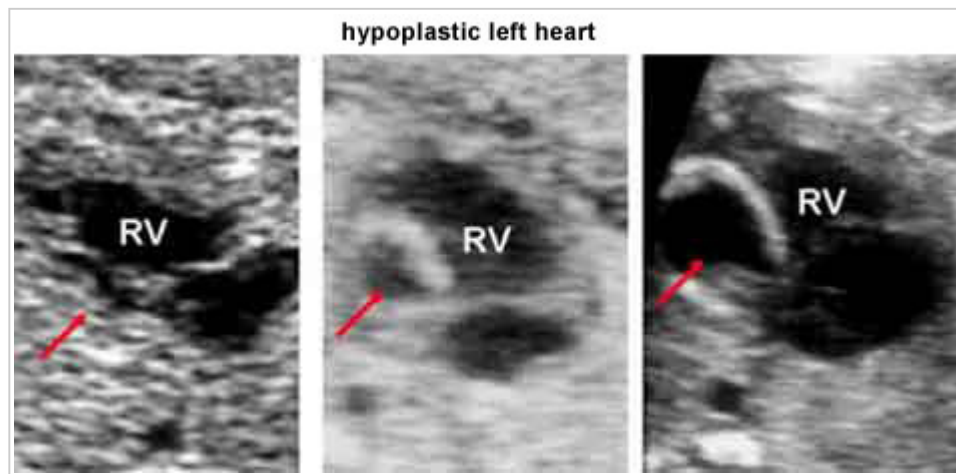
HYPOPLASTIC LEFT HEART SYNDROME

This is a spectrum of anomalies characterized by a very small left ventricle with mitral and/or aortic atresia or hypoplasia. Blood flow to the head and neck vessels and coronary artery is supplied in a retrograde manner via the ductus arteriosus.

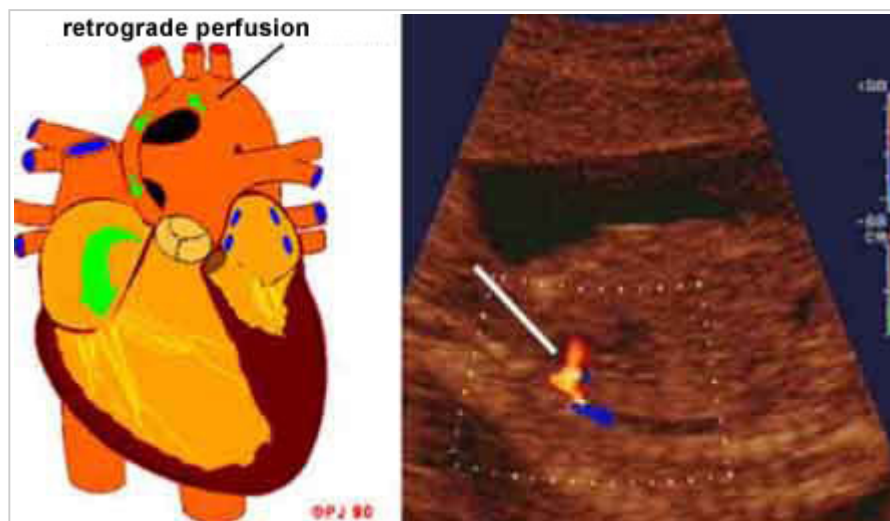


Diagnosis

Prenatal echocardiographic diagnosis of the syndrome depends on the demonstration of a diminutive left ventricle and ascending aorta. In most cases, the ultrasound appearance is self-explanatory, and the diagnosis an easy one. There is however a broad spectrum of hypoplasia of the left ventricle and in some cases the ventricular cavity is almost normal in size. As the four-chamber view is almost normal, we anticipate that these cases will be certainly missed in most routine surveys of fetal anatomy. At a closer scrutiny, however, the movement of the mitral valve appears severely impaired to non-existent, ventricular contractility is obviously decreased, and the ventricle often displays an internal echogenic lining that is probably due to endocardial fibroelastosis.



The definitive diagnosis of the syndrome depends on the demonstration of hypoplasia of the ascending aorta and atresia of the aortic valve. Color flow mapping is an extremely useful adjunct to the real-time examination, in that it allows the demonstration of absent to severely decreased mitral valve flow and of retrograde blood flow within the ascending aorta and aortic arch.



Prognosis

Hypoplastic left heart is well tolerated in utero. The patency of the ductus arteriosus allows adequate perfusion of the head and neck vessels. Intrauterine growth may be normal, and the onset of symptoms most frequently occurs after birth. The prognosis for infants with hypoplastic left heart syndrome is extremely poor and this lesion is responsible for 25 % of cardiac deaths in the first week of life. Almost all affected infants die within six weeks if they are not treated. In the neonatal period prostaglandin therapy is given to maintain ductal patency but still congestive heart failure develops within 24 hours of life. Options for surgery include cardiac transplantation in the neonatal period (with an 80% 5-year survival) and the three-staged Norwood repair. Stage 1 involves anastomosis of the pulmonary artery to the aortic arch for systemic outflow, placement of systemic-to-pulmonary arterial shunt to provide pulmonary blood flow, and arterial septectomy to ensure unobstructed pulmonary venous return; the mortality from the procedure is about 30%. Stage 2 (which is usually carried out in the sixth month of life) involves anastomosis of the superior vena cava to the pulmonary arteries. The overall 2-year survival with the Norwood repair is about 50% but more than 50% of survivors have neurodevelopmental delay.

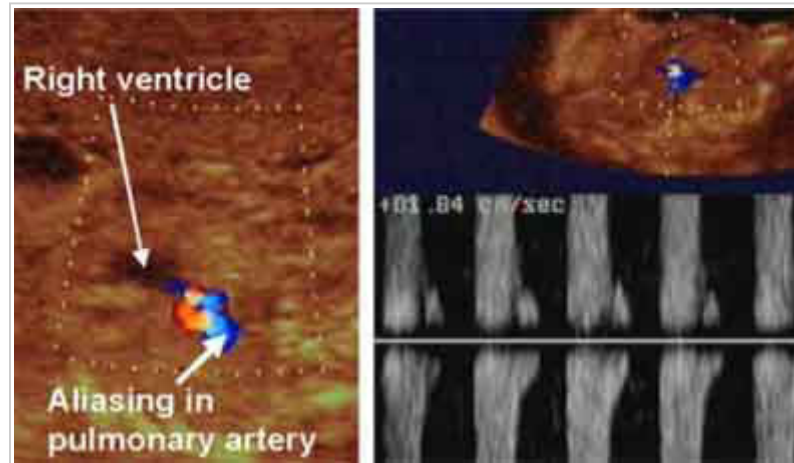
PULMONARY STENOSIS AND PULMONARY ATRESIA

Prevalence

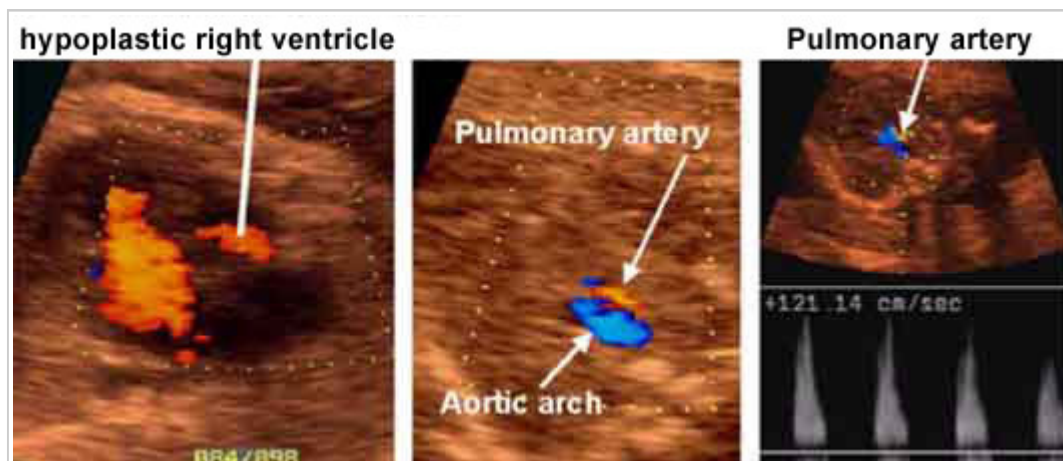
Pulmonary stenosis is found in about 1 per 2,000 births. Pulmonary atresia is rare, and is found in less than 1 per 10,000 births.

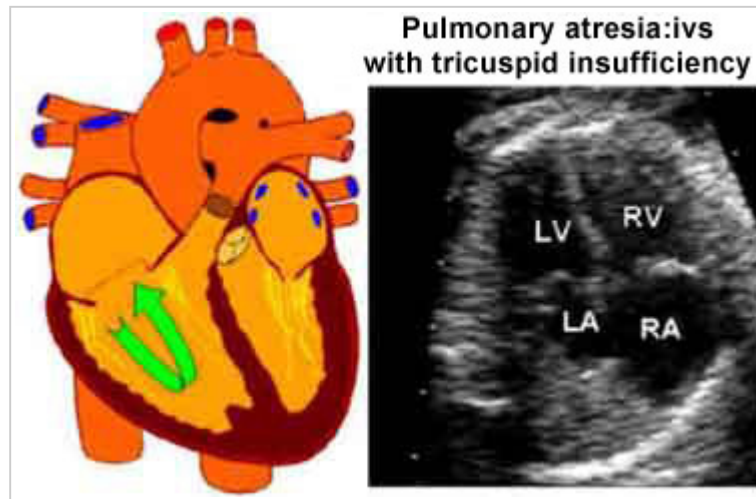
Diagnosis

The most common form of pulmonary stenosis is the valvar type, due to the fusion of the pulmonary leaflets. Hemodynamic is altered proportionally to the degree of the stenosis. The work of the right ventricle is increased, as well as the pressure, leading to hypertrophy of the ventricular walls. The same considerations formulated for the prenatal diagnosis of aortic stenosis are valid for pulmonic stenosis as well. A handful of cases recognized in utero have been reported in the literature thus far, mostly severe types with enlargement of the right ventricle and/or post-stenotic enlargement or hypoplasia of the pulmonary artery.



Pulmonary atresia with intact ventricular septum (PA:IVS) in infants is usually associated with an hypoplastic right ventricle. However, cases with enlarged right ventricle and atrium have been described with unusual frequency in prenatal series. Although these series are small, it is possible that the discrepancy with the pediatric literature is due to the very high perinatal loss rate that is found in "dilated" cases. Enlargement of the ventricle and atrium is probably the consequence of tricuspid insufficiency. Prenatal diagnosis of PA:IVS relies on the demonstration of a small pulmonary artery with an atretic pulmonary valve. The considerations previously formulated for the diagnosis of hypoplastic left heart syndrome apply to PA:IVS as well.





Prognosis

Patients with mild stenosis are asymptomatic and there is no need for intervention. Patients with severe stenosis, right ventricular overload may result in congestive heart failure and require balloon valvuloplasty in the neonatal period with excellent survival and normal long-term prognosis. Fetuses with pulmonary atresia and an enlarged right heart have a very high degree of perinatal mortality. Infants with right ventricular hypoplasia require biventricular surgical repair and the mortality is about 40%.

EBSTEIN'S ANOMALY AND TRICUSPID VALVE DYSPLASIA

Ebstein's anomaly results from a faulty implantation of the tricuspid valve. The posterior and septal leaflets are elongated and tethered below their normal level of attachment on the annulus or displaced apically, away from the annulus, down to the junction between the inlet and trabecular portion of the right ventricle. The anterior leaflet is normally inserted but deformed. The resulting configuration is that of a considerably enlarged right atrium at the expense of the right ventricle. The portion of the right ventricle that is ceded to the right atrium is called the atrialized inlet of the right ventricle. It has a thin wall that may even be membranous and is commonly dilated. The tricuspid valve is usually both incompetent and stenotic. Associated anomalies include atrial septal defect, pulmonary atresia, ventricular septal defect, and supraventricular tachycardia. Ebstein's may be associated with trisomy 13, 21, Turner, Cornelia de Lange and Marfan syndromes. Maternal ingestion of lithium has also been incriminated as a causal factor.

Diagnosis

The characteristic finding is that of a massively enlarged right atrium, a small right ventricle, and a small pulmonary artery. Doppler can be used to demonstrate regurgitation in the right atrium. About 25% of the cases have supraventricular tachycardia (from re-entrant impulse), atrial fibrillation or atrial flutter. Differential diagnosis from pulmonary atresia with intact ventricular septum and a regurgitant tricuspid valve or isolated tricuspid valve insufficiency is difficult and may be impossible antenatally.



Prognosis

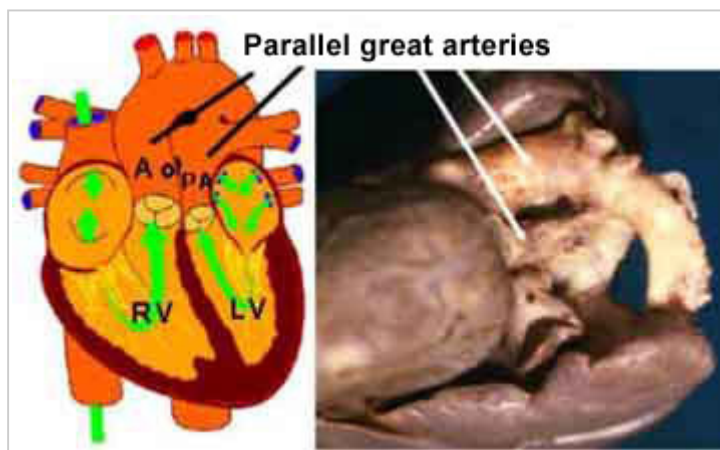
Although the disease has a variable severity with some cases discovered only late in life, Ebstein's anomalies detected prenatally have a dismal prognosis, with essentially all patients dying. This probably reflects that the prenatal variety is more severe than the one detected in children or adults.

CONOTRUNCAL MALFORMATIONS

Conotruncal malformations are a heterogeneous group of defects that involve two different segments of the heart: the conotruncus and the ventricles. Conotruncal anomalies are relatively frequent. They account for 20-30% of all cardiac anomalies and are the leading cause of symptomatic cyanotic heart disease in the first year of life. Prenatal diagnosis is of interest for several reasons. Given the parallel model of fetal circulation, conotruncal anomalies are well tolerated in utero. The clinical presentation occurs usually hours to days after delivery, and is often severe, representing a true emergency and leading to considerable morbidity and mortality. Yet, these malformations have a good prognosis when promptly treated. Two ventricles of adequate size and two great vessels are commonly present giving the premise for biventricular surgical correction. The outcome is indeed much more favorable than with most of the other cardiac defects that are detected antenatally. The first reports on prenatal echocardiography of conotruncal malformations date back from the beginning of the '80s. Nevertheless, despite improvement in the technology of diagnostic ultrasound, the recognition of these anomalies remains difficult. The four-chamber view is frequently unremarkable in these cases. A specific diagnosis requires meticulous scanning and at times may represent a challenge even for experienced sonologists. Referral centers with special expertise in fetal echocardiography have indeed reported both false positive and false negative diagnoses. There is a typical association between conotruncal anomalies and 22q11 deletion, a condition associated with long term implications, including immune deficits, neurological development and speech, that may not be apparent in neonatal life.

TRANSPOSITION OF THE GREAT ARTERIES

Transposition of the great arteries is an abnormality in which the aorta arises entirely or in large part from the right ventricle and the pulmonary artery arises from the left ventricle. Associated cardiac lesions are present in about 50% of cases, including ventricular septal defects (which can occur anywhere in the ventricular septum), pulmonary stenosis, unbalanced ventricular size ("complex transpositions"), anomalies of the mitral valve, which can be straddling or overriding. There are three types of complete transposition: those with intact ventricular septum with or without pulmonary stenosis, those with ventricular septal defects and those with ventricular septal defect and pulmonary stenosis.

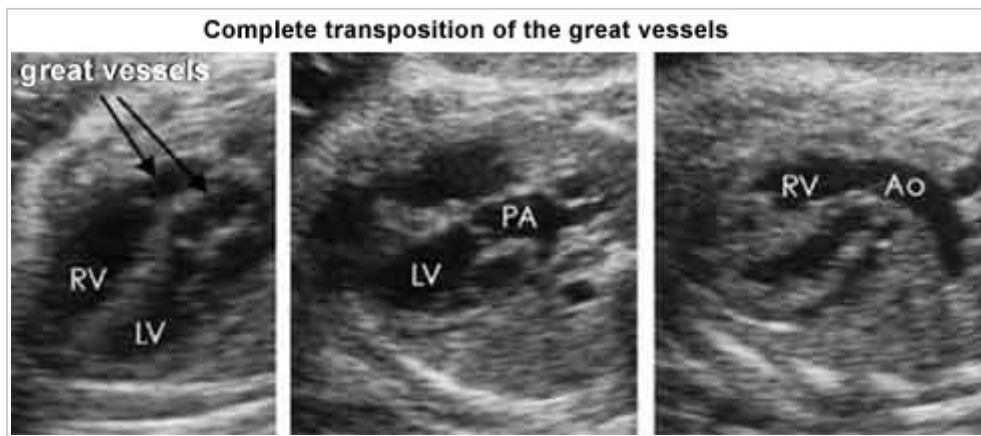


Prevalence

Transposition of the great arteries is found in about 1 per 5,000 births.

Diagnosis

Complete transposition is probably one of the most difficult cardiac lesions to recognize in utero. In most cases the four-chamber view is normal, and the cardiac cavities and the vessels have normal appearance. A clue to the diagnosis is the demonstration that the two great vessels do not cross but arise parallel from the base of the heart. The most useful echocardiographic view however is the left heart view demonstrating that the vessel connected to the left ventricle has a posterior course and bifurcates into the two pulmonary arteries. Conversely, the vessel connected to the right ventricle has a long upward course and gives rise to the brachio-cephalic vessels.



Difficulties may arise in the case of huge malalignment ventricular septal defect with overriding of the posterior semilunar root. This combination makes the differentiation with double outlet right ventricle very difficult. Corrected transposition is characterized by a double discordance, at the atrio-ventricular and ventriculo-arterial level. The left atrium is connected to the right ventricle, which is in turn connected to the ascending aorta. Conversely, the right atrium is connected with the right ventricle, which is in turn connected to the ascending aorta. The derangement of the conduction tissue secondary to malalignment of the atrial and ventricular septa may result in dysrhythmias, namely complete atrioventricular block. For diagnostic purposes, the identification of the peculiar difference of ventricular morphology (moderator band, papillary muscles, insertion of the atrioventricular valves) has a prominent role. Demonstration that the pulmonary veins are connected to an atrium which is in turn connected with a ventricle that has the moderator band at the apex is an important clue, that is furthermore potentially identifiable even in a simple four-chamber view. Diagnosis requires meticulous scanning to carefully assess all cardiac connections, by using the same views described for the complete form. The presence of atrioventricular block increases the index of suspicion.

Prognosis

As anticipated from the parallel model of fetal circulation, complete transposition is uneventful in utero. After birth, survival depends on the amount and size of the mixing of the two otherwise independent circulations. Patients with transposition and an intact ventricular septum present shortly after birth with cyanosis and deteriorate rapidly. When a large ventricular septal defect is present, cyanosis can be mild. Clinical presentation may be delayed up to 2-4 weeks, and usually occurs with signs of congestive heart failure. When severe stenosis of the pulmonary artery is associated with a ventricular septal defect, symptoms are similar to patients with tetralogy of Fallot. The time and mode of clinical presentation with corrected transposition depend upon the concomitant cardiac defects.

Surgery (which involves arterial switch to establish anatomic and physiological correction) is usually carried out within the first two weeks of life. Operative mortality is about 10% and 10-year follow-up studies report normal function but there is uncertainty if in the long term such patients are at increased risk of atherosclerotic coronary disease. In cases with pulmonary stenosis and ventricular septal defect balloon atrial septostomy may be necessary to ensure adequate oxygenation until definitive repair when the patient is older.

TETRALOGY OF FALLOT

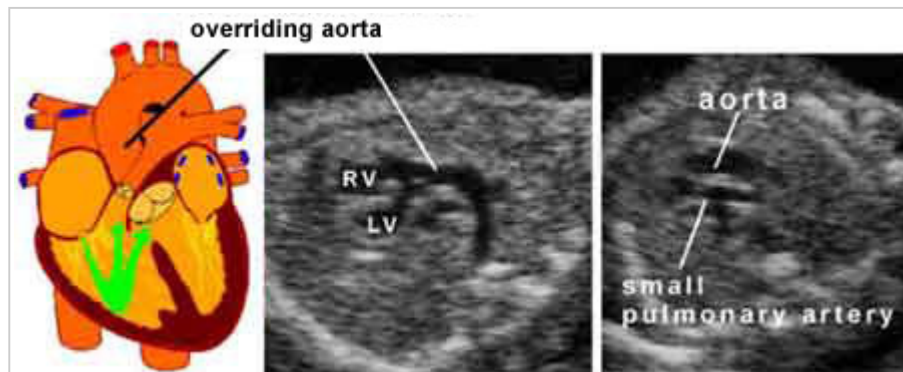
The essential features of this malformation are: (a) malalignment ventricular septal defect with anterior displacement of the infundibular septum associated with subpulmonary narrowing and overriding aortic root and (b) demonstrable continuity between the right outflow tract and the pulmonary trunk. In about 20% of cases this continuity is lacking leading to atresia of the pulmonary valve, a condition that is commonly referred to as pulmonary atresia with ventricular septal defect. Tetralogy of Fallot can be associated with other specific cardiac malformations, defining peculiar entities. These include atrioventricular septal defects (found in 4% of cases), and absence of the pulmonary valve, (found in less than 2% of cases). Hypertrophy of the right ventricle, one of the classic elements of the tetrad, is always absent in the fetus, and only develops after birth.

Prevalence

Tetralogy of Fallot is found in about 1 per 3,000 births.

Diagnosis

Echocardiographic diagnosis of tetralogy of Fallot relies on the demonstration of a ventricular septal defect in the outlet portion of the septum and an overriding aorta. There is an inverse relationship between the size of the ascending aorta and pulmonary artery, with a disproportion that is often striking. A large aortic root is indeed an important diagnostic clue.



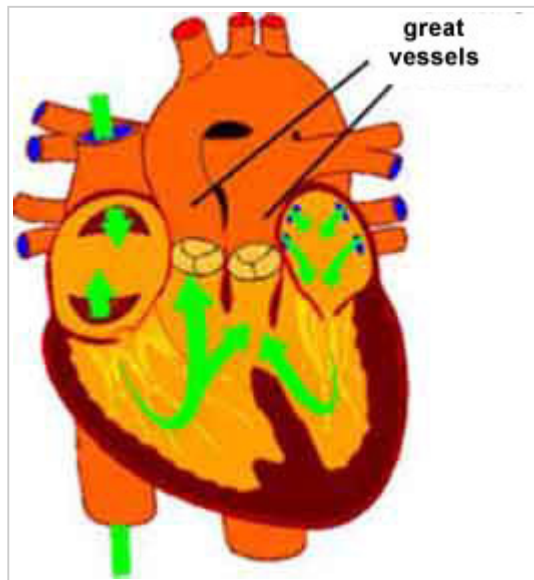
Doppler studies provide valuable information. The finding of increased peak velocities in the pulmonary artery corroborates the diagnosis of Tetralogy of Fallot by suggesting obstruction to blood flow in the right outflow tract. Conversely, demonstration with color and/or pulsed Doppler that, in the pulmonary artery, there is either no forward flow or reverse flow allows a diagnosis of pulmonary atresia. Diagnostic problems arise at the extremes of the spectrum of tetralogy of Fallot. In cases with minor forms of right outflow obstruction and aortic overriding differentiation from a simple ventricular septal defect can be difficult. In those cases in which the pulmonary artery is not imaged, a differential diagnosis between pulmonary atresia with ventricular septal defect and truncus arteriosus communis is similarly difficult. The sonographer should also be alerted to a frequent artifact that resembles overriding of the aorta. Incorrect orientation of the transducer may demonstrate apparent septo-aortic discontinuity in a normal fetus. The mechanism of the artifact is probably related to the angle of incidence of the sound beam. Careful visualization of the left outflow tract with different insonation angles, as well as the use of color Doppler and the research of the other elements of the tetralogy, should virtually eliminate this problem. Abnormal enlargement of the right ventricle, main pulmonary trunk and artery, suggests absence of pulmonary valve. Evaluation of other variables, such as multiple ventricular septal defects and coronary anomalies, would be valuable for a better prediction of surgical timing and operative prognosis. Unfortunately, these findings cannot be recognized for certain by prenatal echocardiography.

Prognosis

Cardiac failure is never seen in fetal life as well as postnatally. Even in cases of tight pulmonary stenosis or atresia, the wide ventricular septal defect provides adequate combined ventricular output, while the pulmonary vascular bed is supplied in a retrograde manner by the ductus. The only exception to this rule is represented by cases with an absent pulmonary valve that may result in massive regurgitation to the right ventricle and atrium. When severe pulmonic stenosis is present, cyanosis tends to develop immediately after birth. With lesser degrees of obstruction to pulmonary blood flow the onset of cyanosis may not appear until later in the first year of life. When there is pulmonary atresia, rapid and severe deterioration follows ductal constriction. Survival after complete surgical repair (which is usually carried out in the third month of life) is more than 90% and about 80% of survivors have normal exercise tolerance.

DOUBLE-OUTLET RIGHT VENTRICLE

In double-outlet right ventricle (DORV) most of the aorta and pulmonary valve arise completely or almost completely from the right ventricle. The relation between the two vessels may vary, ranging from a Fallot-like to a TGA-like situation (the Taussig-Bing anomaly). DORV is not a single malformation from a pathophysiological point of view. The term refers only to the position of the great vessels that is found in association with ventricular septal defects, tetralogy of Fallot, transposition, univentricular hearts. Pulmonary stenosis is very common in all types of DORV, but left outflow obstructions, from subaortic stenosis to coarctation and interruption of the aortic arch, can also be seen.



Prevalence

Double-outlet right ventricle is found in less than 1 per 10,000 births.

Diagnosis

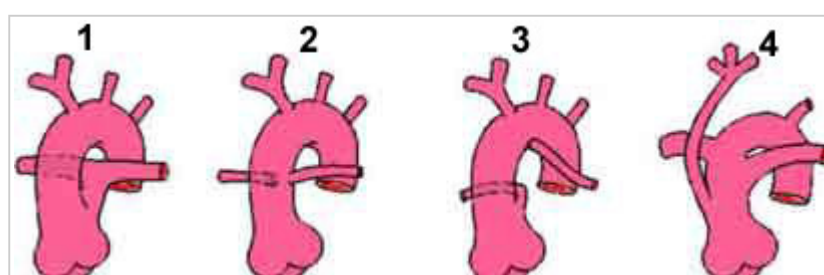
Prenatal diagnosis of DORV can be reliably made in the fetus but differentiation from other conotruncal anomalies can be very difficult, especially with Tetralogy of Fallot and transposition of the great arteries with ventricular septal defect. The main echocardiographic features include (a) alignment of the two vessels totally or predominantly from the right ventricle and (b) presence in most cases of bilateral conus (subaortic and subpulmonary).

Prognosis

The hemodynamic are dependent upon the anatomic type of DORV and the associated anomalies. Since the fetal heart works as a common chamber where the blood is mixed and pumped, DORV is not associated with intrauterine heart failure. However DORV, in contrast to other conotruncal malformations, is commonly associated with extracardiac anomalies and/or chromosomal defects. The early operative mortality is about 10%.

TRUNCUS ARTERIOSUS COMMUNIS

Truncus arteriosus is characterized by a single arterial vessel that originates from the heart, overrides the ventricular septum and supplies the systemic, pulmonary and coronary circulations. The single arterial trunk is larger than the normal aortic root and is predominantly connected with the right ventricle in about 40% of cases, with the left ventricle in 20%, and is equally shared in 40%. The truncal valve may have one, two or three cusps and is rarely normal. It can be stenotic or, more frequently, insufficient. A malalignment ventricular septal defect, usually wide, is an essential part of the malformation. There are three types based on the morphology of the pulmonary artery. In type 1, the pulmonary arteries arise from the truncus within a short distance from the valve, as a main pulmonary trunk, which then bifurcates. In type 2, there is no main pulmonary trunk. In type 3, only one pulmonary artery (usually the right) originates from the truncus, while the other is supplied by a systemic collateral vessel from the descending aorta. Eventually, type 4 is characterized by an interruption of the aortic arch. Similar to tetralogy of Fallot, and unlike the other conotruncal malformations, truncus is frequently (about 30%) associated with extracardiac malformations.



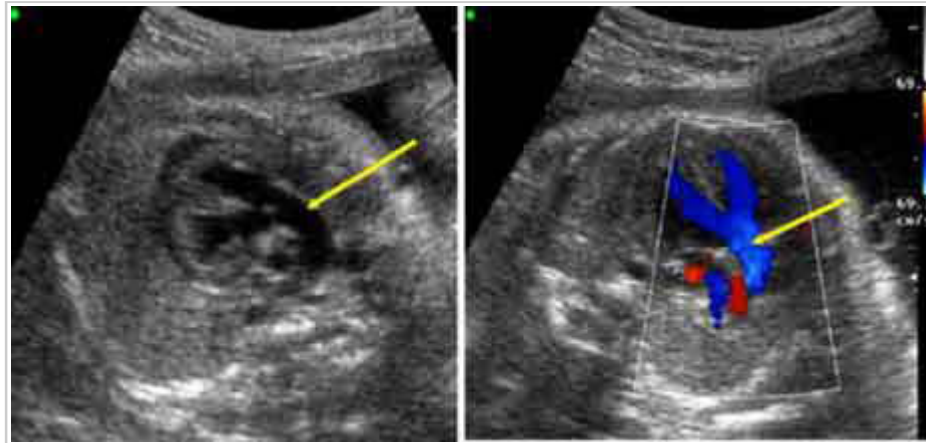
Prevalence

Truncus arteriosus is found in about 1 per 10,000 births.

Diagnosis

Truncus arteriosus can be reliably detected with fetal echocardiography. The main diagnostic criteria are:

(a) a single semilunar valve overrides the ventricular septal defect



(b) there is direct continuity between one or two pulmonary arteries and the single arterial trunk.



The semilunar valve is often thickened and moves abnormally. Doppler ultrasound is of value to assess incompetence of the truncal valve. A peculiar problem found in prenatal echocardiography is the demonstration of the absence of pulmonary outflow tract and the concomitant failure to image the pulmonary arteries. In this situations a differentiation between truncus and pulmonary atresia with ventricular septal defect may be impossible.

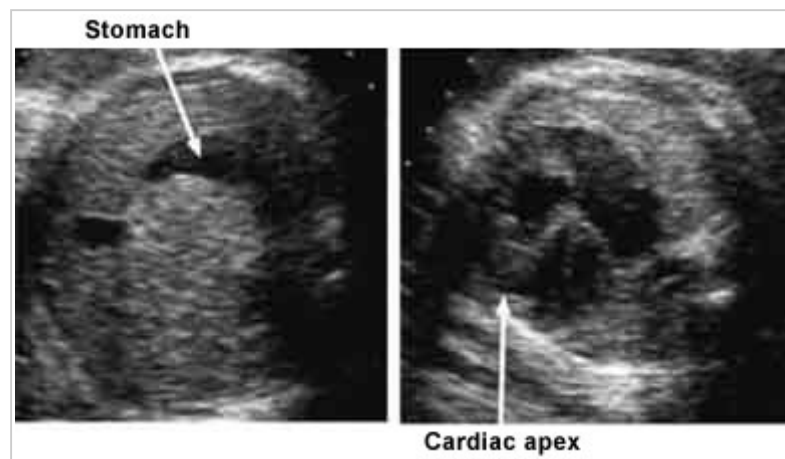
Prognosis

Similar to the other conotruncal anomalies truncus arteriosus is not associated with alteration of fetal hemodynamics. Truncus arteriosus is frequently a neonatal emergency. These patients have usually unobstructed pulmonary blood flow and show signs of progressive congestive heart failure with the postnatal fall in pulmonary resistance. Many patients will present with cardiac failure in the first 1 or 2 weeks of life. Surgical repair (usually before the sixth month of life) involves closure of the ventricular septal defect and creation of a conduit connection between the right ventricle and the pulmonary arteries. Survival from surgery is about 90% but the patients require repeated surgery for replacement of the conduit.

CARDIOSPLENIC SYNDROMES

In cardiosplenic syndromes, also referred to as heterotaxy, the fetus is made of either two left or two right sides. Other terms commonly used include left or right isomerism, asplenia and polysplenia. Unpaired organs (liver, stomach and spleen) may be absent, midline or duplicated. Because of left atrial isomerism (thus absence of right atrium which is the normal location for the pacemaker) and abnormal atrioventricular junctions, atrioventricular blocks are very common. Cardiosplenic syndromes are typically associated with abnormal situs, that is abnormal disposition of

abdominal and/or thoracic organs.



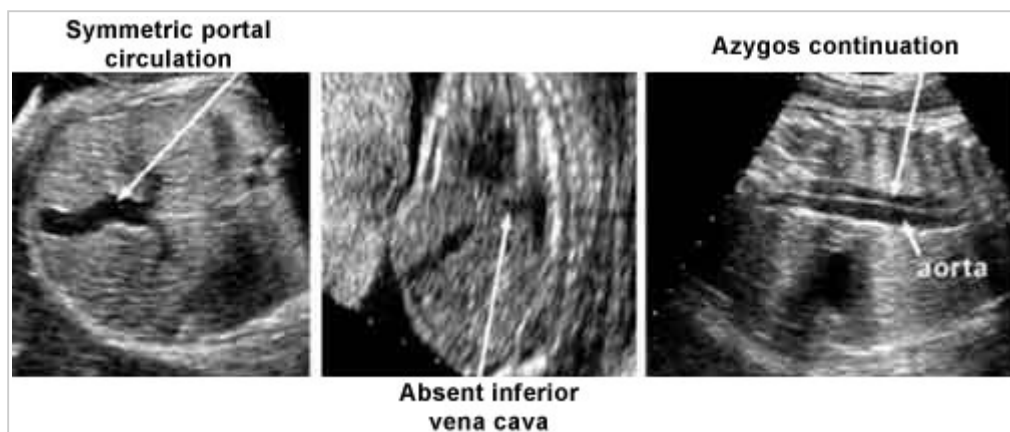
Prevalence

Cardiosplenic syndromes, which represent about 2% of all congenital heart defects, are found in about 1 in 10,000 births.

POLYSPLENIA

In polysplenia, the fetus has two left sides (one in normal position and the other as a mirror image); this is called left isomerism. Multiple small spleens (usually too small to be detected by antenatal ultrasound) are found posterior to the stomach. The liver is midline and symmetric. But the stomach and aorta can be on opposite sides. Cardiac anomalies are almost invariably present, including anomalous pulmonary venous return, atrioventricular canal, and obstructive lesions of the aortic valve. One typical and peculiar finding is the interruption of the inferior vena cava, with the lower portion of the body drained by the azygos vein.

Evaluation of the disposition of the abdominal organs is of special value for the sonographic diagnosis of fetal cardiosplenic syndromes. In normal fetuses, a transverse section of the abdomen demonstrates the aorta on the left side and the inferior vena cava on the right; the stomach is to left and the portal sinus of the liver bends to the right, towards the gallbladder. In polysplenia, a typical finding is interruption of the inferior vena cava with azygous continuation (there is failure to visualize the inferior vena cava and a large venous vessel, the azygos vein, runs to the left and close to the spine and ascends into the upper thorax). Symmetry of the liver can be sonographically recognized in utero by the abnormal course of the portal circulation that does not display a clearly defined portal sinus bending to the right.



The heterogeneous cardiac anomalies found in association with polysplenia are usually easily seen, but a detailed diagnosis often poses a challenge; in particular, assessment of connection between the pulmonary veins and the atrium (an element that has a major prognostic influence) can be extremely difficult. Associated anomalies include absence of the gallbladder, malrotation of the guts, duodenal atresia and hydrops.

ASPLENIA

In asplenia, the fetus has two right sides (right isomerism). As in polysplenia, evaluation of the disposition of the abdominal organs is a major clue to the diagnosis. The liver is generally midline and the stomach right- or left-sided. The aorta and cava are on the same side (either left or right) of the spine. The spleen cannot be seen and the stomach is found in close contact with the thoracic wall. Cardiac malformations are severe, with a tendency towards a single structure replacing normal paired structures: single atrium, single atrioventricular valve, single ventricle and single great vessel, and are usually easily demonstrated.

Diagnosis

Cardiosplenic syndromes may be inferred by the abnormal disposition of the abdominal organs. The presence of complex cardiac abnormalities is almost the rule.

Prognosis

The outcome depends on the amount of cardiac anomalies, but it tends to be poor. Atrioventricular insufficiency and severe fetal bradycardia due to atrioventricular block may lead to intrauterine heart failure.

ECHOGENIC FOCI

Prevalence

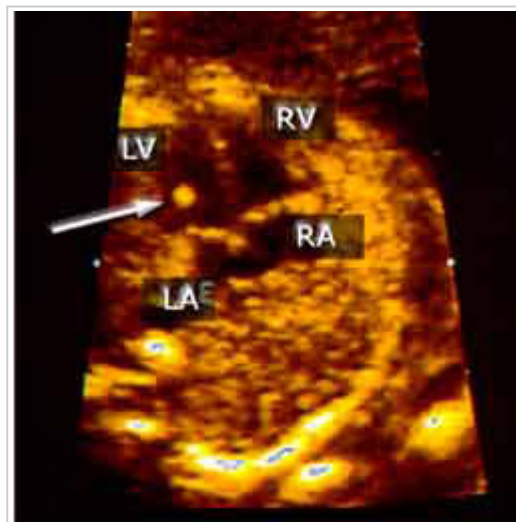
Echogenic foci in the heart are found in about 4% of pregnancies and in 12% of fetuses with trisomy 21.

Etiology

Histological studies have shown these foci to be due to mineralization within a papillary muscle.

Diagnosis

Echogenic foci are detected in the four-chamber view of the heart. In about 95% of cases they are located in the left ventricle and in 5% in the right ventricle; in 98% they are unilateral and 2% bilateral. Ventricular function is normal and the atrioventricular valves are competent.



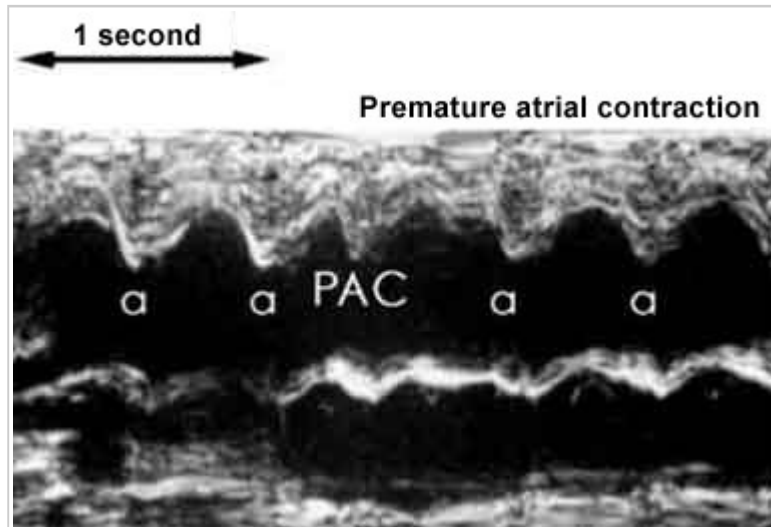
Four-chamber view. Note the white arrow pointing the echogenic foci in the left ventricle.

Prognosis

Echogenic foci are usually of no pathological significance and in more than 90% of cases they resolve by the third trimester or during pregnancy. However they are sometimes associated with cardiac defects and chromosomal abnormalities. For isolated hyperechogenic foci the risk for trisomy 21 may be three-times the background maternal age and gestation related risk.

CARDIAC DYSRHYTHMIAS: PREMATURE CONTRACTIONS

Ectopic heart beats are common but they are abnormal only when they occur at a frequency of more than 1 in 10 beats. Premature contractions may be of atrial (much more common) or ventricular origin. Immaturity of the conducting system may be the origin. The diagnosis is made by passing an M-mode cursor through one atrium and one ventricle. Premature atrial contractions are spaced closer to the previous contraction than normally and may be transmitted to the ventricle or blocked.

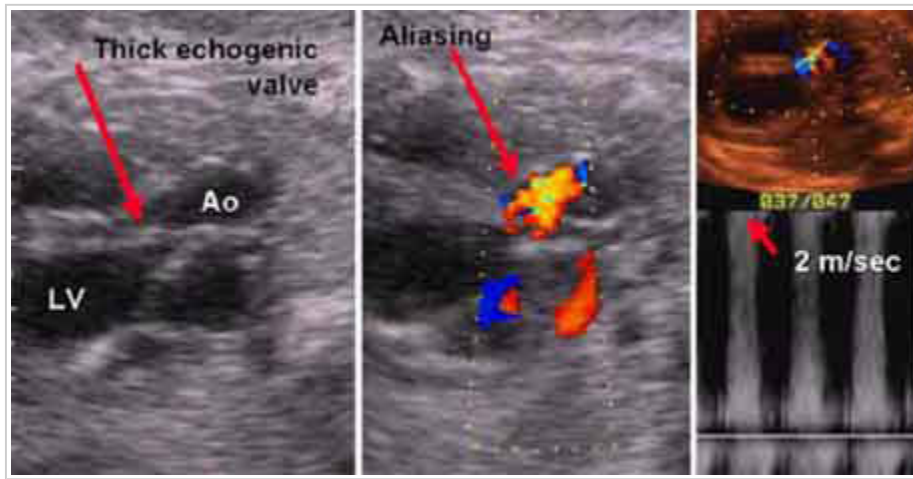


Premature ventricular contractions present in the same way but are not accompanied by an atrial contraction. Premature ventricular contractions are often followed by a compensatory pause due to the refractory state of the conduction system; the next conducted impulse arrives at twice the normal interval, and the continuity of the rhythm is not broken. Premature atrial contractions are usually followed by a non-compensatory pause; when the regular rhythm resumes, it is not synchronous with the rhythm before the extrasystole. The distance between the contraction that preceded the premature contraction and the one following it is not twice the distance between two normal contractions but a little shorter. Another approach to the sonographic diagnosis is to evaluate the waveforms obtained from the atrioventricular valves, hepatic vessels or inferior vena cava, which demonstrate pulsations corresponding to atrial and ventricular contractions.

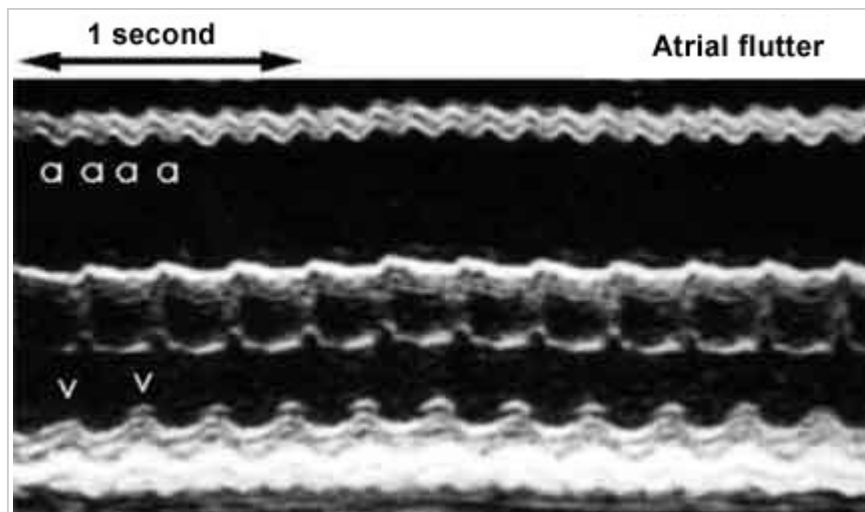
Premature contractions are benign, tend to disappear spontaneously in utero, and only rarely persist after birth. It has been suggested that in some cases there may be progression to tachyarrhythmia, but the risk if any is certainly very small.

CARDIAC DYSRHYTHMIAS: TACHYARRHYTHMIAS

Tachyarrhythmias are classified according to the origin and the number of beats per minute. In the majority of cases the abnormal electrical impulse originates from the atria. Atrial tachyarrhythmia includes supraventricular tachycardia, atrial flutter and atrial fibrillation. Since atrial rhythms greater than 240 bpm are usually associated with varying degrees of atrioventricular block, the ventricular rate is usually reduced to 60 to 160 bpm. Ventricular tachycardia has been occasionally encountered during fetal life. Supraventricular tachycardia is the most common form of tachyarrhythmia, and the ventricular response is 1:1. It is characterized by a heart rate of 200-300 bpm. Supraventricular tachycardia may be due to an autonomous focus, in which case the rhythm is monotonous, or to a re-entry mechanism, in which case sudden conversion from an abnormal to a normal rhythm can be seen. Cardiac malformations are rare.



Atrial flutter is associated with a heart rate 300-400 bpm. The ventricular response is equal to or less than 2:1. Occasionally, atrioventricular block of high degree with ventricular bradycardia are seen. Structural anomalies are more common than in supraventricular tachycardia and include Ebstein's anomaly and pulmonic stenosis.



Atrial fibrillation is characterized by an atrial rate greater than 400 bpm and completely irregular ventricular rhythm, with constant variation of the distance between systole. The atrial contractions are usually too small to be detected by M-mode. A combination of different atrial arrhythmias may coexist in the same fetus.

Ventricular tachycardias are rare, and have typically a ventricular frequency of 200 bpm or less. Associated anomalies include atrial septal defect, atrial septal aneurysm, mitral anomalies, endocardial cushion defect, endocardial fibroelastosis, Ebstein's anomaly, cardiac tumors (rhabdomyoma), anomalies of the conduction system, Coxsackie B infection and cardiomyopathy. Tachycardia is commonly associated with hydrops, as a consequence of low cardiac output.

Diagnosis

The heart rate, atrial and ventricular, can be analyzed by either M-mode sonography of the cardiac chambers or pulsed Doppler evaluation of atrioventricular inflows, hepatic veins and inferior vena cava. A heart rate of about 240 bpm with atrioventricular conduction of 1:1, is pathognomonic of supraventricular tachycardia. An atrial rate greater than 300 bpm with an atrioventricular response of 1:2 or less indicates atrial flutter. A very fast atrial rate with irregular ventricular response is indicative of atrial fibrillation. A ventricular rate in the range of 200 bpm with a normal atrial rate is suggestive of ventricular tachycardia.

Prognosis

Sustained tachycardia is associated with suboptimal ventricular filling and decreased cardiac output. This results in atrial overload and congestive failure. Fetuses with supraventricular tachycardia that occasionally convert to sinus rhythm can tolerate well the condition. Sustained tachycardias of greater than 200 bpm frequently result in fetal

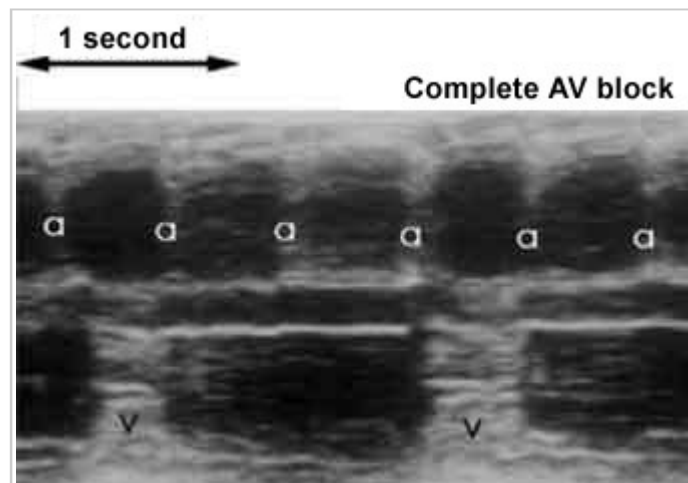
hydrops. The combination of hydrops and dysrhythmia has a poor prognosis (mortality of 80%) independently of the nature of the tachycardia.

Fetal therapy

After 32 weeks of gestation the fetus should be delivered and treated ex utero. Prenatal treatment is the standard of care for premature fetuses that have sustained tachycardias of more than 200 bpm, particularly if there is associated hydrops and/or polyhydramnios. The treatment depends on the type of tachycardia, and the aim is to either decrease the excitability or increase the conduction time to block a re-entrant mechanism. Although a vagal maneuver (such as simple compression of the cord) may sometimes suffice, the administration of antiarrhythmic drugs is often necessary. The drugs used include propranolol, verapamil, procainamide, quinidine, flecainide, amiodarone and adenosine; combination of these drugs is also possible but the optimal approach remains uncertain. These drugs are usually administered to the mother but they can also be given directly to the fetus (intraperitoneally, intramuscularly in the thigh or intravascular through the umbilical cord). The usual response to treatment is conversion to a normal rhythm, followed by shorter episodes of tachycardia that are more interspersed, and finally the presence of extrasystole alone. Fetuses with normal rhythm but persistent hydrops are still at risk of death. The survival rate of fetuses with tachyarrhythmias treated in utero is more than 90%.

CARDIAC DYSRHYTHMIAS: COMPLETE ATRIOVENTRICULAR BLOCK

In complete atrioventricular block, the atria beat at their own rhythm, and none of their impulses is transmitted to the ventricles. The ventricles have a slow rate (40-70 bpm).



In 50% of cases structural anomalies are present (mostly left isomerism and corrected transposition of the great arteries). In the remaining cases, the condition is almost exclusively caused by the presence of maternal autoantibodies anti-Ro (SS-a) or anti-La (SS-B). Most mothers are asymptomatic but in a few cases connective tissue disease is present (lupus erythematosus, scleroderma, rheumatoid arthritis and Sjogren's syndrome). Fetuses with cardiac malformations have heart block starting from the first trimester. Atrioventricular block secondary to maternal autoantibodies develops slowly throughout gestation; a normal cardiac rhythm may be found in the second trimester.

Atrial and ventricular contractions are identified by either M-mode or pulsed Doppler, as previously described. The prognosis depends on the presence of cardiac defects, the ventricular rate and the presence of hydrops; usually, fetuses with a ventricular rate greater than 55 bpm have a normal intrauterine growth and do not develop heart failure. Conversely, hydrops is almost the rule for greater degrees of ventricular bradycardia. Intrauterine treatment by the administration of beta-mimetic agents has been used (with the aim of increasing electric excitability of the myocardial cells and thus ventricular rate), but the results have been disappointing. Maternal administration of steroids (Dexamethasone 8 mg/day) has been advocated for complete heart block secondary to maternal autoantibodies, but the value of this treatment remains, however, unproven. Invasive fetal cardiac pacing has been attempted but thus far there have been no survivors.