16

Anomalies of the right heart

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Introduction

This chapter covers significant lesions of the right side of the heart that can be observed during prenatal life. It summarizes our experience gained from 10 903 fetal ultrasonographic cardiocirculatory assessments performed in our Fetal Cardiology Unit from 1990 to 1999. For each condition, after a brief anatomical description, circulatory pathophysiology, echocardiographic diagnosis, clinical presentation, prognosis and, finally, impact on obstetric and perinatal management are covered. For simplicity and clarity, first-line prenatal ultrasonographic studies will refer to routine screening performed in all pregnant women during the early second trimester to eliminate major malformations; second-line echocardiography will relate to ultrasonographic study focused on the cardiocirculatory system of the fetus, realized in a specialized unit by an expert sonographer.

Pathophysiology common to all prenatal right heart dysfunctions

One of the major implications of the parallel disposition of the two ventricles which characterizes fetal hemodynamics is that the respective output of each ventricle could be different. Actually, during the third trimester of gestation, Doppler investigation has demonstrated that, in the human fetus, the right ventricular stroke volume is 28% greater than the left ventricular stroke volume.[1]

Any significant impairment to forward flow through the right-sided channels, be it at the atrial, ventricular or arterial levels, will cause an increase in the amount of blood crossing the foramen ovale to reach the left-sided cavities. In these circumstances, systemic output can be maintained if the following two conditions are met: adequate size of the foramen ovale, and the absence of left ventricular failure. Normal reference values for foramen ovale dimensions and Doppler velocity pattern throughout human pregnancy have been reported.[2,3] It must be recognized, however, that in the presence of right-sided obstructive lesions, adequate size means that the diameter of the foramen ovale has to be greater than normal values to avoid any restrictive effect. Combined ventricular output will then be predominantly made up of blood coming from the left side of the heart in a proportion dictated by the severity of the right-sided lesion. Flow through the lungs will comprise blood coming from either the right or the left ventricle, depending on the amount of blood ejected by the right ventricle. If this amount is significantly reduced, the ductus arteriosus will channel blood from the aorta towards the pulmonary circulation. Consequently, recording of flow direction through the ductus arteriosus is a reliable means of assessing the degree of severity of all lesions situated on the right side of the heart during prenatal life. Finally, any significant interference with the filling patterns of the right-sided cavities of the fetal heart should alter flow velocity waveforms in the systemic veins.[14]

These various hemodynamic adjustments can have major influences on secondary cardiac morphological development and on the clinical condition, both before and immediately after birth, as well as on the long-term prognosis of the disease.

Anomalies of the inlet

The right atrium

Idiopathic enlargement of the right atrium

This is a rare entity, described predominantly in the adult population. A few cases have been reported in the pediatric literature[5–8] and during prenatal life.[5,9,10]

On anatomic examination, the right atrium appears to be extremely dilated, and the tricuspid valve is normally positioned. Histologically, the right atrial wall shows widespread muscular degeneration and diffuse fibrosis.

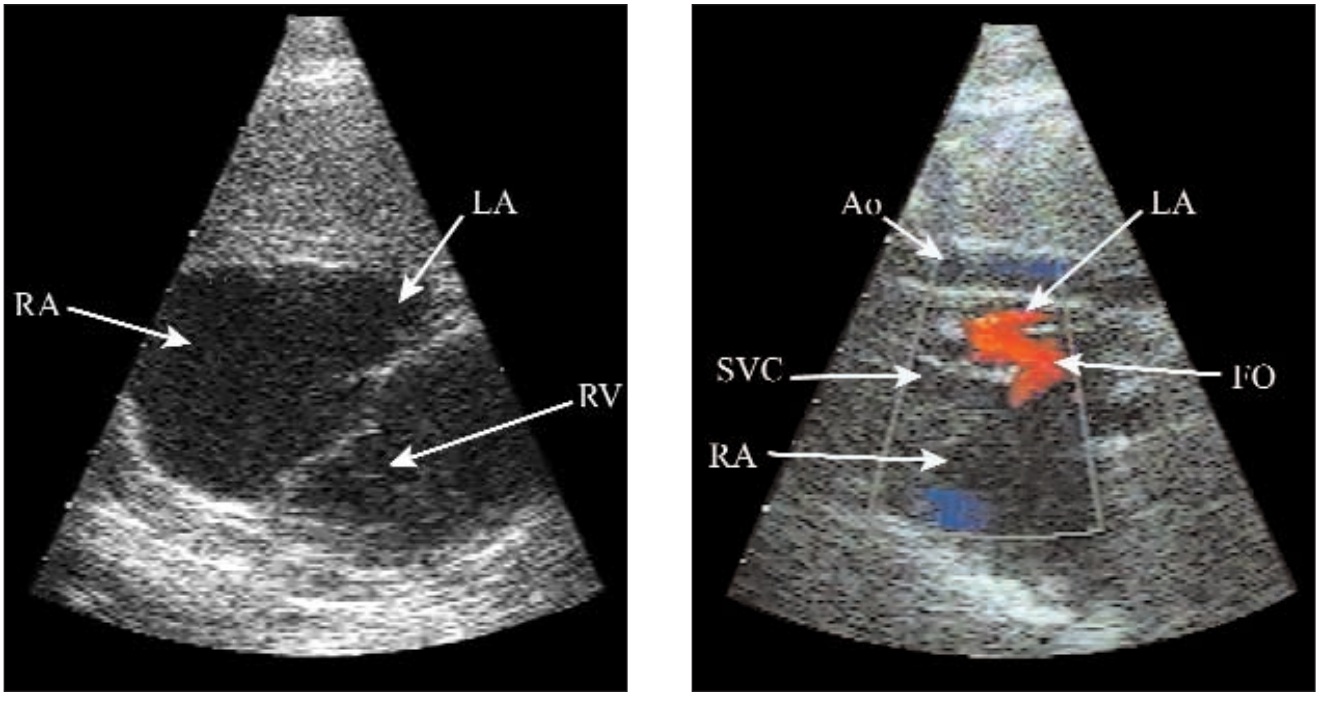

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Figure 16.1
(a) Echocardiographic real-time picture recorded in a fetus with an idiopathic dilatation of the right atrium (RA). This view shows the markedly dilated right atrium and helps to rule out an Ebstein's anomaly on the base of the normal attachment of the tricuspid valve. (b) The same fetus is scanned in a saggital view. The two venae cavae can be seen entering the dilated RA. The color-Doppler investigation confirms that the foramen ovale is not restrictive. (SVC: superior vena cava; Ao: aorta; LA: left atrium; FO: foramen ovale.)

Prenatal ultrasonographic diagnosis is easy, since the enormous right atrium markedly alters the four-chamber view. The second-line sonographer must, however, make sure that no other malformation is present. Various degrees of tricuspid insufficiency have been described, leading to the erroneous diagnosis of Ebstein's anomaly.[9,10] The few fetuses reported with idiopathic right atrial enlargement had no sign of circulatory failure. However, one neonate was seen in cardiac failure related to atrial tachycardia.[5] A search in our prenatal database revealed only one case, identified at 39 weeks of pregnancy, delivered vaginally without problems (Figure 16.1). Postnatal echocardiographic study confirmed the diagnosis. The child is still asymptomatic at age 20 months.

The tricuspid valve

Tricuspid dysplasia

This classification encompasses a wide spectrum of anomalies, from the simple thickening of all three leaflets of the tricuspid valve to loss of mobility related to involvement of the chordae tendineae. Tricuspid dysplasia must be distinguished from Ebstein's anomaly on the basis of the absence of tethering of the leaflets to the posterior ventricular wall and, more frequently, to the septal surface. The dysplasia can be either isolated or, more frequently, associated with other malformations usually causing increased right ventricular pressure. In our database, 17 fetuses have been classified with this diagnosis, and it was an isolated finding in only five cases.

The isolated form of tricuspid dysplasia can be easily overlooked by the first-line sonographer since both the four-chamber view and the relative position of the great arteries will look normal globally. During a detailed echocardiographic study, suspicion of tricuspid dysplasia raised by greater echogenicity of the valve will be confirmed by evidence of significant regurgitation on Doppler interrogation. This Doppler criterion is, however, plagued by its subjectivity, since some tricuspid insufficiency is commonly observed in normal fetuses. With the help of color Doppler investigation, criteria based on the extent of and surface area covered by the regurgitant jet have been proposed in an attempt to

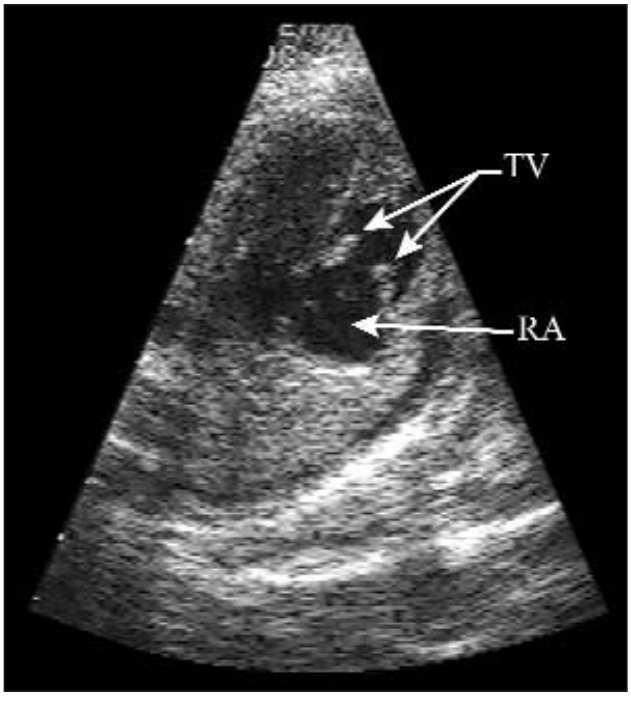


Figure 16.2
Four-chamber view of the heart of a 34 week fetus illustrating the hyperechogenecity of the dysplastic tricuspid valve. This fetus had also a ventricular septal defect (membranous type) and the caryotype revealed a trisomy 21. (TV: tricuspid valve; RA: right atrium.)

overcome this drawback.[11] Somewhat disturbing is the occasional observation of tricuspid valvular dysplasia associated with right ventricular echogenic foci in fetuses with trisomy 21. In a retrospective review of our files, we found 10 such fetuses out of a total number of 21 infants with trisomy 21; six had no cardiac malformation (Figure 16.2). This raises the question of considering tricuspid dysplasia as a minor marker of chromosome abnormalities.

Clinically, isolated tricuspid dysplasia is usually a fortuitous finding in an otherwise normal fetus. Significant tricuspid regurgitation causing right ventricular dilatation and dysfunction has, however, been reported.[12] The prenatal prognosis is also dependent on the associated lesions, the more frequent being stenosis or atresia of the right ventricular outlet.[13] Isolated tricuspid insufficiency carries a good fetal prognosis as long as the foramen ovale is wide enough to accommodate the volume overload caused by the regurgitant flow. In our group of fetuses with isolated tricuspid dysplasia, the anomaly was well tolerated throughout pregnancy in all cases. Vaginal delivery is always possible when the regurgitation is well tolerated. After birth, the evolution is usually uneventful since the postnatal fall in right ventricular afterload causes a rapid decrease in the volume of regurgitation. The situation is completely different in the presence of major associated lesions which will dictate the management and influence the outcome.

Ebstein's anomaly

Although this malformation covers a wide spectrum in terms of presentation and severity, its anatomical characteristics are specific enough to allow reliable prenatal echocardiographic identification. The problem comes from abnormal attachments of the septal and posterior tricuspid valve leaflets. The leaflets are grossly deformed, tethered onto the septal surface and inferior wall, showing some mobility only at their tips. This produces two chambers within the right ventricle: one, the atrialized portion, made up of parts of the ventricular free wall and septum above the functional opening of the tricuspid valve; the other formed by the infundibulum. A ballooning anterior leaflet guards the outlet of the newly-formed atrialized portion. Exceptional cases of Ebstein's anomaly can be observed on the left side of the heart in cases of ventricular inversion. One of our 14 cases of Ebstein's disease diagnosed before birth was of this form.

From a hemodynamic point of view, the redundant and relatively fixed tricuspid leaflets are both stenotic and regurgitant, causing marked dilatation of the "new" right atrial cavity. Flow through this dilated chamber is disturbed not only by the regurgitant tricuspid jet but also by the fact that ventricular depolarization causes myocardial contraction on both sides of the functional opening of the tricuspid apparatus. Anterograde flow through the main pulmonary artery will depend on many factors, among which are the severity of the tricuspid insufficiency, the functional capacity of the remaining infundibular portion of the right ventricle and also the possible presence of stenosis at the subpulmonary and/or pulmonary valvular levels. In prenatal life, the permeability of the outflow tract can be difficult to assess with the Doppler technique, since the entire right ventricular ejection fraction could go backward through the leaking tricuspid valve, which offers lower resistance then the pulmonary valve, which opens against pulmonary and systemic resistance. In severe tricuspid insufficiency, the pulmonary circulation will be essentially maintained by retrograde flow coming from the ductus arteriosus, even though the right ventricular outlet could be anatomically permeable. The right-to-left shunt normally observed through the foramen ovale is, therefore, significantly increased. The foramen is usually large and nonrestrictive; combined ventricular output can thus be maintained by an increase in left ventricular stroke volume.

Evidence of a dilated right atrium on the four-chamber view will raise suspicion during first-line sonographic

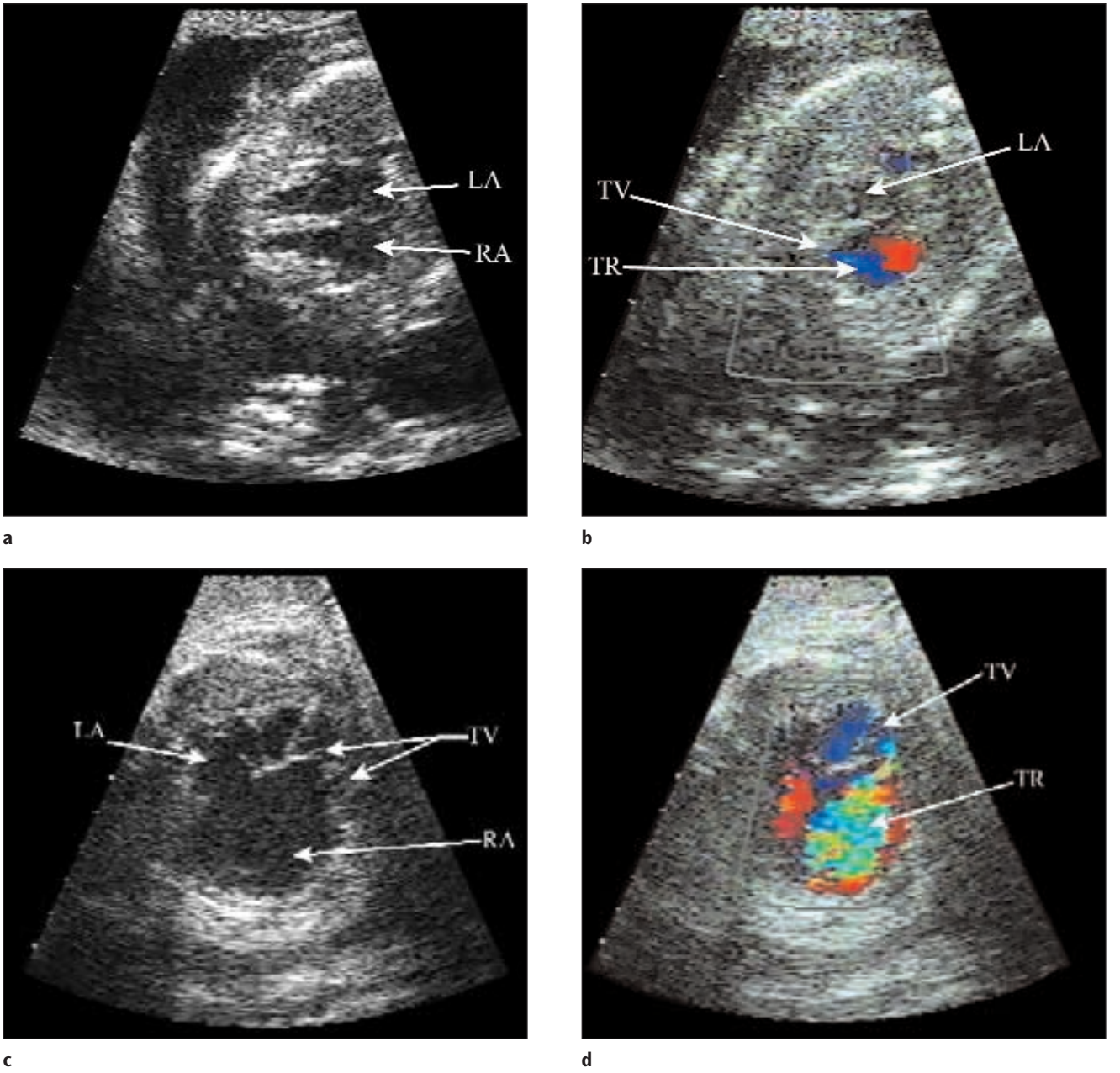


Figure 16.3
Top: *At 19 weeks of gestation*. (a) This four-chamber view shows a slightly dilated right atrium without clear evidence of tethering of the septal leaflets. (b) Color-Doppler investigation disclosed tricuspid insufficiency of moderate severity. Bottom: *Same fetus at 34 weeks of gestation*. (c) The right atrium is markedly dilated; the tricuspid leaflets are dysplastic, abnormal attachments of the redundant anterolateral leaflet are clearly identified. (d) On color-Doppler mode, a severe tricuspid insufficiency is now documented. (LA: left atrium; RA: right atrium; TR: tricuspid regurgitation; TV: tricuspid valve.)

screening. However, in the incomplete form of Ebstein's anomaly, where only the septal leaflets have a lower attachment than usual,[14] the right atrial cavity may appear normal. Furthermore, even in the more complete form, the four-chamber view may not appear suspicious early in the second trimester, since the right atrium may not yet be significantly enlarged (Figure 16.3). It is crucial that the first-line sonographer realize that identification of the malformation early in gestation is essentially based on a four-chamber view, preferably in a vertical position, which includes both atrioventricular valves; lack of mobility associated with abnormal opening of the tricuspid leaflets might be the only clue for diagnosis at this stage of pregnancy (Figure 16.4). The second-line sonographer

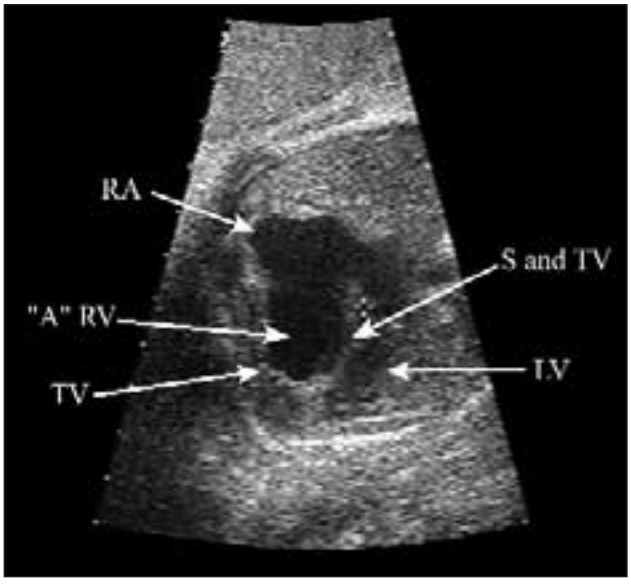


Figure 16.4
Cardiac picture of a 31 week fetus with an Ebstein's anomaly. This vertical four-chamber view allows reliable assessment of 1) the tethering of the septal leaflet (S and TV); 2) the morphology of the anterior leaflet of the tricuspid valve (TV) which is redundant and loosely attached to the ventricular wall; 3) the extent of the atrialized portion of the right ventricle ("A" RV); 4) the degree of dilation of the new atrium formed by the anatomical right atrium (RA) + the atrialized right ventricle.

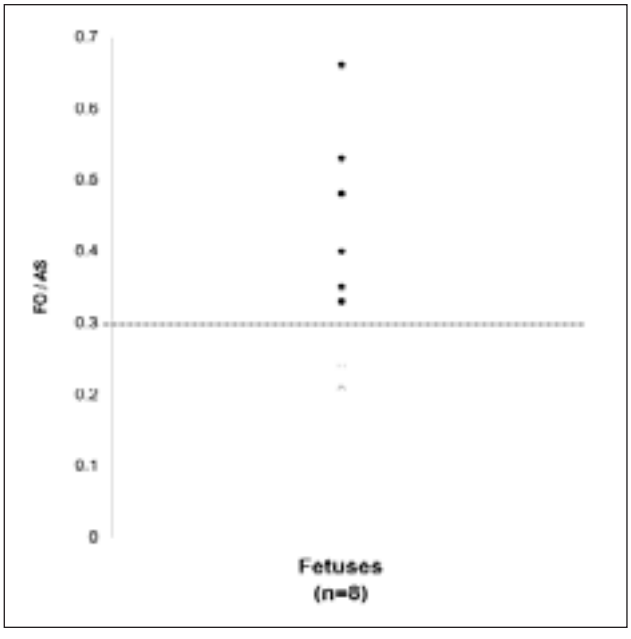


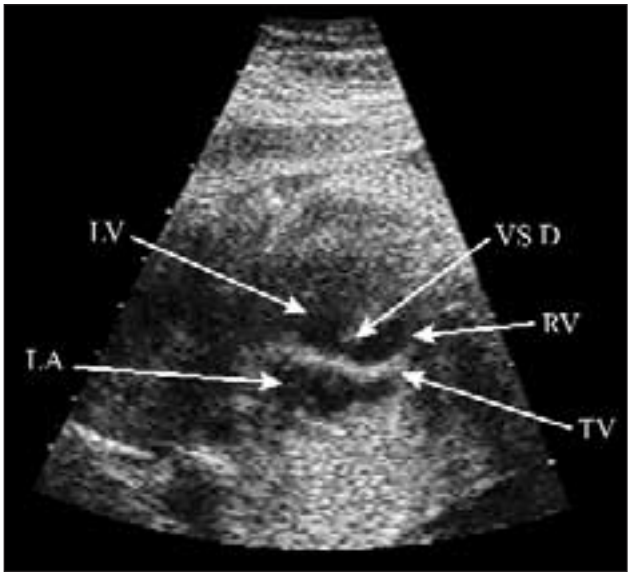
Figure 16.5
Distribution of the ratio, size of the fossa ovale (FO) over length of the interatrial septum (AS) in relation to the outcome of eight fetuses with Ebstein anomaly. All fetuses with a ratio lower than 0.3 developed hydrops fetalis. Adapted from reference 16.

has the responsibility of completing the anatomic and hemodynamic assessments by obtaining the following information, which could have major prenatal and/or postnatal prognostic implications:

1. The ratio of diameters of the functional tricuspid opening over the annulus;
2. The degree of displacement (ratio of the distance from the tricuspid annulus to the apex over the functional opening to the apex);
3. The surfaces of the right atrium + atrialized right ventricle over the functional right ventricle + left atrium + left ventricle;[15]
4. The severity of tricuspid regurgitation;
5. The presence and type of right ventricular outflow tract obstruction better assessed on the short-axis view at the base of the heart;
6. The ratio of fossa ovale diameter over the length of the atrial septum on a horizontal four-chamber view;[16]
7. Left ventricular output;
8. The cardiothoracic ratio;[17]
9. The flow pattern through the main pulmonary artery and the ductus arteriosus (appearance of retrograde systolic and/or diastolic flows);
10. Evidence of atrial or ventricular arrhythmia.

All the measurements of points 1–4 can be obtained from a vertical four-chamber view.

Despite all this information, however, the chance of a given fetus with Ebstein's anomaly reaching term without problems remains difficult to establish. Indeed, the criteria of severity proposed for extrauterine life do not necessarily apply to the parallel disposition of the fetal ventricles. In an effort to designate prognostic criteria specific to fetal life, we retrospectively studied eight fetuses with Ebstein's anomaly.[16] This investigation suggested that the prenatal prognosis could be significantly influenced by the ability of the foramen ovale to decompress the right atrium (Figure 16.5). All six fetuses with a ratio of foramen ovale/septal atrial length greater than 0.3 went on to show normal circulatory function throughout pregnancy. The high risk of fetal death in the presence of a restrictive foramen ovale could explain why the majority of Ebstein's anomalies seen in postnatal life are associated with large interatrial septal defects and a right-to-left shunt.



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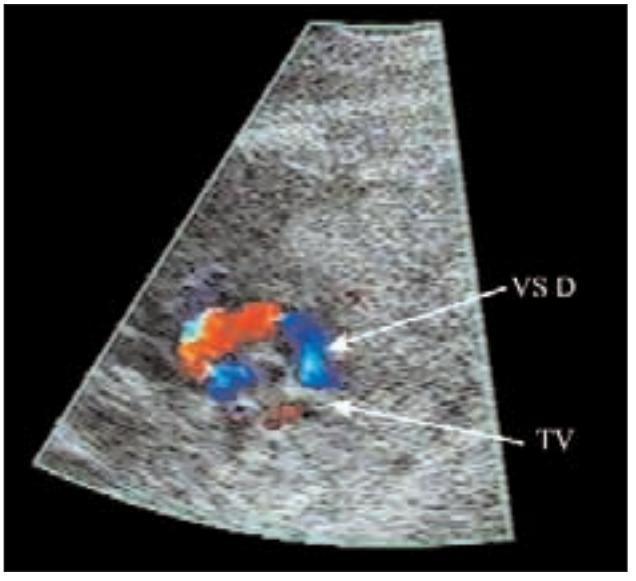

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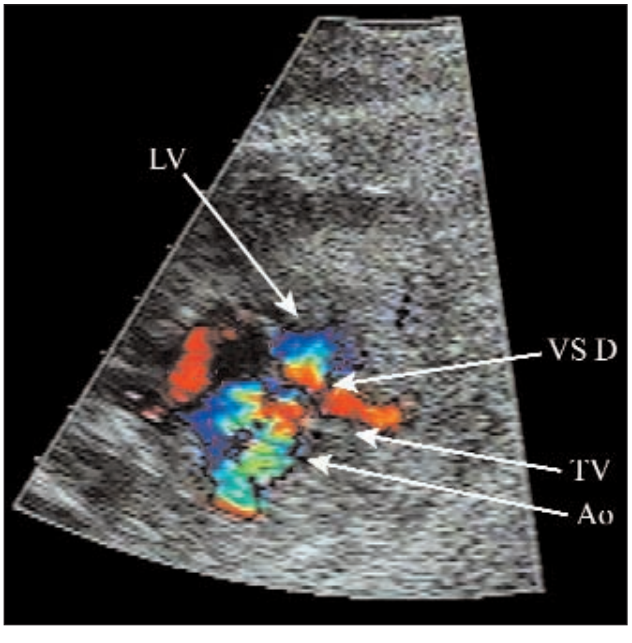

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Figure 16.6
(a) Four-chamber view recorded in a 20 week fetus with a tricuspid atresia, ventricular septal defect and normally related great arteries. The relative hypoplasia of the right ventricle is obvious in this picture. (b) The color-Doppler investigation shows in diastole that blood is entering into the left ventricle through the mitral valve and being shunted into the right ventricle through the ventricular septal defect. (c) During the following systole, blood velocities are seen going towards the aorta from the right ventricle because of the presence of an associated pulmonic stenosis. (LA: left atrium; LV: left ventricle; VSD: ventricular septal defect; RV: right ventricle; TV: tricuspid valve; Ao: aorta.)

Arrhythmia due to extreme dilatation of the right atrium is another factor which, in all likelihood, might be a cause of sudden intrauterine death, even if flow through the foramen ovale is not restricted.

Fetuses with Ebstein's anomaly without cardiac failure or hydrops can usually tolerate vaginal delivery without major problems. The situation is more dramatic in the presence of hydrops fetalis, which usually appears toward the end of the second or the early part of the third trimester. The attending team is then faced with the necessity of performing fetal extraction by Cesarean section which will, in effect, add the risk of prematurity to that of severe circulatory failure in a fetus already endangered by a major cardiac malformation. The risk of postnatal death is thus very high in this group of infants. Irrespective of the condition of the fetus, the major challenge that will influence the immediate postnatal outcome is the need to establish efficient flow through the

lungs. Following this, factors such as the degree of compression of the lungs by the dilated right atrium, the indices of severity of tricuspid impairment based on anatomy and the degree of regurgitation, the permeability of the right ventricular outflow tract and the level of pulmonary vascular resistance will all come into play.

Tricuspid atresia

In postnatal life, tricuspid atresia is associated with great arteries that are either normally related (approximately 80% of cases) or transposed, with or less frequently without a ventricular septal defect.[18] All but one of the 17 fetuses seen in our unit had normally related great arteries. The common feature in all these cases is the relative lack of growth of the right ventricle associated with an enlarged left ventricular cavity. This explains why tricuspid atresia is frequently classified under the hypoplastic right heart syndrome. Right ventricular hypodevelopment is, however, less marked in the presence of a ventricular septal defect; even though it is small, the cavity can then be well identified and the tricuspid valve appears as either an imperforate membrane or fused echogenic leaflets with little or no mobility. Hypodevelopment of either pulmonary artery or aorta will also be observed, depending on which of these arteries arises from the right ventricle.

Fetal survival is based on major hemodynamic adjustments. In cases of isolated tricuspid atresia and normally related great arteries, survival is possible through accommodation of the entire systemic return by the widely patent foramen ovale. Because of the parallel disposition of the two ventricles, this adjustment is compatible with normal peripheral perfusion throughout gestation. A major overload of the left sided cavities is then observed. Secondary dilatation of the aorta associated with variable pulmonary artery hypodevelopment is also part of the classical picture. The pulmonary circulation is provided by retrograde flow through the ductus arteriosus.

In tricuspid atresia with transposition of the great arteries, the widely patent foramen ovale remains an absolute necessity; overload of the left atrial and ventricular cavities remains part of the picture. At the level of the great arteries, however, the pulmonary artery is dilated while the ascending aorta and the aortic arch are relatively hypoplastic, with an increased risk of coarctation of the aorta at birth; in these cases, the aortic arch and its arterial branches going to the head and arms as well as the coronary arteries are perfused by retrograde blood flow from the aortic isthmus and the pulmonary artery.

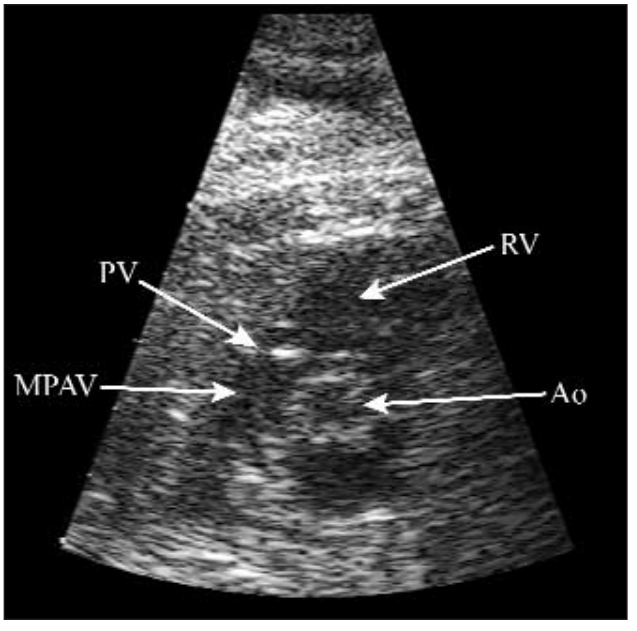
With both normally related and transposed great arteries, the presence of a large ventricular septal defect will cause passage of flow from the left to the right ventricle and some development of the right ventricular cavity. Pulmonary flow could even be normal or slightly decreased, depending on the size of the defect, and the main pulmonary artery or aorta may be within normal limits.

The prenatal diagnosis of tricuspid atresia can be easily suspected during routine obstetric ultrasound examinations. On the four-chamber view, asymmetric development of the two ventricles is obvious (Figure 16.6a). The second-line investigation will confirm the diagnosis, not only by real-time examination of the inlet of the right ventricle showing the absence of tricuspid valve movement, but also by the lack of flow velocities across the tricuspid valve in pulsed and color Doppler investigations. The following additional points must be clarified: the size of the fossa ovale and the mobility of the membrane of the foramen; the size and function of the left ventricle; the integrity of the ventricular septum; the relative position of the main arteries; the sizes of the pulmonary artery and aorta; the size and direction of flow through the ductus arteriosus (Figure 16.6b–d). All these elements should help to establish the prognosis either before birth or immediately after birth. In reviewing our cases, it was surprising to see that all 17 had good left ventricular function and no sign of circulatory failure. The most likely explanation is that cases of tricuspid atresia with a relatively small foramen ovale do not survive beyond the first trimester of gestation.

In the absence of hydrops, vaginal delivery is certainly possible in a fetus with tricuspid atresia. The need, however, for immediate care of the neonate in a tertiary center must be underlined. Arterial oxygen content will be primarily dependent on the respective proportion of pulmonary and systemic venous return that will enter the left ventricle. In the absence of a ventricular septal defect, the survival of these neonates will lie entirely on the patency of the ductus arteriosus, which represents the only source of pulmonary flow. The situation is not quite the same, however, in the presence of a large ventricular septal defect, where forward pulmonary blood flow can be efficiently maintained through the defect; such cases can even develop cardiac failure due to high cardiac output. When tricuspid atresia is associated with transposition of the great arteries, pulmonary flow is normal or increased, and the neonate may not have significant cyanosis; in these cases, however, cardiac failure, the size of the aorta and the possibility of coarctation or arch interruption are all elements of concern.

Anomalies of the outlet: pulmonary stenosis

The presence or absence of a ventricular septal defect profoundly modifies the dynamics of obstructive lesions along the right ventricular outlet.



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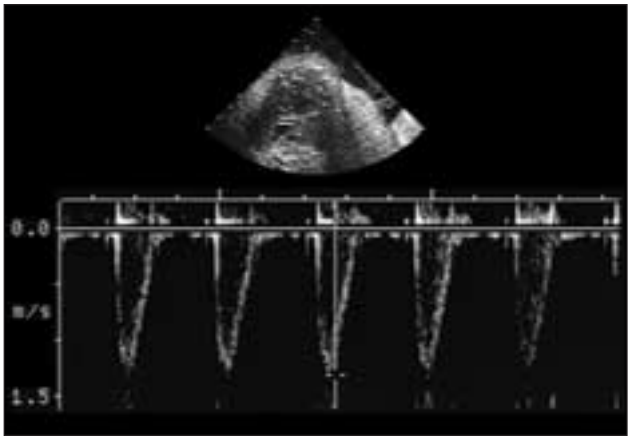

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Figure 16.7
(a) Short axis view at the base of the heart showing the outflow tract of the right ventricle and the pulmonary artery around the aorta. The leaflets of the pulmonary valve are echogenic but the infundibulum and the pulmonary artery are of normal size. (b) The pulsed-Doppler tracing recorded a few millimeters beyond the pulmonary valve reveals a peak velocity of 1.5 m/s which is above the normal limits of 0.8 m/s. After birth, a gradient of 20 mmHg was found through the pulmonary valve. (PV: pulmonary valve; MPA: main pulmonary artery; RV: right ventricle; Ao: aorta.)

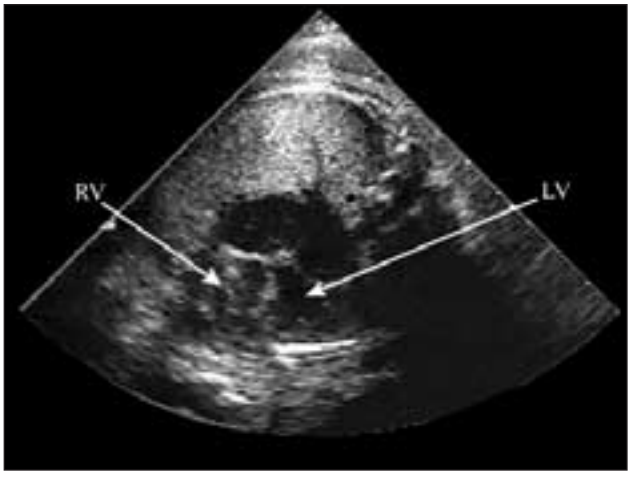
Without a ventricular septal defect

On the basis of morphologic appearance, clinical presentation and prognosis, mild-to-moderate pulmonary stenosis has to be distinguished from critical stenosis or complete atresia of the valve.

In the mild-to-moderate form, the thickness and mobility of the pulmonary valve are variable. The morphology of the right ventricle can be normal. In the moderate form, some right myocardial hypertrophy might be present, particularly at the end of gestation. It is important to remember, however, that in prenatal life, the appearance of myocardial hypertrophy could decrease ventricular diastolic compliance and consequently end-diastolic volume. The extent of this fall in preload will vary according to the gestational age at which the hypertrophy occurs.

Mild-to-moderate pulmonary stenosis can be very difficult to detect on routine obstetric ultrasound because of the relatively minor changes observed in cardiac morphology. The four-chamber view can appear completely normal. Careful examination of the pulmonary valves might, however, disclose abnormal echogenicity of the leaflets. An increase in peak flow velocities through the valve could be the only clue to the diagnosis (Figure 16.7). This is the main reason why second-line sonographers should always perform a Doppler flow velocity investigation through the semilunar valves in all high-risk patients screened for cardiac malformation. The relationship between the increase in peak velocity through the stenotic valve and the severity of the lesion remains linear as long as the diastolic function of the right ventricle is not altered by myocardial hypertrophy.[19] In the presence of moderate-to-severe stenosis, right ventricular filling characteristics change and end-diastolic pressures tend to rise, favoring an increase in the right-to-left shunting through the foramen ovale; at that point, the secondary fall in right ventricular output renders the modified Bernoulli equation based on the peak velocity measurements[20] unreliable for the assessment of the severity of the stenosis. From a total of 40 pulmonary vascular stenoses found in our database, 36 fetuses had a mild-to-moderate form. The relatively low prenatal incidence of this form is, in all likelihood, related to the difficulty in identifying the lesion during routine screening in the second trimester. The second-line sonographer who makes the diagnosis of mild-to-moderate pulmonary stenosis in prenatal life must complete the study and be sure to:

1. Look at the integrity of the septal wall, both on the five-chamber and on the short-axis views at the base of the heart to eliminate ventricular septal defects;



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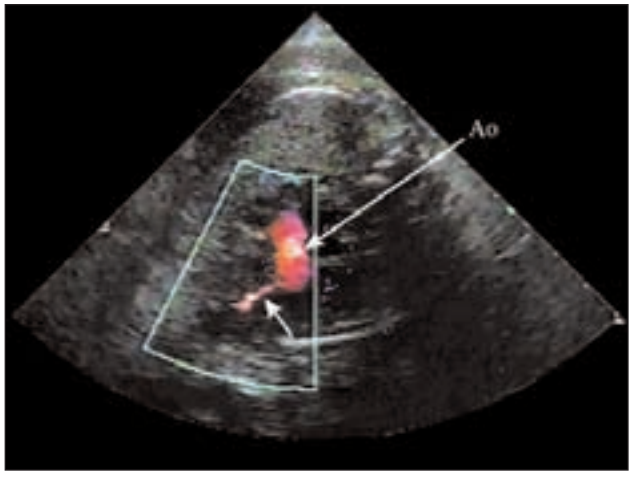

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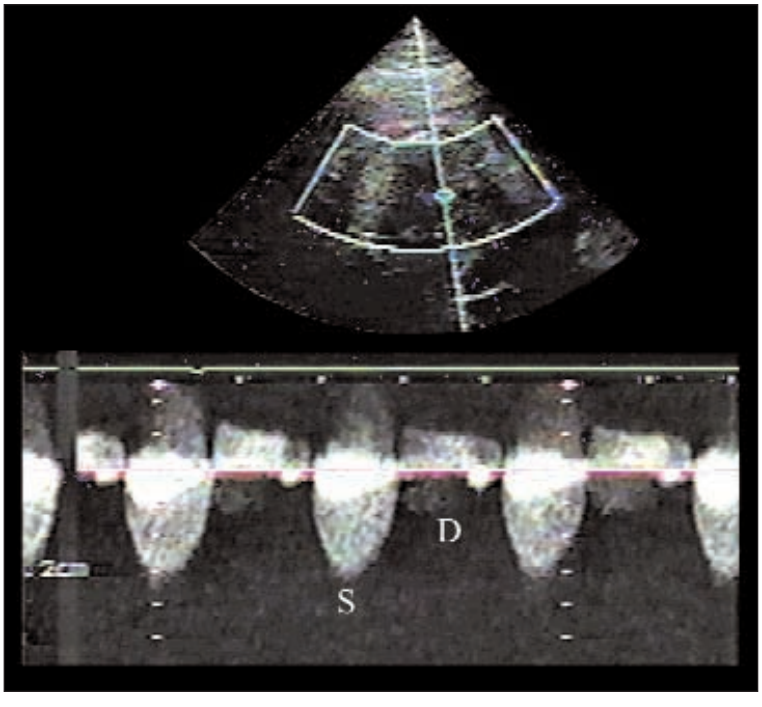

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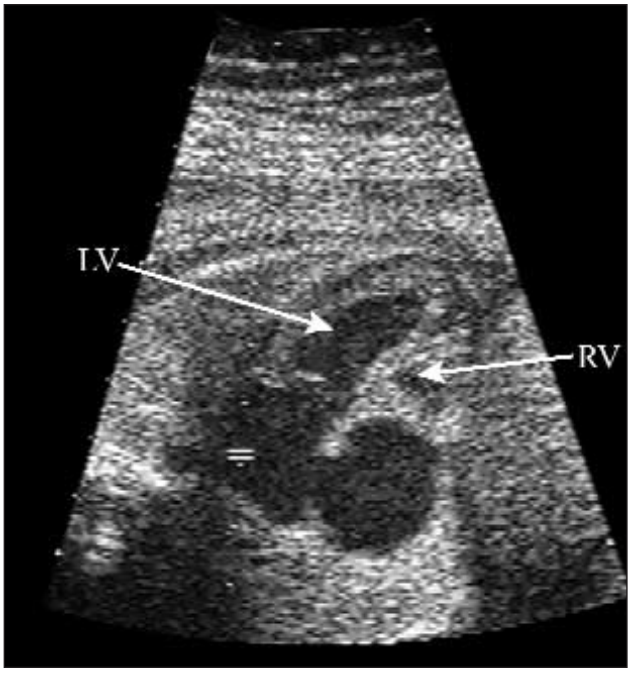
Figure 16.8
(a) Bidimensional real-time picture of the four-chamber view in a 20 week fetus with pulmonary atresia and intact ventricular septum. An hypoplastic and trabeculated right ventricle (RV) is seen with very thickened free walls. The left-sided cavities are dilated. (LV: left ventricle.) (b) In the same fetus, a color-Doppler interrogation recorded in systole reveals a dilated branch of the coronary artery (arrow) which is draining blood from the right ventricular cavity towards the aorta (Ao) suggesting the persistance of sinusoïds within the myocardium. (c) A pulsed-Doppler recording of flow velocities within the same dilated coronary artery seen in B (but with the cardiac apex pointing towards the top of the picture) shows that in systole (S) the blood is circulating from the myocardium towards the aorta at the peak velocity of 3 m/s (gradient of 43 mm between right ventricle and aorta); in diastole (D), a reverse flow is noted from aorta towards the right ventricle.

2. Investigate the tricuspid valve to rule out tricuspid regurgitation;
3. Record flow through the ductus arteriosus to see whether it is retrograde or fully anterograde;
4. Measure the ratio of the size of left to right ventricular end-diastolic diameters as well as the mitral and tricuspid annuli;
5. Measure the size of the pulmonary valve annulus.

The prenatal prognosis of mild-to-moderate cases of valvular pulmonary stenosis is excellent. A progressive increase in severity of the stenosis is rare, and an elevation of the observed gradient could well be related to the physiological rise in flow through the right side of the heart. Delivery in these cases can be achieved by the vaginal route. Usually, the neonate does not require any specific postnatal care.

In critical stenosis or complete atresia of the pulmonary valve, the anatomy of the lesions varies according to the status of the tricuspid valve.[21] In the absence of tricuspid insufficiency, the right ventricle is markedly hypertrophied. The cavity itself is small and almost virtual. On



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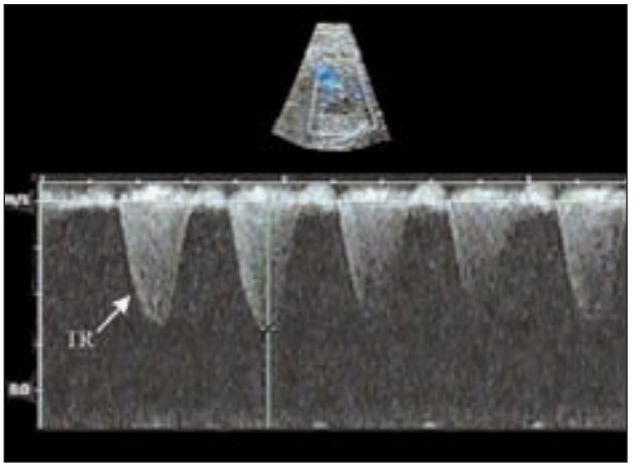

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Figure 16.9
(a) Real-time picture of the heart of a fetus with pulmonary valvular atresia and severe tricuspid regurgitation. In this view, the right ventricle (RV) appears trabeculated but relatively well developed and the diameter of the tricuspid annulus is only slightly smaller than that of the mitral valve. (LV: left ventricle.) (b) Recording of the pulsed-Doppler in the right atrium showing a marked tricuspid regurgitation (TR) with a peak velocity of 5.8 m/sec.

histology, muscle cell disorganization has been described.[22] Major anomalies are also present in the coronary arteries, characterized by abnormal origin and distribution, the absence of proximal aorto-coronary connections, coronary stenosis or interruption.[23] Sinusoids are sometimes present, connecting the ventricular cavity with the coronary circulation (Figure 16.8). A recent experimental investigation showed that, with an increase in pressure within the right ventricular cavity of fetal lambs, marked accumulation of free oxygen radicals was found within the myocardium.[24] A link between these findings and the histopathologic anomalies seen in pulmonary atresia with an intact ventricular septum is a possibility which is now speculative. By contrast, in pulmonary atresia associated with significant tricuspid regurgitation, the blood flowing back and forth through the incompetent valve causes some growth of the ventricular cavity and prevents an increase in ventricular pressure above the systemic level. In these cases, the myocardium appears less hypertrophied and has almost normal organization of myocytes. Sinusoids are usually absent (Figure 16.9).

In both cases, the diagnosis can be made quite easily at the first-line routine screening. The four-chamber view is abnormal and shows variable degrees of right ventricular hypoplasia. In addition, the increase in right-to-left shunting to the foramen ovale is responsible for enlargement of the left-sided cavities.

The cardiologist assessing a fetus with critical pulmonary stenosis and intact ventricular septum must: study the tricuspid valve morphology and rule out significant leaks; in the presence of tricuspid regurgitation, evaluate the severity of insufficiency to establish the type of pulmonary atresia; carefully examine the right ventricular myocardium, using the color Doppler mode, looking for sinusoids (Figure 16.8); determine the orientation of flow through the ductus arteriosus as an important element of diagnosis, since retrograde flow should be expected; measure the diameter of the pulmonary valve annulus compared to that of the aorta; the size of the main pulmonary artery should also be assessed. This evaluation will influence postnatal management inasmuch as it will help establish the indication of perforation followed by dilatation of the valve in the cardiac catheterization laboratory (Figure 16.9). Furthermore, the cardiologist must evaluate the size and function of the left ventricle as well as the size of and flow through the foramen ovale. The intrauterine prognosis of critical stenosis or complete atresia of the pulmonary valve depends on both the size of the foramen ovale and left ventricular function.

The ten fetuses seen in our unit with pulmonary atresia or critical pulmonary stenosis were all in good clinical condition, suggesting that they represented survivors from a wider spectrum from which fetuses

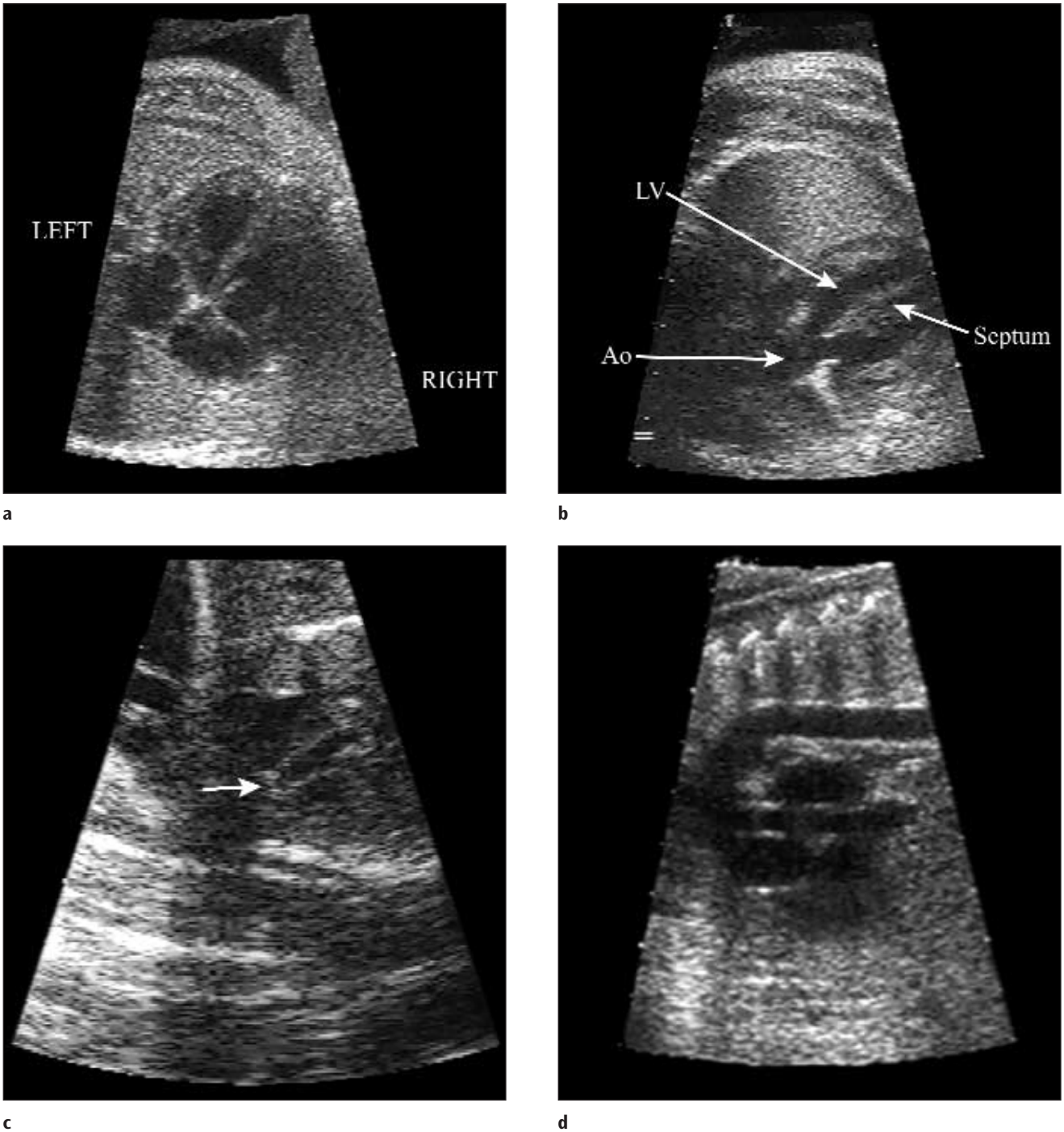

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Figure 16.10
These images were obtained from a fetus with the classical form of tetralogy of Fallot. (a) This four-chamber view taken posteriorly at the level of the A-V valves could be described as normal. (b) On the five-chamber view, the sub-aortic ventricular septal defect is clearly observed as well as the dilated ascending aorta (Ao) and the septo-aortic discontinuity. (LV: left ventricle.) (c) A truncus arteriosus is ruled out and the diagnosis of tetralogy of Fallot established by the identification of a small pulmonary valve annulus (arrow) connected to the right ventricle, associated with pulmonary artery hypoplasia. (d) Saggital view of the same fetus showing the aortic arch which is dilated. The reduction in diameter usually observed at the level of the isthmus is not present.

with a restrictive foramen ovale were eliminated, owing to intrauterine death early in gestation. The mode of delivery is decided on, according to the functional condition of the left ventricle. Usually, vaginal delivery is possible. Any sign of left ventricular dysfunction, such as shortening fraction lower than 25%, evidence of progressive flow restriction through the foramen ovale, or fluid accumulation in either the pleural or the peritoneal cavities should be an indication for Cesarean section.

During the immediate postnatal period, pulmonary atresia with an intact septum represents a typical example where arterial oxygenation is entirely dependent on patency of the ductus arteriosus. Urgent initial treatment is, therefore, the intravenous administration of prostaglandin. Subsequent management of the neonate will be based on echocardiographic evidence of a right ventricular cavity with sufficient functional ability to warrant balloon dilatation of the valve (Figure 16.9). The presence of sinusoids establishing wide communication between the ventricular cavity and the coronary circulation is an absolute contraindication to any attempt at opening the right ventricular outlet; in these cases, surgical palliation will have to be considered. Significant coronary artery stenosis is another factor that will influence survival.

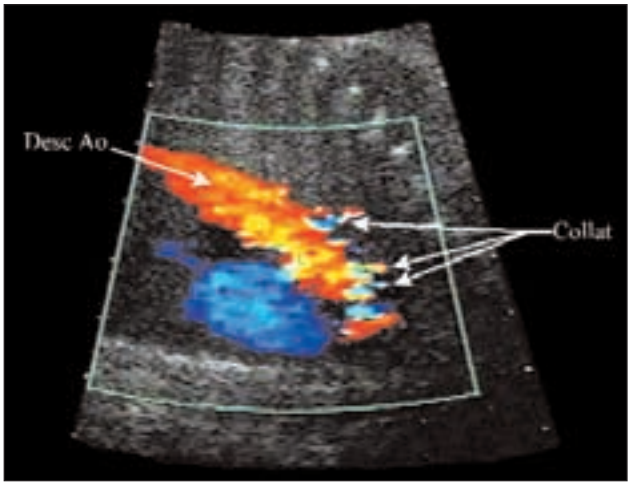

Figure 16.11
The Doppler-color investigation of this fetus with tetralogy of Fallot and pulmonary atresia, discloses the presence of aorto-pulmonary collaterals (collat) originating from the thoracic descending aorta (desc Ao).

With ventricular septal defect

Classical tetralogy of Fallot This malformation is a consequence of anterior displacement of the infundibular septum, causing narrowing of the right ventricular outlet chamber. The ventricular septal defect is large, because of the malalignment of the infundibular septum. The aorta is dilated. The sizes of the pulmonary annulus and artery vary according to the severity of the stenosis. Characteristically, they are always smaller than the aortic annulus and ascending aorta.

Tetralogy of Fallot can be easily missed during first-line sonographic screening unless adequate sonographic views are recorded. If the four-chamber view is obtained posteriorly, at the level of the atrioventricular valves, the septum will look perfectly intact and the view will be described as normal (Figure 16.10a). The relative position of the great arteries will, of course, be normal. Prenatal diagnosis of tetralogy of Fallot is established on the five-chamber view where the aorta appears dilated, overriding the septum (Figure 16.10b). In this view, the ventricular septal defect is usually obvious. When the diagnosis of tetralogy of Fallot is confirmed, the second-line sonographer must specify the following criteria of severity; first, the ratio of pulmonary/aortic annulus diameters; second, the degree of right ventricular outflow tract obstruction. Doppler investigation is unreliable for this purpose, since the amount of blood that flows through the infundibulum is inversely related to the severity of the stenosis; this is due to the presence of the ventricular septal defect, which allows decompression of the right ventricle towards the aorta. Only visual assessment is therefore possible, preferably on the short-axis view at the base of the heart (Figure 16.10c). Third, the pattern of flow through the ductus arteriosus is assessed. This should be one of the best criteria for severity assessment: reverse flow will be observed through the ductus arteriosus if right ventricular output is not sufficient to maintain normal flow through the lungs.

The clinical condition of fetuses with tetralogy of Fallot is usually good. Combined cardiac output remains within normal limits. The only change will be the significant increase of the portion of combined output that comes from the ascending aorta compared to that from the pulmonary artery. Consequently, the aortic arch and isthmus are well developed and coarctation of the aorta is, for all practical purposes, never described in association with tetralogy of Fallot (Figure 16.10d). All of our 39 patients with this classical form of tetralogy of Fallot had no sign of circulatory failure. This good fetal hemodynamic picture can, however, be darkened by the relatively high incidence of chromosomal and extracardiac anomalies in this group.[25] Microdeletion of chromosome 22 may be found in up to 20% of infants with tetralogy of Fallot.[26] There is, however, no indication, in isolated tetralogy of Fallot, for extraction by Cesarean section. The immediate postnatal condition and management will be influenced by the severity of the stenosis and associated

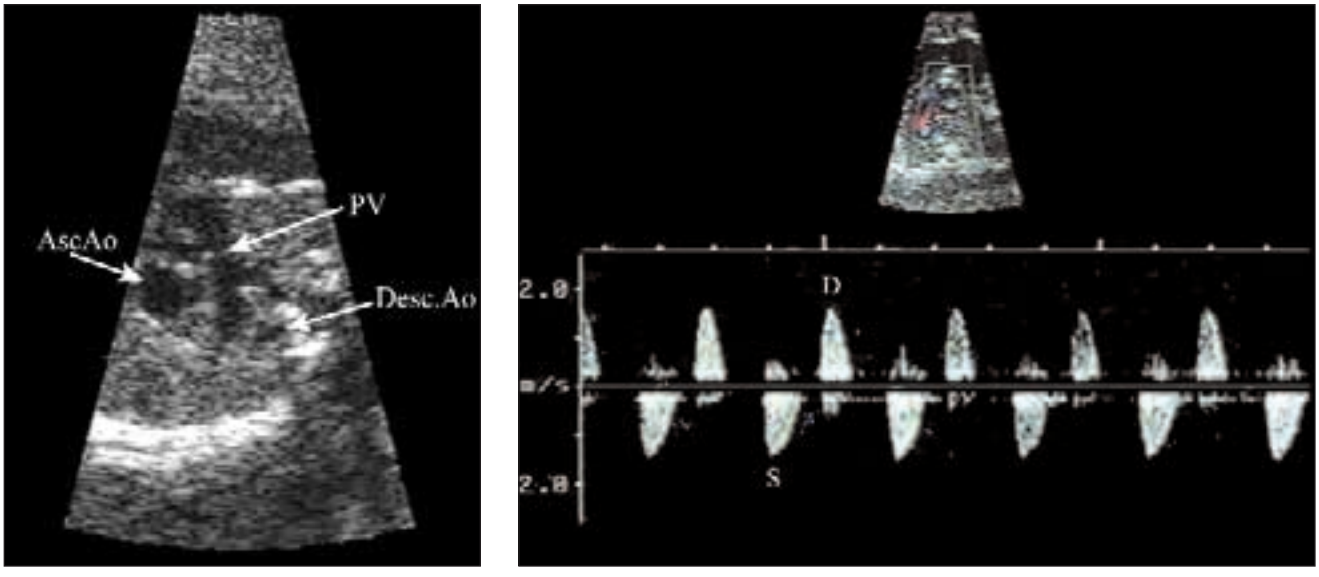

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Figure 16.12
Ultrasonographic pictures taken from a fetus with tetralogy of Fallot with rudimentary pulmonary valve. (a) Short axis view at the basis of the heart showing the pulmonary valve (PV) which is echogenic and dysplastic; the ascending aorta (Asc. Ao) is dilated; the main pulmonary artery and both branches are well visualized. Note the absence of a ductus arteriosus between the pulmonary artery and descending aorta (Desc. Ao). (b) Pulsed-Doppler recording in the main pulmonary artery above the valve illustrating the systolic anterograde (S) and diastolic retrograde (D) velocities.

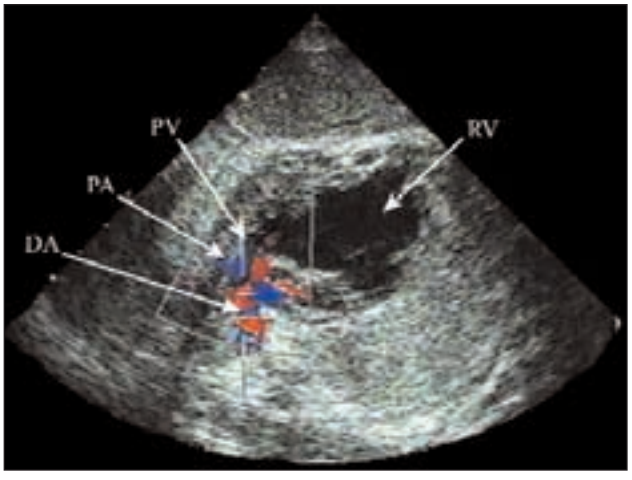
extracardiac anomalies. Cases with decreased or diastolic retrograde flow through the ductus arteriosus in prenatal life can be expected to require specialized care immediately after birth to maintain the patency of the ductus. Ideally, all fetuses with tetralogy of Fallot should be delivered in a tertiary center; even in less severe cases, close monitoring of the clinical condition is justified after normal closure of the ductus arteriosus.

Tetralogy of Fallot with pulmonary valve atresia This is considered an extreme form of the disease characterized by complete obstruction of the right ventricular outlet. In this condition, the main pulmonary artery is small or sometimes absent. Perfusion of the lungs comes from the ductus arteriosus, which appears tortuous, and from aortopulmonary collaterals. This form of tetralogy of Fallot is less frequent; we identified four such cases in our files.

Prenatal ultrasonographic diagnosis is based first on an abnormal five-chamber view showing the very dilated aorta overriding the septum with a large ventricular septal defect. This picture is sometimes misinterpreted as being that of a truncus arteriosus. The latter diagnosis is ruled out by identification of the blind outlet of the right ventricle followed by a small pulmonary artery. In cases of truncus arteriosus, the pulmonary artery arises directly from the trunk. The second element of diagnosis of tetralogy of Fallot with pulmonary atresia is the presence of aortopulmonary collaterals, which can be seen in prenatal ultrasonographic study coming from the thoracic descending aorta (Figure 16.11).

The cardiocirculatory condition of these fetuses is usually good, for the same reasons given for the classical form of tetralogy of Fallot. These fetuses are usually able to support vaginal delivery. They must, however, undergo cardiocirculatory evaluation immediately after birth to assess the efficacy of the collaterals and of the ductus arteriosus in maintaining adequate pulmonary blood flow and sufficient oxygenation of arterial blood.

Tetralogy of Fallot with an absent or dysplastic pulmonary valve This entity, although rare, needs to be identified during prenatal screening. Its anatomic features are: large ventricular septal defect with an overriding aorta, aneurysmal dilatation of the pulmonary trunk, appearance of the dysplastic or rudimentary pulmonary valve, absence of the ductus arteriosus and, finally, right ventricular dilatation, which is frequently observed, unlike the classical form of tetralogy of Fallot. Studies of rat fetuses with tetralogy of Fallot and absence of the pulmonary valve created by maternal administration of bis-diamine led to the conclusion that neural crest cells are important in formation of the pulmonary valve and that enlargement of the pulmonary arteries and bronchial compression develop in fetal life.[27]



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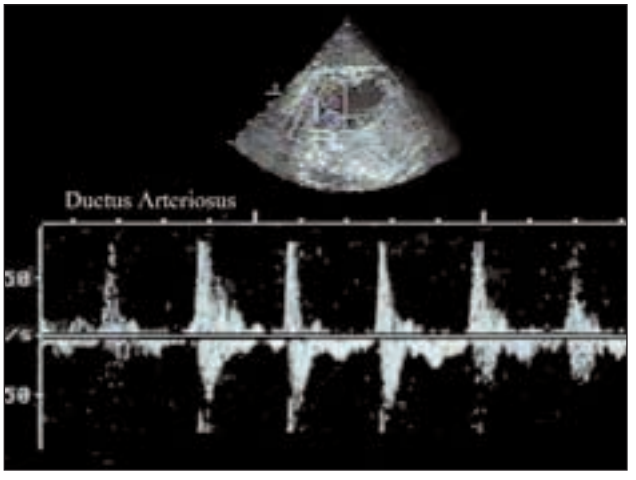

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Figure 16.13
Images of a fetus with Uhl's anomaly. (a) The Short axis view reveals the marked dilatation of the right ventricle (RV) and the thinness of the myocardium. With color-Doppler interrogation, it is possible to observe some anterograde flow (blue color) through the pulmonary artery (PA); retrograde flow (red color) coming from the ductus arteriosus is however also documented. (b) Pulsed Doppler flow velocity recording in the ductus arteriosus shows reverse flow early in systole (above the zero-velocity line) followed by the normal anterograde flow in end-systole and during diastole. This pattern is compatible with a late right ventricular contraction (right bundle branch block).

Ultrasonographic diagnosis of this form of tetralogy of Fallot is easier than in the classical form.[28] During routine ultrasonographic screening, suspicion is raised by dilatation of the right ventricular cavity on the four-chamber view. Here again, the diagnosis is confirmed on the five-chamber view. Close examination of the right ventricular outflow tract will show the dilated pulmonary artery with abnormal or absent pulmonary valves. Doppler investigation of the dilated pulmonary artery will disclose systolic antegrade and diastolic retrograde flows caused by severe pulmonary insufficiency (Figure 16.12). In the lungs, the dilated peripheral pulmonary artery can be clearly seen with color Doppler interrogation. Careful investigation with both real-time and color Doppler echocardiography will confirm the absence of the ductus arteriosus in the majority of cases.

The intrauterine prognosis of tetralogy of Fallot with absent pulmonary valves is uncertain. The two cases from our database showed no sign of cardiocirculatory failure throughout pregnancy. There are, however, reported cases of fetuses that developed polyhydramnios[29] and/or hydrops fetalis.[30] Tracheobronchial and esophageal compression by the dilated pulmonary artery is considered to be the etiology of the polyhydramnios. On the other hand, the to-and-fro movement of blood between the right ventricle and the dilated pulmonary artery may result in elevated right ventricular end-diastolic pressure, leading to a possible increase in venous systemic pressure and hydrops fetalis. Major respiratory problems occur after birth, owing to the associated abnormal development of bronchi which, in addition, are frequently compressed by the markedly dilated pulmonary artery.

Anomalies at the myocardial level

Primary anomalies

Uhl's anomaly

This myocardial impairment specifically involving the right ventricle has been rarely described in prenatal life. It is essentially characterized by the lack of development of myocytes.[31] On macroscopic examination, the right ventricular free wall appears thin and translucid. On microscopic studies, only the pericardial and endocardial layers are present with some adipose tissue and a few myocytes. The right ventricular cavity is markedly enlarged and hypotonic.

Echocardiographic diagnosis is relatively easy. On first-line screening examination, the four-chamber view will be abnormal. Suspicion of the specific diagnosis will be based on thinness of the right ventricular free wall with the

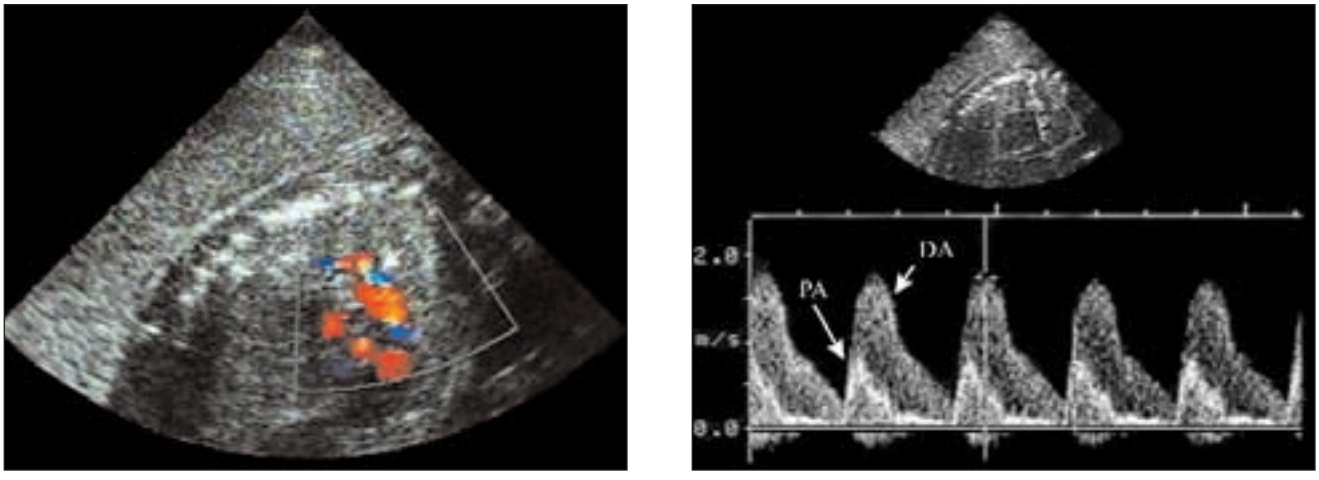

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Figure 16.14
(a) Doppler color flow imaging of the ductus arteriosus of a fetus on indomethacin for polyhydramnios. Note the hour-glass appearance of the ductus arteriousus. (b) In this tracing taken in the same fetus, the pulsed-Doppler sample volume encompasses both the pulmonary artery (PA) and the ductus arteriosus (DA). The flow velocity waveforms of the two arterial segments are superimposed and reveal a significant increase in peak velocities through the ductus, both in systole and diastole.

absence of any apparent contraction (Figure 16.13a). Despite this major myocardial impairment and systemic pressure in the fetal pulmonary circulation, anterograde flow through the pulmonary valve was documented in our two cases (Figure 16.13b). Another hemodynamic problem is related to frequently associated tricuspid insufficiency. To establish the postnatal prognosis, the second-line sonographer will have to assess flow through the main pulmonary artery as well as the size and function of the left ventricle. A decision concerning the type of delivery will be based on the clinical condition of the fetus. Those fetuses which are able to reach term without evidence of circulatory failure should, in theory, be able to tolerate vaginal delivery. After birth, assessment of the capability of the right ventricle to maintain pulmonary flow is mandatory. Short- and long-term prognosis is reserved. One of our two cases died suddenly at home at the age of 14 months presumably from arrhythmia. It is not known whether adult patients reported with this disease had the full pathological picture since birth.[31] Morbidity and mortality later in life are frequently related to major ventricular arrhythmia and this anomaly is alternatively named ventricular dysplasia or arrhythmic right ventricle.

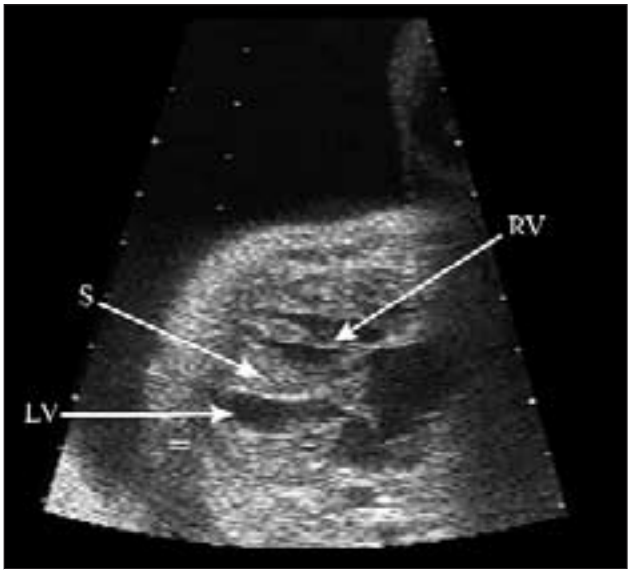
Secondary anomalies

Some fetal conditions can cause secondary myocardial changes that predominantly involve the right ventricle. These conditions deserve mention, as they are not infrequent.

Restrictive ductus arteriosus

During prenatal life, the normal pulmonary arch is made up of the main pulmonary artery and the ductus arteriosus. The ductal segment can be absent in certain types of malformation, as mentioned in the section on tetralogy of Fallot. More frequently, it can become restrictive after maternal administration of prostaglandin synthetase inhibitors, such as indomethacin, used for suppression of premature labor or for reduction of polyhydramnios. A similar effect on the ductus arteriosus has been reported with the administration of betamethasone,[32] a glucocorticoid frequently given for fetal lung maturity induction. Any decrease in the diameter of the ductus will cause a gradient between the main pulmonary artery and the aorta; suprasystemic pressure will then be present not only in the pulmonary circulation but also in the right ventricle. Progressive right ventricular hypertrophy associated with tricuspid regurgitation is then observed.

Ultrasonographic diagnosis of restrictive ductus arteriosus is based on both two-dimensional imaging and the Doppler flow velocity signal through the ductus. The real-time picture frequently shows an hourglass appearance of the ductus (Figure 16.14a). With the Doppler technique, increases in peak systolic velocities of



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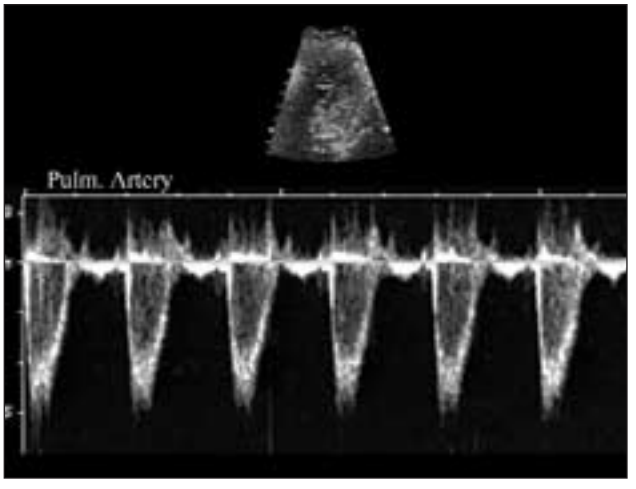

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Figure 16.15
(a) Four-chamber view of the heart of the recipient twin in the context of a twin-to-twin transfusion syndrome. Note the thickening of the septum and the free walls of the ventricle. (S: septum; RV: right ventricle; LV: left ventricle.) (b) Pulsed-Doppler taken above the pulmonary valve of the same recipient twin showing an increase in peak velocity of 1.5 m/s.

> 140 cm/s, diastolic velocities of > 35 cm/s and a pulsatility index ((systolic velocity – diastolic velocity)/mean velocity) of < 1.9 have been proposed as expressions of ductal constriction.[33] An example of these changes is shown in Figure 16.14b.

These fetuses must be identified quickly, since cardiocirculatory failure has been described in this condition.[34] The prognosis, however, is good as long as the medication is discontinued; disappearance of Doppler evidence of ductal constriction is usually observed within 24–48 hours after the arrest of medication.

The twin–twin transfusion syndrome

This syndrome is observed in monochorionic twins and is characterized by arteriovenous connections within the placenta, causing passage of blood from one fetus (the donor) to the other (the recipient). The recipient twin becomes polycythemic and plethoric. One of the features of this condition is that the myocardium of the recipient twin tends to become thickened and echogenic. Although this myopathy involves both sides of the heart, cases of subpulmonary stenosis have been described.[35] We documented such right ventricular outlet stenosis in one case of twin–twin transfusion (Figures 16.15a,b). Both myopathy and stenosis usually regress after birth, but a few cases have been described where progression of right ventricular outflow tract obstruction was observed.[36]

Diastolic overload of the right ventricle

Overload of the right ventricle can be observed in all conditions affecting fetal left ventricular function because of the parallel disposition of the two ventricles. These conditions, such as hypoplastic left heart syndrome, mitral disease, restrictive foramen ovale or coarctation of the aorta, are discussed in Chapter 29. Some prenatal circulatory anomalies, however, could cause isolated right ventricular diastolic overload while the left heart is normal. At birth, the neonates will show essentially right ventricular hypertrophy on the electrocardiogram. This situation is typically observed in intracranial cerebral arteriovenous fistula. The most frequent form of cerebral fistula is characterized by aneurysmal dilatation of the vein of Galen draining a network of cerebral arteries. The degree of shunting through the fistula is variable but, for obvious reasons, the greater the shunts, the earlier will be the time of appearance of neurologic and cardiocirculatory symptoms. All four cases of aneurysm of the vein of Galen found in our database had massive arteriovenous shunting (Figure 16.16a,b).

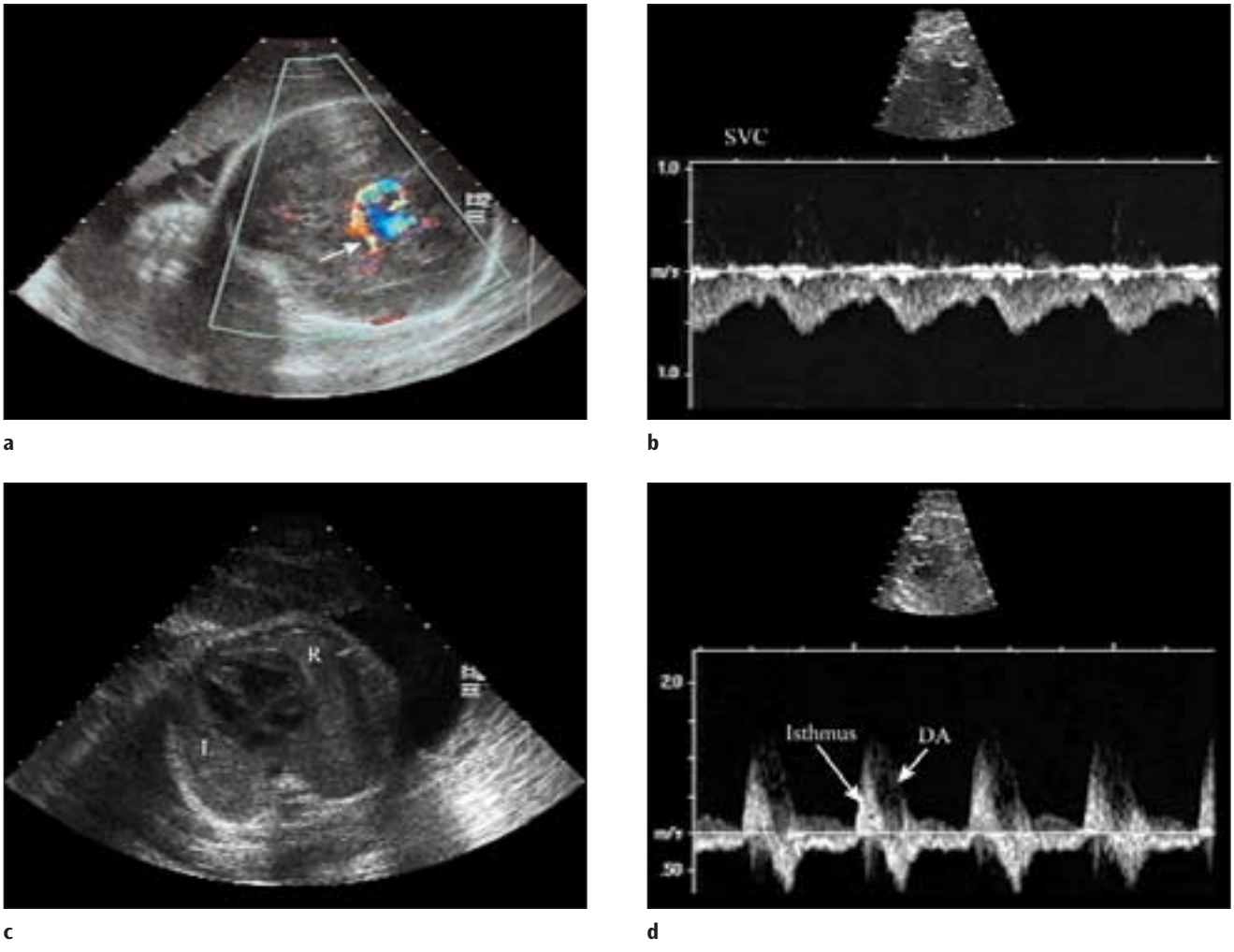

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Figure 16.16
(a) Color-Doppler interrogation in a fetus with aneurysm of the vein of Gallen. Direct connection of an anterior cerebral artery (arrow) into the dilated vein can be seen causing a jet of blood curling around into the aneurysm. (b) Because of the direct arterio-venous connection, the flow velocities through the superior vena cava (SVC) present an arterial pattern with marked forward flow during diastole. (c) In the same fetus, the right sided cavities are mildly dilated (R: right; L: left). (d) Simultaneous recording of Doppler flow velocities in both the aortic isthmus and the ductus arteriosus illustrates the clear preponderance of the right ventricular ejection volume: blood flow is retrograde in the isthmus during the second half of systole and the entire diastole.

The prenatal hemodynamic changes are related to the marked increase in volume of flow drained by the superior vena cava going into right-sided cavities. Besides causing dilatation of the right atrium and ventricle, this volume overload is transmitted to the pulmonary circulation and ductus arteriosus. Retrograde diastolic flow of blood coming from the ductus arteriosus is observed through the aortic isthmus (Figure 16.16c,d).[37]

The prognosis of cerebral arteriovenous fistula diagnosed in prenatal life is somber. In addition to cerebral damage, intrauterine cardiac failure is a frequent complication. A team approach is essential for the management of both fetuses and neonates.

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