THE HEART

Sonologists and sonographers usually do not "do" fetal echocardiography: the anatomy is considered mysterious, anomalies perceived as innumerable, and "cardiac experts" try to close the field to outsiders by obfuscating their explanations with eponyms and esoteric terminology such a "D-loop", "criss-cross heart", "conotruncal", "concordance", "isomerism", "inversion", etc[1]. There is also a common belief that to "understand hearts" one needs an in-depth review of enigmatic embryology. While some of this may be true to a certain degree, not everyone ought to be a cardiac expert, and the basic knowledge required to correctly interpret the vast majority of examinations can be derived from a simple study of the heart. It is the purpose of this chapter to provide as much information as can be incorporated without resorting to arcane theories.

The heart is usually examined by real-time and, in some circumstances, with M-mode or Doppler. We will first describe the normal anatomy in the different planes, and then we will review the sequential approach to the heart, as it is adapted to the examination of the fetus.

THE FETAL CIRCULATION

The fetal circulation differs from the adult circulation in many respects. The adult circulation is a *sequential* circulation. If one could travel on a red blood cell, the journey would pass through the right atrium, right ventricle, pulmonary artery, lungs, pulmonary veins, left atrium, left ventricle, aorta and finally back through the cava. Each location is visited sequentially.
In the fetus the situation is different. Let us first travel on a red blood cell that just returned from the placenta for oxygenation. The journey starts with the umbilical vein, ductus venosus, inferior vena cava, and right atrium. Here is the first change: instead of continuing into the right ventricle, the red blood cell will probably go through the foramen ovale into the left atrium, left ventricle, aorta, brachiocephalic vessels, head or upper limbs, then return by the superior vena cava into the right atrium. The blood flow is thus separated in the right atrium into a right heart flow (essentially deoxygenated blood from the head and upper limbs) and a left heart flow (oxygenated blood from the placenta). This results from streaming of the blood as it enters the right atrium.

| Adult circulation | Fetal circulation |
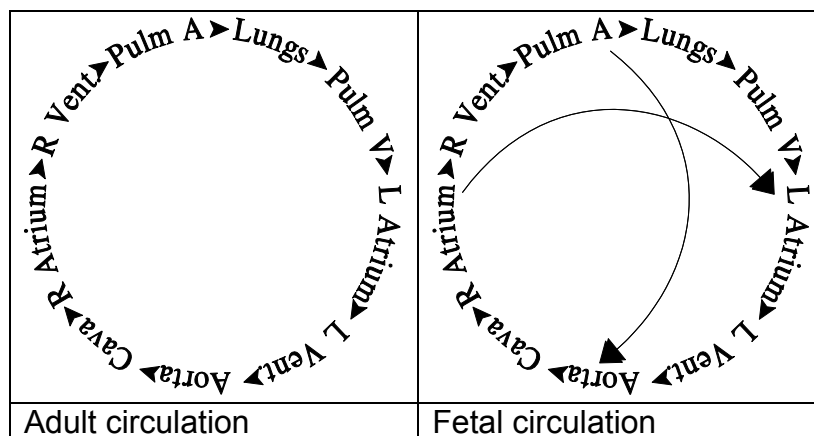
The Eustachian valve (the junctional fold between the inferior vena cava and the right atrium) directs the inferior vena caval flow toward the **foramen ovale** that is very close to the inferior vena cava. The inferior caval flow itself is divided into two components: the oxygenated blood coming from the left hepatic vein (and ductus) and the desaturated blood from the rest of the inferior vena cava. The oxygenated blood enters the foramen ovale, while the desaturated blood goes through the tricuspid valve[2]. The foramen ovale is bordered on its inferior edge by the septum primum that is in the left atrium side and forms the foramen ovale valve. The septum secundum makes the superior border and is on the right atrial side. The foramen ovale opening, thus, is patent for a flow that is oriented from bottom to top and is against the direction of the flow of the superior vena cava that is in the direction of the tricuspid valve. After traveling through the upper part of the body, the red blood cell has lost some of its oxygen and will go on to perfuse the body and get a refill in the placenta.

Coming from the superior vena cava, it will go through the tricuspid valve to the right ventricle and pulmonary artery. Here is another change: instead of going through the lungs it will go through a fetal bypass called the **ductus** and arrive directly into the descending aorta. Since the lungs are not ventilated *in utero*, passing through them would not oxygenate blood, and only about 10% of the pulmonary circulation perfuses the lungs.
Of course the separation of the inferior and superior vena cava flows is not perfect, and there is some mixing of the two circulations. Yet, because of the streaming, the most oxygenated blood perfuses the heart and the brain. The fetal circulation is therefore not a sequential circulation, but a *parallel* circulation with a bifurcation at the right atrium into the left or right heart and a bypass at the ductus arteriosus, skipping the left heart.

Another feature of the fetal circulation is the **ductus venosus**. The ductus venosus allows blood to bypass the hepatic circulation and thus prevent a loss of pressure in the returning circulation. In the lamb only 40-50% of the flow passes through the hepatic sinusoid, the rest passes through the ductus. This explains why the ductus venosus is difficult to image: if most of the flow passed through the ductus, its caliber would be equal to that of the umbilical vein, which it is not. The ductus venosus is believed to regulate the flow to the fetal heart by preventing overload when uterine contractions express blood from the placenta into the fetal circulation. Although the ductus walls contain smooth muscle, the presence of a sphincter is debated. While some authors have found evidence of a sphincter[3], others have not[4].
In fetal anemia, increased liver hematopoiesis is probably responsible for compression of the venous system, which produced the ascites that is observed. In hypoxemic states ("placental insufficiency" for instance) the flow is redistributed so that a constant supply of oxygen is provided to the brain, myocardium and adrenal glands. Blood flow to the lungs decreases progressively, while flow to the gastrointestinal tract, musculoskeletal system and kidneys decreases abruptly[5]. The decreased perfusion of the kidney leads to a decrease in glomerular filtration and production of urine and thus to oligohydramnion.

THE NORMAL CARDIAC ANATOMY

REAL-TIME EXAMINATION

The heart can be observed in infinity of planes, but a few sections are the basis on which most of the diagnoses are made[6]. These planes include:

- the four-chamber view,
- short axis (or axial),
- left and right chambers and
- great vessels views.

Although it is convenient to refer to these standardized views for description purposes, in practice it may be difficult to reproduce these exact sections, and the operator should be familiar with small variations of these planes. It is important to examine the heart with the least number of active focal zones on the transducer. This increases the frame rate, decreases blurring due to averaging of systolic and diastolic frames, permits a better motion analysis and allows a true determination of the fetal heart rate. You can easily verify that when all the focal zones are turned on, the heart rate slows down noticeably, giving a false impression of bradycardia.

FOUR-CHAMBER VIEW

The four-chamber view is obtained by making a section that is practically axial to the fetal chest [7]. The four-chamber view can be obtained either with the long axis of the heart in the axis of the beam or perpendicular to the beam. The orthogonal view is best to study the septum (both interatrial and interventricular). Otherwise the sound waves are reflected at a shallow angle and away from the transducer. This creates the appearance of a septal defect. This section is now part of the routine (Level I) examination and detects roughly one-third of the cardiac anomalies[8],[9]. The important landmarks to identify are:
- The spine,
- The transverse descending aorta,
- The interatrial septum,
- The left and rigth atrium,
- The interventricular septum,
- The right and left ventricle and
- The two atrioventricular valves (tricuspid and mitral valve)

It is important to begin the analysis of the four-chamber view by localizing the spine and the transverse descending aorta, which is a circle laying anterior to the spine. Usually in a normal fetus the descending aorta is in the left side and points to the left atrium. To make sure this atrium is really the anatomically left, we have to look for the foramen ovale valve, which is

inside the left atrium always and has a funny movement that makes it easy to recognize (see further down). The atria and the ventricles should have equal size and thickeness. The atrioventricular valves should have the same size and this is easy to analyse in real time image. The valve ring is better visualized during diastole and the leaflets during sistole. The thickness of the interventricular septum and of the free ventricular walls is the same. Notice that the heart is not midline but shifted to the left side of the chest. The axis of the interventricular septum is about 45º to 20º to the left of the anteroposterior axis of the fetus[9]. Because of the left-sided position of the heart the right ventricle is anterior and closest to the anterior chest wall, while the left atrium is the most posterior chamber and closest to the spine. These relations are not true in congenital malformations, as we will see later, but, for now, are convenient simplifications.

Other important landmarks should be recognized. In the right atrium, two thin lines distinct from the interatrial septum can occasionally be seen. The *Eustachian valve*, a crest between the inferior vena cava and the wall of the right atrium, is located close to the inferior vena cava. The *Chiari network* is composed of abnormal lacelike strands that attach to the Eustachian valve and the crista terminalis. It results from the incomplete resorption of the septum spurium, which should be completed by the 3rd month and exists in about 1% of patients[10]. 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. In the four chamber view the most anterior vein is the inferior pulmonary vein; the most posterior is the superior pulmonary vein. The right ventricle appears foreshortened compared to the left because of a large muscle bundle at its apex: the *moderator band*. In favorable cases one can note the difference in lining of the two ventricles: the right ventricle has a more coarse lining than the left due to a coarser trabeculation. Even more difficult to observe is that a papillary muscle (the muscle of the septal leaflet of the tricuspid valve) implants on the septum in the right ventricle, while the left side of the interventricular septum is free of papillary muscle. In the four-chamber view, both ventricles should have almost the same width (right over left = 1.1).

When the plane is slightly angled cranial, the intersection of the septa and the atrioventricular valves is replaced by a round structure: the root of the aorta between the two atria. This section is nicknamed the *five-chamber view* and is used to assess the origin of the aorta. 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 LONG AXIS VIEW / LEFT HEART VIEWS*

This section demonstrates important landmarks: the aorta arising from the left ventricle and the mitral valve is seen between the left atrium and the left ventricle. Note that the posterior leaflet is shorter than the anterior leaflet. The anterior leaflet is in continuity with the posterior wall of the aorta. The anterior wall of the aorta is in continuity with the interventricular septum. The aortic valve can be seen at the base of the aorta. The continuity between the left ventricle and the aorta resembles the ballerina feet aspect.

4

Left outflow tract

This section demonstrates the right ventricle and the 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. The pulmonary valve is anterior and cranial to the aortic valve.
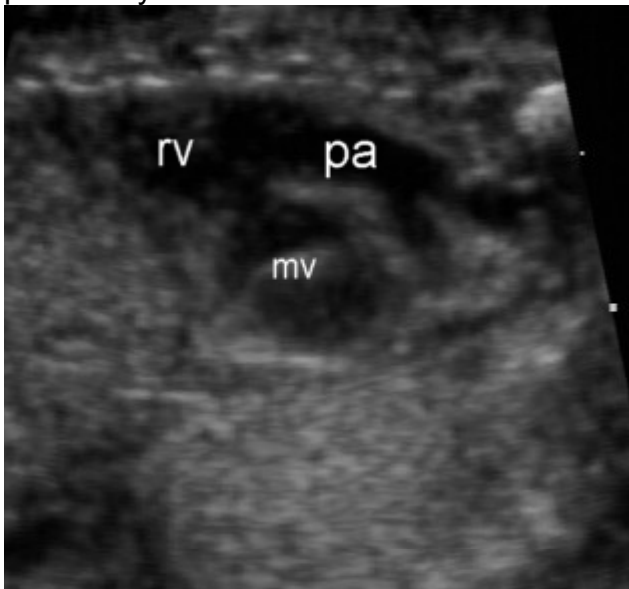
The appearance of the short axis views depends on the level at which they are obtained in the heart from the apex to the base. At the apex, a figure *8* is seen with the two ventricles separated by the interventricular septum. Both ventricles have the same morphology and size. Round structures in the ventricular cavities represent sections of papillary muscle. When the section is closer to the base, the valves are visible. The section of the mitral valve has a typical fish-mouth or oval shape; the tricuspid section resembles more an arrowhead. At the base of the heart the axial section demonstrates the right heart wrapped around the aorta. The section resembles the Yellow Pages logo ("Let your fingers do the walking"). This section is perpendicular to the ascending aorta and demonstrates the right atrium, tricuspid valve, right

ventricle, pulmonary valve, main pulmonary artery and ductus. This is the best section to demonstrate the pulmonary valve.

THE VALVES

The implantation of the tricuspid valve on the septum is more apical than that of the mitral valve. The tricuspid valve has three leaflets: a large anterior leaflet, a scalloped posterior leaflet, and a small septal leaflet. The anterior leaflet of the mitral valve should be in continuity with the posterior wall of the aorta. The anterior leaflet is longer than the posterior leaflet, which may be difficult to see. In the short axis view of the heart the valves can be seen to make a smaller inner structure within the ventricle. The image of the aortic valve in the short axis of the aorta is an inverted *Y* or a *Mercedes-Benz sign*. Sometimes the coronary arteries are visible alongside the aorta.

THE 3-VESSELS VIEW

This is a special form of the right-outflow tract that demonstrates the pulmonary artery (pa), ascending aorta (a) and superior vena cava (svc), almost aligned. The anterior aspect of the vessels should be compared as well as their sizes.
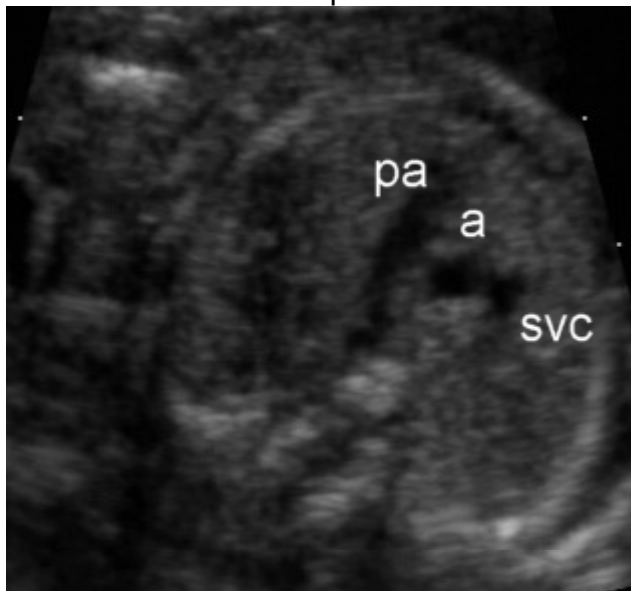

THE VESSELS

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

CARDIAC MEASUREMENTS

Cardiac measurements are simple to obtain and were an easy source of publication in the early days of fetal echocardiography. Some authors have advocated simple measurements that do not require the knowledge of the cardiac cycle[11], while others insisted on rigorous frame-by-frame analysis or M-mode tracing to distinguish between the two[12]. Although some authors considered the measurements reliable[13], usually the errors on the measurements are

so great that the resulting nomograms are limited to linear regressions. Nomograms of small structures show 5th and 95th confidence limits that encompass variations of size in the 30 to 80% range[14]; thus, normal variations are greater than the variations induced by pathology. Intraobserver variation can be as great as 40%[15], yet intraobserver variability is usually much smaller than interobserver variability. The landmarks used for standardization may be altered in malformed hearts, and, finally, most anomalies are easily detectable without using any nomogram. Thus, over the years we have matured to realize that nomograms were not necessary to the diagnosis of cardiac anomalies, and have abandoned even our own cardiac nomograms.

Though measurements are of little help, using other cardiac structures for reference can be quite beneficial, and a few simple rules are sufficient to keep in mind. The normal heart occupies roughly one-third of the chest. Since the pressure on both sides of the heart is the same (equalized by the ductus and foramen ovale) the workload is the same too. Thus the heterolateral structures should have similar diameters: the two ventricles and atria have essentially the same diameter[16]. When compared to the aorta, the pulmonary artery is larger by 20%, while the isthmus and the ductus respectively measure only 70% and 90% of the aorta at its origin[17].
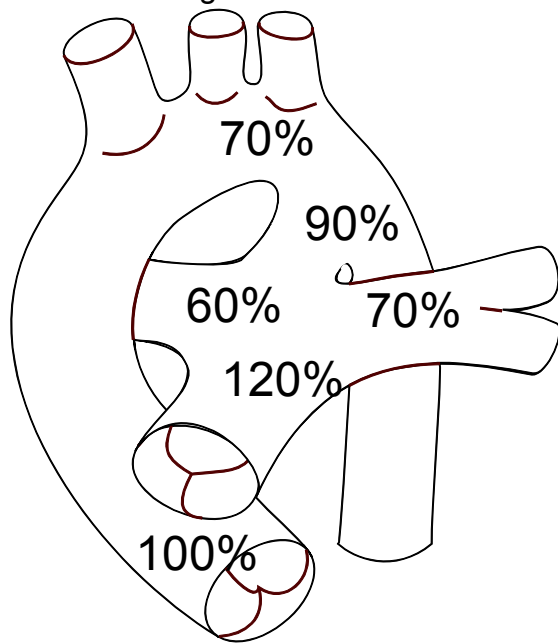
Deviations from this rule should suggest anomalies. The biventricular shortening (a measure of the contractility) ranges from 23 to 35%[18].

IDENTIFICATION OF THE CARDIAC STRUCTURES

The simplifications described earlier are not valid when examining fetuses at risk of cardiac anomalies since they may have dextrocardia or ventricular inversion. A stricter method of identification uses the following *intrinsic* criteria.

Recognition of the atria
❑ "The atria follows the viscera": this dictum refers to the fact that the position of the stomach predicts the side of the left atrium *as long as the fetus does not have heterotaxy* (therefore, check that the apex of the heart and the stomach are on the same side). A corollary of this rule is that the position of the atria can be inferred from the bronchial anatomy. While we

cannot assess the bronchus, it is sometimes possible to recognize a left lung from a right lung. When a pleural effusion (common in non-immune hydrops) dissects between the lobes, the number of fissures (one on the left lung, two on the right lung) can be counted.
- ❑ The pulmonary veins drain into the left atrium. Exception: anomalous venous return.
- ❑ The foramen ovale flap beats towards the left atrium. Exception: in mitral atresia the flap is imobile or slightly herniates in the right atrium.
- ❑ The right atrium is the chamber that drains the inferior vena cava. Exception: in polysplenia the cava does not necessarily end in the right atrium.

Recognition of the ventricles
- ❑ The left ventricle has a smoother inner surface than the right ventricle, but this is difficult to recognize.
- ❑ *The valves follow the ventricle*; thus a bicuspid valve is an indicator of left ventricle, while a tricuspid valve marks a right ventricle.
- ❑ There are only two papillary muscles in the left ventricle; three in the right ventricle.
- ❑ The right ventricle has a prominent papillary muscle in its apex called the *moderator band*.
- ❑ The tricuspid valve inserts on the interventricular septum closer to the apex than the mitral valve.
- ❑ Papillary muscles insert on the septum only on the right ventricle.

Recognition of the great arteries
- ❑ The great arteries originate from the heart crossing over each other in a 90° angle. They never emerge from the heart in a parallel position. Thus seeing two arteries side by side is always abnormal. Further back in the thorax however, they merge.
- ❑ The pulmonary artery is slightly bigger than the aorta.
- ❑ Two arterial valves should always be present.
- ❑ The pulmonary artery arises anterior and cranial to the aorta.

WHAT DO YOU MEAN YOU CAN'T SEE ALL THAT?

Neither can we, at least not in every fetus. You should be able to see the four-chamber view in 99%, the five-chamber view in 95% and the short axis view in 70%[19]. There are, unfortunately, no special tricks except for good 1) spatial orientation, 2) hand-eye coordination, 3) equipment and 4) patience. Practice is what will make you successful. The common refrain that "We do not do enough cardiac anomalies to be good at it" is not a good excuse. The first step is to detect that an anomaly is present. Since cardiac anomalies are among the most frequent, your chance of finding one is high. You might want to be able to give the correct diagnosis, but that is not as important as being able to describe to the pediatric cardiologist or your local guru what the findings are. She/he will then help you sort out the problems.

M-MODE

Since the fetal ECG is difficult to derive, one uses the M-mode recording to deduce from the mechanical events the electrical signal that caused them. 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. Historically, M-mode was just recorded with a pencil-like transducer, and orientation was a major headache. Current equipment displays a two- dimensional image alongside the

M-mode recording, which simplifies the orientation. Most machines allow toggling between a display of the M-mode, the real-time or a combination of the two. The gain and magnification of the M-mode can often be set independently from that of the real-time. Since the M-mode recording is along a single line, there is no focal zone to set.
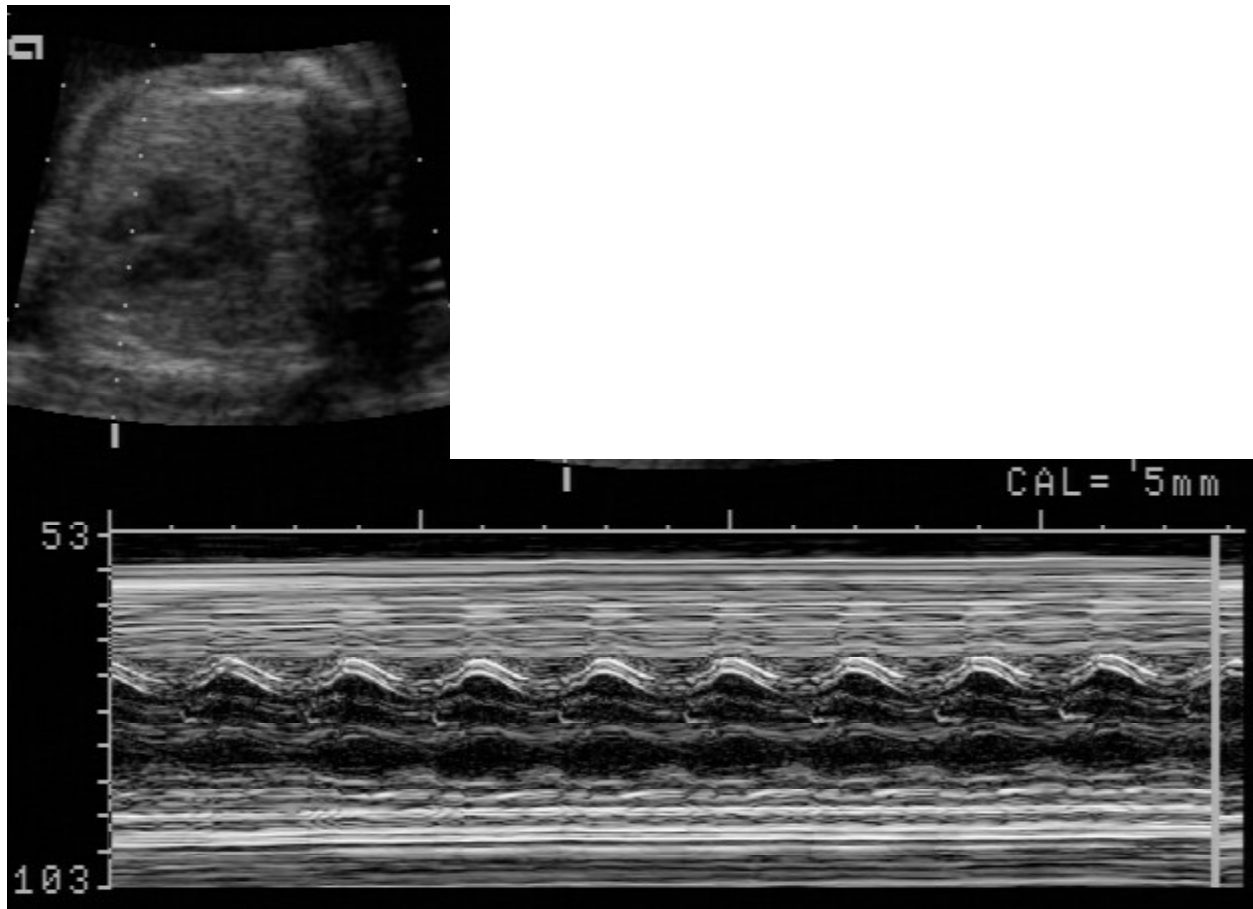

Biventricular M-mode

The most common use for M-mode is in documenting fetal cardiac activity. One simply "drops" an M-mode line over the fetal heart and records the activity. The machine allows calculation of the fetal rhythm. A grid of dots is overlaid on the image. The vertical spacing of the dots is one centimeter; the horizontal spacing is 0.5 seconds (on some machine it is 0.2 seconds). This allows evaluation of the fetal rhythm even if it was not computed at the time of the examination. If the beats are simultaneous with every horizontal marker, the rhythm is 120 per minutes (one every half second); if it is every two markers, 60 beats per minute (bpm); and every three markers, 40 beats per minute. Two beats per marker (thus 4 per second) represent a tachycardia at 240 bpm.

M-mode was also used to measure the diameters of cardiac chambers. The two-dimensional images are far easier to interpret, and M-mode is now obsolete for this application. Finally, some authors have attempted to derive other values of cardiac activity such as pre-ejection fraction, rate of fractional shortening, etc. This can safely be ignored since they have not contributed to improved diagnostic accuracy.

When the transducer is placed perpendicular to the interventricular septum, one can recognize from top to bottom: the anterior wall and ventricle (with flashes of atrioventricular valve echoes), the septum, the distal ventricle and the posterior wall. A small amount of pericardial fluid can sometimes be seen during systole on the outside of the epicardium and medial to the bright echo that represents the pericardium[20]. Systole is marked by a nearing of the anterior and posterior wall; diastole by a separation of these echoes. Note that in the fetus there is minimal motion of the septum.

This biventricular M-mode is of little clinical use. A more important section is obtained by dropping the M-mode line through an atrium and a ventricle. In this view, the middle echoes will represent either the interventricular or interatrial septum, or an atrioventricular valve with, on either side, an atrial wall and a ventricular wall. This permits an analysis of the transmission of the impulse from the atrium to the ventricle and allows the detection of atrioventricular blocks.
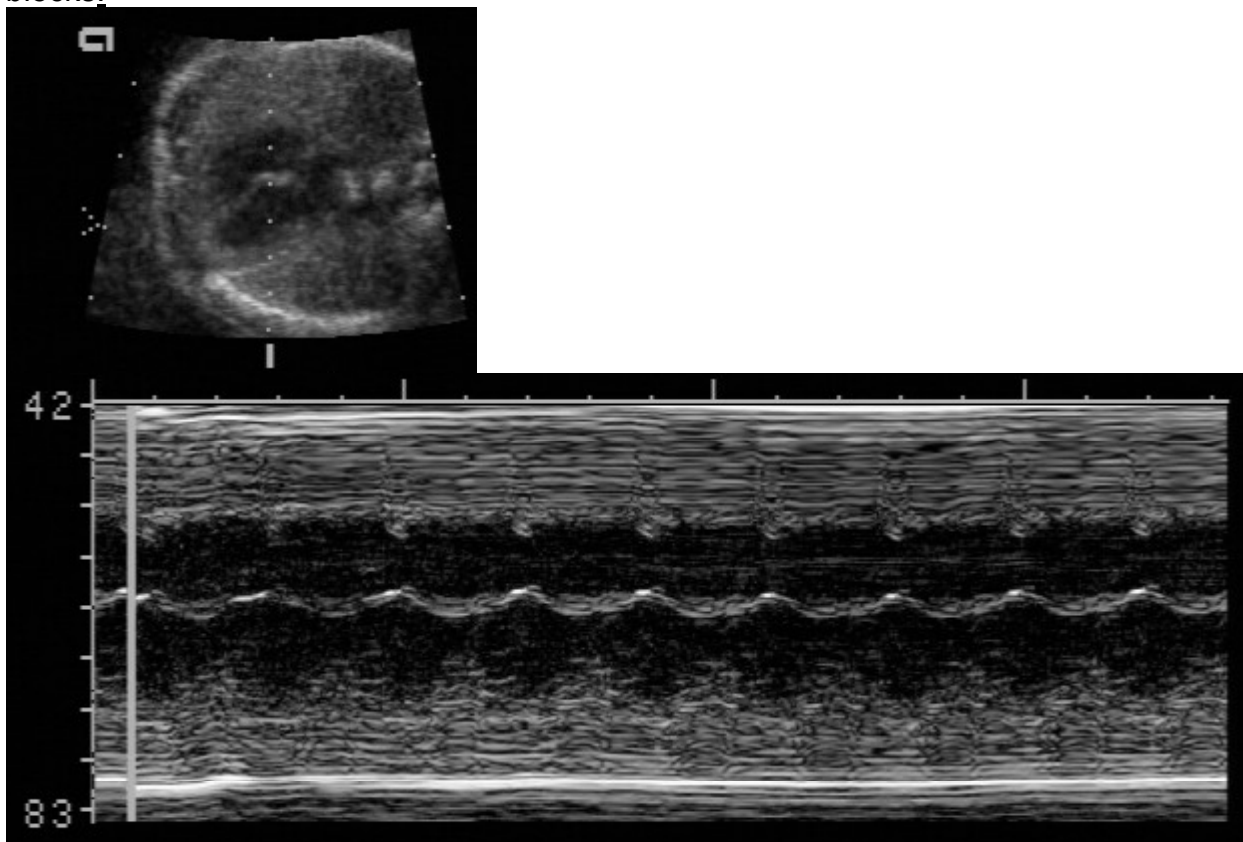
FORAMEN OVALE MOTION

The movement of the foramen ovale is complicated. The valve opens and closes twice during the cardiac cycle. It opens a first time during ventricular systole when returning blood cannot go through the closed tricuspid valve and passes through the foramen ovale toward the left atrium. At the beginning of the diastole, the tricuspid valve opens, thus releasing the pressure, and the foramen ovale valve closes. The opening of the atrioventricular valve is soon followed by contraction of the atria. This pushes blood from the right atrium into the left and opens the foramen ovale for the second time. The valve then closes for the second time at the end of the atrial kick. Thus there will be two periods of opening: a long one during diastole and a short one during systole.
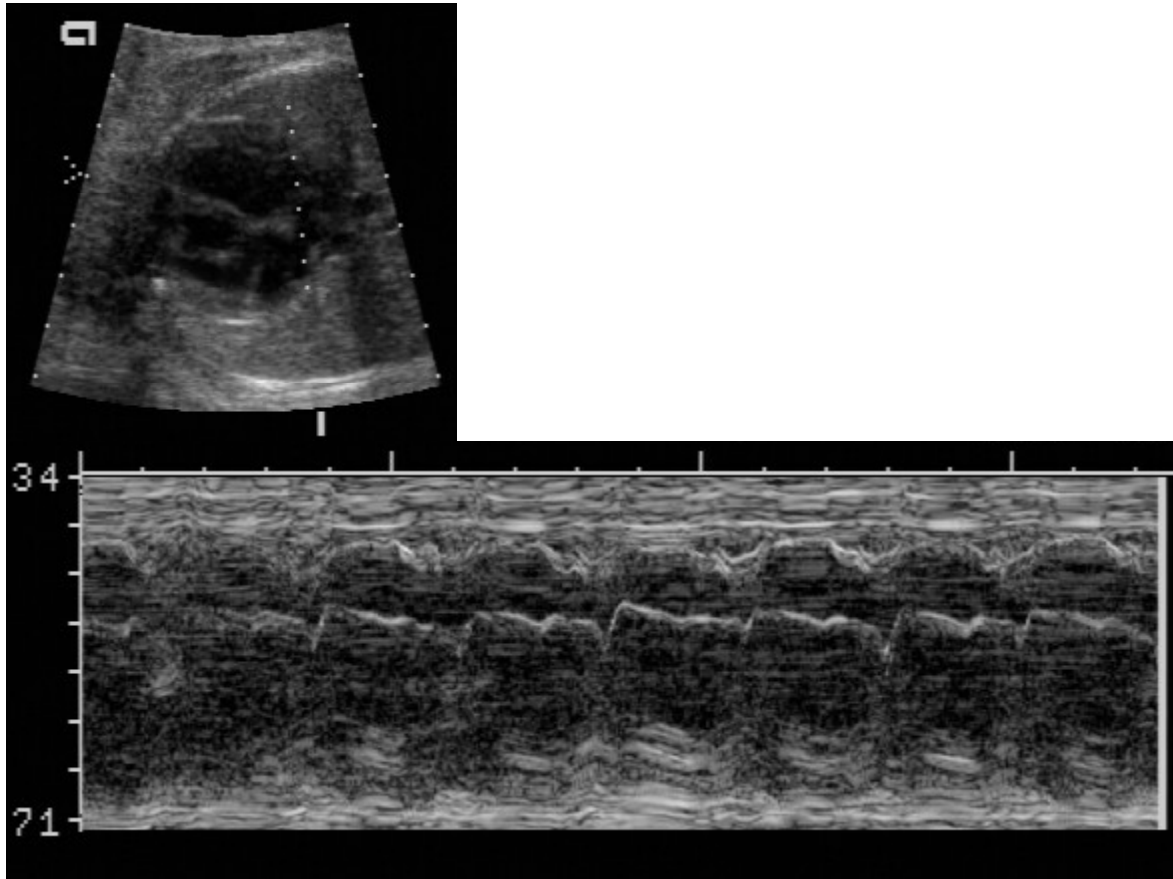
In atrial septal aneurisms, the double motion of the foramen ovale flap is attenuated or eliminated.

VALVULAR MOTION

The mitral and tricuspid valves
The anterior leaflet of the mitral valve has a typical *M-shaped* motion. In early diastole the rush of blood into the left ventricle rapidly opens the valve, and the leaflet moves towards the interventricular septum. After the initial filling of the ventricle, the flow slows, and the leaflet moves away from the septum. This creates a "peak" (the E point), and the motion away from the "peak" is called the EF segment. The atrial kick increases the flow again, pushing the leaflet towards the septum. This creates another ascending segment (FA). The leaflet closes by mowing away from the septum. The initiation of the ventricular contraction causes an undulation (the B point) then the closure of the valve (C). The valve remains closed until the onset on diastole (the D point). The posterior leaflet is shorter and has a smaller motion that mirrors the motion of the anterior leaflet: it moves towards the posterior wall instead of the septum.
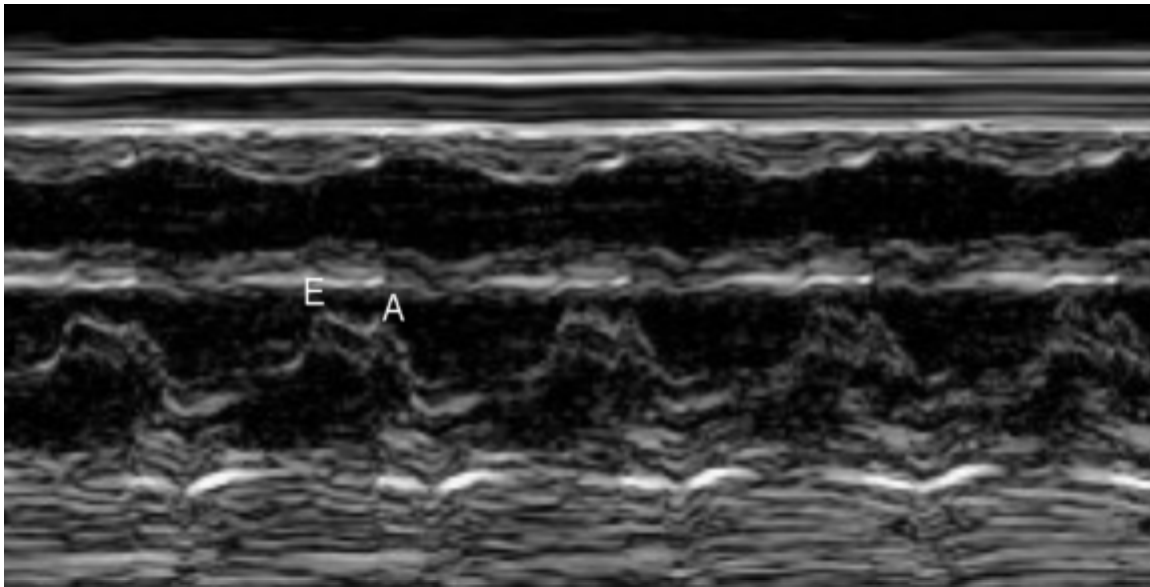
The aortic and pulmonary valves

The M-mode motion of the aortic valve has a typical "box" appearance. The free edge of the valve is seen during diastole in the middle of the lumen of the aorta as a bisecting line. The opening of the aortic valve is very rapid. The semilunar valves move toward the aortic wall. This rapid opening describes the left side of the "box". The box remains open during the whole systole. An equally brisk closure forms the right side of the box. The same image can be obtained from the pulmonary valve, but is usually technically more difficult to obtain. When the walls are moving parallels, it means that it is a great vessel, if it were a ventricle the walls would be moving away and towards to each other.
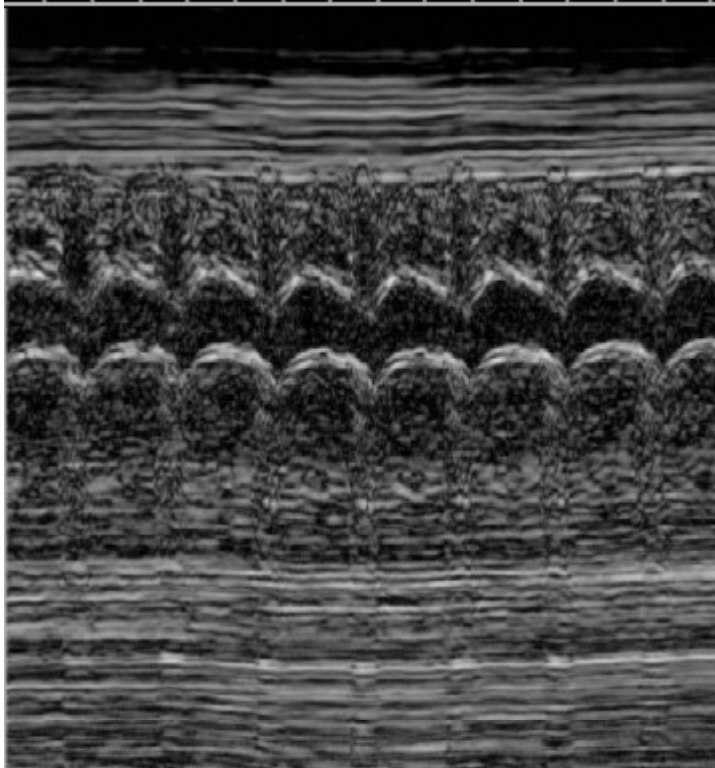
DOPPLER

Doppler first described the effect that now carries his name in the description of the color of stars in 1842[21]. Buys Ballot adapted the concept to sound a few years later[22], and Satomura was the first to apply the idea to cardiac examination in 1956[23].

CONTINUOUS WAVE

Continuous wave Doppler lacks spatial resolution and thus has not been used in the cardiac examination, except to establish cardiac activity or for fetal monitoring.

PULSED WAVE DOPPLER

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). Measurements are obtained during fetal apnea. The spectral analysis is independent of the angle of interrogation and thus is the most operator-independent measurement. Flow velocity assumes that the angle between the ultrasound beam and the flow is correctly estimated (and less than 30º). Flow measurements add to this restriction that the exact size of the section of the vessel is known and that the flow has a flat profile (all the red cells travel at the same speed, and those on the edge of the vessel are not slower). Unfortunately the more physiologic measurements are thus the least reliable.

The PW signal in the ventricle demonstrates early filling (the E wave) and the atrial kick (A wave).
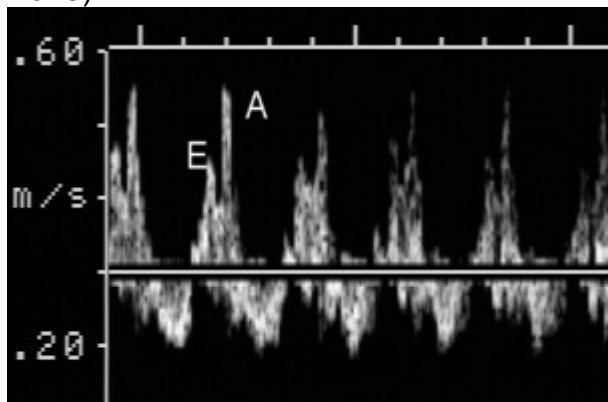
PULSED WAVE DOPPLER IN CARDIAC ANOMALIES

In cardiac anomalies that reroute the whole flow predominantly through one great vessel, velocity measurements at the level of this vessel usually reveal increased velocities[24]. The absence or reversal of diastolic flow in the umbilical artery is associated with a dismal prognosis[25]. In arrhythmias, the spectral analysis can be made in the descending aorta. Premature contractions or tachycardia result in peaks of lower maximal velocity than normal contractions. Some of these may be too feeble to be heard on the audio output, and the rhythm may then be assumed to be slower than it is. Regurgitant flow is seen as peaks that are in the opposite direction to the normal flow and occur during the incorrect part of the cardiac cycle. Instead of a series of peaks separated by no or low signal intervals, the image is that of alternating peaks above and below the baseline.

The atrioventricular flow shows a biphasic profile with a large early (passive filling) and a smaller late diastolic peak (atrial kick). The ratio between the two peaks tends to diminish with gestational age, from 1.5 around 20 weeks to 1.2 at term.
The flow velocities (peak and average) at the four valves can be measured by placing the Doppler sample after the valve[26].

Placing the sample before the valve permits the detection of regurgitation. Aside from sampling the heart, some arteries are commonly investigated. These include the carotid, intracranial arteries, descending aorta and umbilical arteries. The pressure gradient (P) across a stenosis (aortic, pulmonary, mitral and ventricular septal defect) can be estimated with the formula:

Pressure = 4 times V^2 where V is the peak velocity in the jet.

There is a consensus that the right output exceeds the left by about 20-30%[27], but the difference decreases to about 10% in the third trimester[28].
The summation of the right and left flow provides an estimate of the cardiac output. Each ventricular output can be calculated by multiplying the atrioventricular area or the great vessel area by the mean temporal velocity obtained at the appropriate level. Measurements at the atrioventricular valve level are preferred over those at the semilunar valves since the area is larger and the flow slower (no aliasing). The cardiac output is estimated at about 500 ml/min/kg and appears constant through gestation. It should be remembered, however, that this expression of the flow is the result of so many calculations that the summation of the errors (on the estimation of the angle, valve area, cardiac frequency, velocity, flat profile of the flow and estimated fetal weight) renders this estimation of little clinical use.
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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. However, because of the tremendous computer power required and the time required to collect the data for each frame, the frame rate (sampling) is slower than for pulsed wave Doppler. Color Doppler is useful to assess normal anatomy and physiology[31], valvular regurgitation or stenosis, shunting[32] and the orientation of flows to obtain the most representative pulse-wave spectrum[33]. Color Doppler also has the potential to be used to grade valvular regurgitation. The degree of regurgitation at a valve correlates with the prognosis and outcome of the lesion. Regurgitation is commonly assessed radiographically by dividing the cavity into which regurgitation occurs into four equal and concentric zones. Regurgitation of contrast (or color Doppler) is graded from Grade I (zone closest to the regurgitant valve) to Grade IV (zone most distal from the valve).

Color M-mode
Color Doppler lacks temporal resolution: whether images are obtained in systole or diastole can only be derived by deduction (direction of the flow, position of the valve etc). Because of that limitation, it is practical to do a combined M-mode color and color Doppler. Some equipment even allows the simultaneous display of the color M-mode, color Doppler overlaid over the gray-scale image and a recording of the pulse Doppler.

THE STEP BY STEP ANALYSIS

A systematical approach to the heart simplifies its study. The approach widely used by pathologists or pediatric cardiologists relies on the identification of the left and right atria, ventricles and great vessels. This is unfortunately rarely feasible in the fetus since the heart is too small and the resolution insufficient to detect the identifying criteria. Structures such as the atrial appendages or bronchus are essentially invisible in the fetus, especially before 24 weeks. Further, common clues such as the presence of cyanosis and pulmonary overcirculation simply do not exist in the fetus.

The following approach is a derivative of the pathologist's approach, adapted to what can be recognized in the fetus. It starts with the identification of readily recognizable landmarks and progresses to more subtle findings. The step-by-step approach that we use reviews 1) the identification of the fetal position, 2) the position of the heart in relation to the body, 3) the number of chambers and their connections, and finally 4) the rhythms. Before that we must review the criteria used to identify the cardiac structures.

FETAL AND CARDIAC POSITION

To assess the cardiac situs, observe the fetal position: is it cephalic or breech? Then identify the cardiac apex. This usually does not present any problem (see the anatomy section). Finally, assess the position of the aortic arch and that of the stomach; both should be on the same side as the cardiac apex. The descending aorta can be seen slightly on the side of the spine. When in doubt about its position, mentally divide the fetal chest in two equal halves by a line that traverses the middle of the vertebra. The aorta should be on one side of this line and not be divided by it.

THE FETUS IN CEPHALIC POSITION

The fetal spine can either be on the mother's left (right of the screen) or on the mother's right (left of the screen). Remember that it is important to adhere to the AIUM standard orientation here: no creativity allowed until you are quite confident about what you do!
When the fetal spine is on the mother's left, the transducer is closer to the right side of the fetus than to its left side. Therefore, the stomach, apex and aortic arch ought to be on the "far side" of the fetus (away from the transducer): this is situs solitus. If they are on the proximal side the fetus has a situs inversus; in any other condition, the fetus has heterotaxy.
Similarly, when the fetal spine is on the mother's right, the transducer is closer to the left side of the fetus than to its right side. Therefore, the stomach, apex and aortic arch ought to be close to the transducer (situs solitus). If they are on the "far side" the fetus has a situs inversus, in any other condition the fetus has heterotaxy.

Fetus in cephalic position with the spine to the mother's right	Fetus in cephalic position with the spine to the mother's left
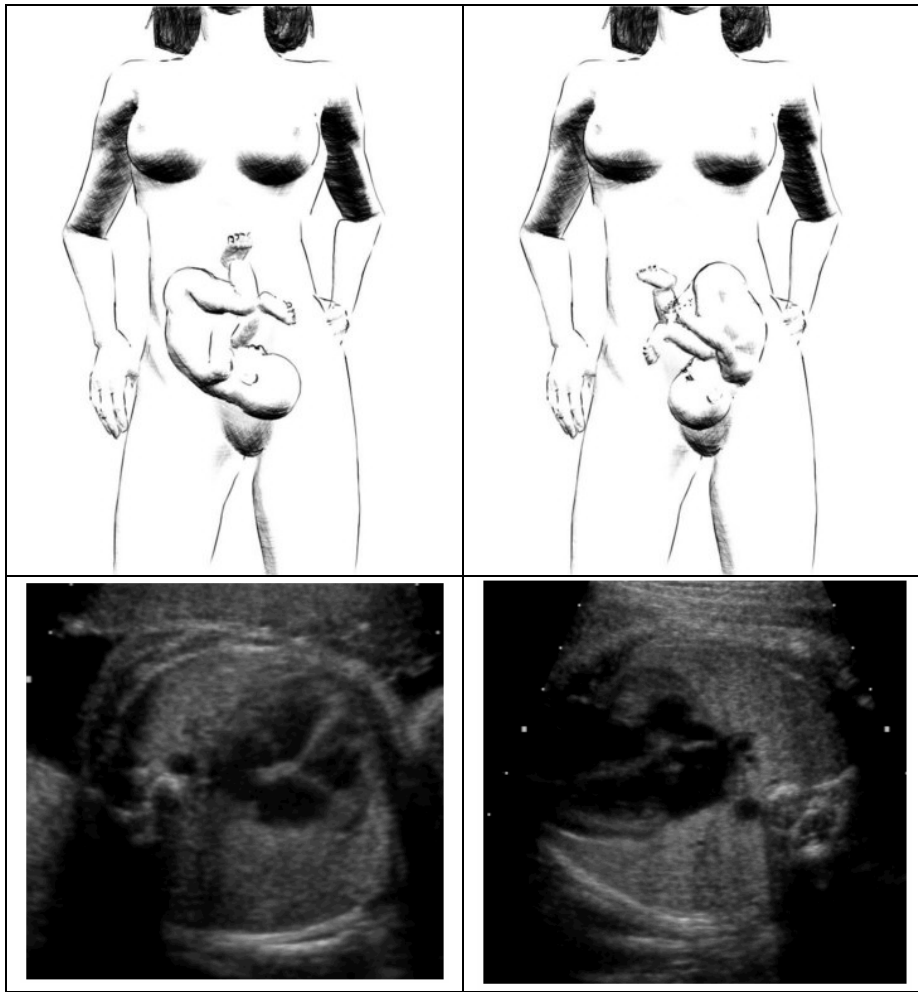
THE FETUS IN BREECH POSITION

The same reasoning applies to the breech fetus. When its spine is on the mother's left, its stomach, apex and aortic arch should be close to the transducer (situs solitus). If they are away, the fetus has situs inversus; if they are discordant, the fetus has heterotaxy.
When the spine is on the mother's right, its stomach, apex and descending aorta should be away from the transducer (situs solitus). If they are close, the fetus has situs inversus; if they are discordant, the fetus has heterotaxy.

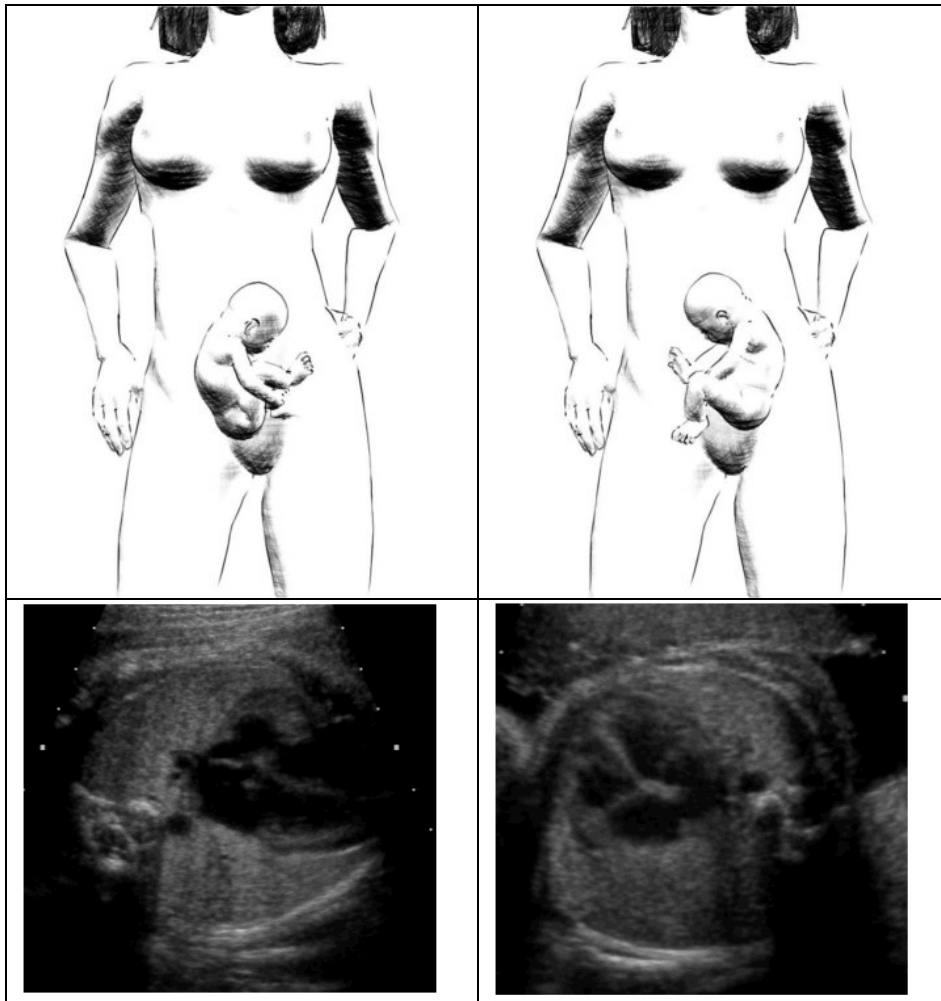| Fetus in breech position with the spine to the mother's right	Fetus in breech position with the spine to the mother's left

Once the fetal position, the apex, the aortic arch and the stomach are identified, one can establish the situs. But before examining the different combinations, let's review what the usual combinations are.

DEFINITIONS

The normal situation — cardiac apex, stomach and aortic arch on the left — is called *situs solitus*. A mirror image of the situs solitus is called *situs inversus*. If some of the organs are on the correct side while others are on the opposite of their expected side, the situation is called *heterotaxy* or *situs ambiguus*. Heterotaxy can be divided according to which organ is abnormal, into *dextrocardia* when the heart is on the right side and the stomach on the left side, and *visceral situs* when the heart is on the left and the stomach on the right. The first condition is also referred to as *situs solitus with dextrocardia*, while the second is referred to as *situs inversus with levocardia*. When the heart and/or the viscera are not frankly on one side but tend to be midline, the condition is called *visceral heterotaxia*. Very rarely, the heart will be in a midline position. This is referred to as *mesocardia*.

Before deciding that the heart is on the "wrong" side, one has to distinguish between two conditions that may be confused. The heart may be on the right side because the heart has an intrinsic abnormality: this is referred to as *dextrocardia*. Sometimes, however, the heart can be on the right side because of an abnormality which is *extrinsic* to the heart. This is called *dextroposition*. The heart is either pushed away from the left to the right by a diaphragmatic

hernia, congenital lobar emphysema or a cystadenomatoid malformation of the lung or it occupies a void on the right in case of right lung agenesis.

The determination of the situs is important since it is an important predictor of the presence of cardiac anomalies: in situs solitus the frequency of congenital anomalies is roughly 1%; in situs inversus it is doubled to 2%. Although the frequency of cardiac anomalies is low in situs solitus, situs solitus is by far the most common configuration; thus, most cardiac anomalies occur in those patients. In heterotaxy, the frequency of cardiac anomalies is considerably higher: over 75% in dextrocardia and over 95% in visceral heterotaxia. In dextrocardia one should look for left to right shunts (atrial septal defects, anomalous venous return or ventricular septal defects) and obstruction to the right outflow (pulmonic stenosis or atresia). There is no specific prevalence of disorders in visceral heterotaxia. Congenitally corrected transposition of the great arteries is common in both visceral heterotaxia and dextrocardia and is also increased in situs inversus.

Great vessels and atrial connections
A section high in the mediastinum is used to assess the side of the aortic arch. One can also look for the position of the descending aorta in the high chest. This is more delicate since whichever side the aorta is on it will ultimately enter the abdomen through the esophageal hiatus and thus be almost midline. The relative position of the aorta and the vena cava should also be noted. In situs solitus and in situs inversus, the aorta and vena cava are on the contralateral side of the midline with the cava ipsilateral to the right atrium[34]. This relation is not true in atrial isomerism. In polysplenia, the cava is interrupted and continued into the hemiazygos that is ipsilateral and posterior to the aorta. In asplenia, the cava is ipsilateral and anterior to the aorta, and the hepatic vein enters the atrium independently from the cava.

Atrioventricular connections
The following connections may exist: two atria connected to separate ventricles or to the same ventricle, or one atria connected to a single ventricle. If the atria are connected to their respective ventricles they are said to be *concordant*, while they are *discordant* when they connect to the opposite anatomical ventricle. When both atria connect to a single ventricle, the condition is called *double inlet* ventricle.

Ventriculo-arterial connections
Finally, the concordance between the ventricles and the great vessels and the position of the vessels should be assessed. Just as before, the connections are concordant when the correct ventricle is connected to the corresponding great vessel, and discordant when it is connected to the opposite vessel. When more than half of both great vessels originate from one ventricle, the situation is called *double outlet* ventricle. Finally, a *single outlet* heart corresponds to the emergence of a single great vessel from the heart: a truncus, an aorta with pulmonary atresia, or a pulmonary artery with aortic atresia.

Fetal cardiac activity is detectable from 6 weeks on by suprapubic ultrasound[35] and about one week earlier by transvaginal ultrasound. In very early pregnancy, the cardiac activity may be detectable before the embryo, especially when the fetus is on the side of the gestational sac. The normal fetal heart rate varies with gestational age. It is around 100 beats per minute (bpm) at 8 weeks, reaches 175 bpm by 10 weeks, 150 at 15 weeks[36][37] and slows further to about 140 æ 20 bpm at 20 weeks and 130 $\pm$ 20 bpm at term[38].

When the rate is greater than 160 beats per minute, one talks about tachycardia; when it is below 100, the condition is referred to as bradycardia. Short episodes of bradycardia, sometimes as slow as 50 bpm, are probably physiologic, especially in the second trimester. The heart rate is influenced by maternal smoking[39] and maximal maternal effort[40] but not by submaximal (65%) exercise[41] or terbutalin treatment[42].

WHEN AND WHY DO A CARDIAC EXAMINATION

WHEN

A full cardiac examination is a time-consuming investigation, which cannot be performed on every patient. Unless there is a special reason to do so, we limit our examination to the following: fetal position, situs, four-chamber view, pulmonary vein return and outflow tracts. When possible we also obtain the aortic arch. Unless the anatomy or rhythms is abnormal we do not obtain Doppler signals. This allows the detection of a large number of anomalies, not only cardiac but also gastrointestinal (diaphragmatic hernia) and pulmonary (cystic adenomatoid malformation, lung agenesis)[43]. The rest of the investigation belongs to the dedicated cardiac examination[44]. Cardiac examinations are easiest to perform between 20 and 24 weeks. Earlier examinations are more difficult because of the small size of the heart; while increasing calcification of the shoulders, arms and ribs impairs later examinations.

WHY

Dedicated examinations (often called "fetal echo" or "echocardiography") are performed for familial/maternal or fetal reasons[45]. The result of the examination will affect the prenatal care in several ways. When the examination is normal, the parent can be reassured—with the *caveat* that some anomalies can still be overlooked. Some of the tachyarrhythmias can be treated *in utero*. When the anomaly is treatable and the fetal condition is worsening, premature delivery and/or referral of the infant to a center familiar with the treatment of the disease should be encouraged. When a lethal anomaly is discovered, interruption of the pregnancy can be offered or, when after the legal limit of termination, non-interventional obstetrical care given.

FAMILIAL REASONS

Familial reasons include a sibling or a history of cardiac anomaly, maternal diabetes, toxic exposure (drugs, medications, alcohol, etc.), and infections. The recurrence rate of cardiac anomalies is 2% overall, but some anomalies such as hypoplastic left heart syndrome, coarctation of the aorta and the cardiosplenic syndromes may have a recurrence rate as high as 10%[46]. Table below lists some of the cardiac anomalies in the offspring of mothers exposed to certain drugs or disease. The number of cases reported in the literature is immensely greater, but few of the reports allow differentiating between a coincidental association and a true statistical relation[47]. Those listed are those thought to have a statistical relation. Although maternal administration of indomethacin (to prevent premature labor) has been reported to affect the tricuspid valve and constrict the ductus[48], we have not been able to detect significant adverse reactions in fetuses that we have studied.

MATERNAL MEDICATIONS AND CARDIAC ANOMALIES

Alcohol[49]
❑ atrial septal defect

- ventricular septal defect
- endocardial cushion defect
- pulmonary aplasia
- tetralogy of Fallot

Anticonvulsants[50,51]
- ventricular septal defect
- tetralogy of Fallot
- atrial septal defect
- aortic stenosis
- transposition of the great arteries

Antineoplastic
- tetralogy of Fallot

Barbiturates[52]
- ventricular septal defect
- coarctation of the aorta
- pulmonary stenosis

Chlorotheophylline[53]
- various

Exogenous female sexual hormones[54]
- ventricular septal defect
- aortic stenosis
- tricuspid atresia
- patent ductus arteriosus
- transposition of great arteries
- tetralogy of Fallot
- double outlet right ventricle
- atrial septal defect
- Ebstein's anomaly

Indomethacin[55]
- premature closure of the ductus

Lithium[56]
- coarctation of the aorta
- tricuspid regurgitation
- atrial flutter
- Ebstein's anomaly
- pulmonary atresia

Phenothiazines[57]
- various

Prochlorperazine[58]
- ventricular septal defect

Salicylates[59,60]
- atrial septal defect
- left heart hypoplasia
- ventricular septal defect

Thalidomide[61]
- ventricular septal defect
- atrial septal defect
- tetralogy of Fallot
- truncus arteriosus communis

- ❑ pulmonary stenosis

Trimethobenzamide[62]
- ❑ various

Vitamin A[63]
- ❑ various

MATERNAL DISORDERS AND CARDIAC ANOMALIES

Coxsackie B[64]
- ❑ myocarditis

Cytomegalovirus[65]
- ❑ tetralogy of Fallot

Diabetes[66]
- ❑ transposition of great arteries
- ❑ ventricular septal defect
- ❑ coarctation of the aorta
- ❑ atrial septal defect
- ❑ endocardial cushion defect
- ❑ left heart hypoplasia

Epilepsy[67]
- ❑ transposition of great arteries
- ❑ atrial septal defect
- ❑ tetralogy of Fallot
- ❑ coarctation of the aorta

Hyperphenylalaninemia[68]
- ❑ ventricular septal defect
- ❑ atrial septal defect
- ❑ tetralogy of Fallot

Lupus[69]
- ❑ congenital heart block
- ❑ atrial septal defect
- ❑ pulmonary stenosis

Mumps[70]
- ❑ Endocardial fibroelastosis

Phenylketonuria[71]
- ❑ ventricular septal defect
- ❑ coarctation of the aorta
- ❑ tetralogy of Fallot
- ❑ pulmonary atresia
- ❑ pulmonary stenosis

Rubella[72,73]
- ❑ atrial septal defect
- ❑ ventricular septal defect
- ❑ tricuspid valve atresia
- ❑ pulmonary stenosis
- ❑ pulmonary valve stenosis
- ❑ aortic valve stenosis
- ❑ aortic arch anomalies
- ❑ coarctation of the aorta
- ❑ Ebstein's anomaly

Toxoplasmosis[74]
- ❑ myocarditis
- ❑ aortic stenosis
- ❑ ventricular septal defect

FETAL INDICATIONS

Fetal indications include:
- ❑ **signs of trisomy 13, 18, 21**: search for endocardial cushion defect, atrial septal defect, ventricular septal defect, tetralogy of Fallot, double outlet right ventricle, univentricular heart, truncus, transposition of the great vessels, hypoplastic left heart syndrome and tricuspid atresia, among others[75].
- ❑ **hydrops or polyhydramnios**: this is a very typical association that suggests circulatory failure. The causes of circulatory failure include 1) obstructive diseases such as malformations (aortic atresia, calcinosis, etc.), torsion of the great vessels by an extracardiac mass (cystic adenomatoid tumor of the lung, cardiac teratoma or diaphragmatic hernia), 2) arrhythmias (either bradycardia or, more commonly, severe tachycardia) or 3) decreased oxygen carrying capacity of the blood usually from anemia (isoimmunization, fetomaternal hemorrhage, etc.) or other causes (increased blood viscosity in the recipient twin of a twin-to-twin transfusion).
- ❑ **anomaly of situs**
- ❑ **bradycardia**: search for an anomaly of the conducting system, either due to an absent or anomalous connection in the connecting system (atrial septal defect, endocardial cushion defect, transposition) or damage due to autoimmune reactions (maternal lupus).
- ❑ **growth retardation**: either "symmetrical" (think of TORCH infections or chromosomal anomalies and their associated cardiac anomalies) or "asymmetrical" growth retardation[76] is associated with cardiac anomalies.
- ❑ **cystic hygroma**: should suggest Turner syndrome and thus coarctation of the aorta and hypoplastic left heart syndrome.
- ❑ **vertebral anomalies**: search for anomalies of the VACTERL association (ventricular septal defect) or Klippel-Feil syndrome (atrial septal defect, coarctation).
- ❑ **sacral meningoceles** have also been associated with conotruncal anomalies[77].
- ❑ **hand and feet anomalies**: numerous syndromes associated with acromelic and cardiac anomalies.
- ❑ **first branchial arch anomalies** (mandible and lower facial anomalies) are associated with conotruncal anomalies (great vessel anomalies)[78].
- ❑ **single umbilical artery**: numerous anomalies have been reported including: atrial septal defect, ventricular septal defect, hypoplastic ventricle, tetralogy of Fallot, truncus, transposition, anomalous pulmonary venous return, coarctation, dextrocardia.
- ❑ **persistent right umbilical vein**: almost always associated with a variety of cardiac defects.

Cardiac anomalies are associated with extracardiac anomalies in 5-10% (combined data[79],[80]). Conversely, non-cardiac anomalies occur in 7-17% of fetuses with a cardiac anomaly (combined data of CNS[81], gastrointestinal[82], ventral wall[83] and genitourinary[84]). Because of these associations we perform a fetal echo and karyotype for every fetus in which an anomaly is found.

CARDIAC ANOMALIES AND GROWTH RETARDATION

The impression that cardiac anomalies are well tolerated by the fetus and are not a cause of growth retardation is a bias of pediatric cardiologists. The more severe anomalies can be associated with severe growth retardation that leads to stillbirth[85].

FREQUENCY OF CARDIAC ANOMALIES

Congenital heart diseases occur in about 0.6% of newborns. The distribution of anomalies in newborns is described in figure ***. The distribution of anomalies detected in fetuses is strongly biased toward the more severe anomalies. When stillborn and early fetal deaths are included, the number of anomalies rises. Approximately 5% of the defects are associated with chromosomal defects in the pediatric population, while in the fetal groups the frequency rises to 40% when the anomaly is detected around 20 weeks[86] and decreases to 13% close to term, with an overall risk of 25%[87]. By far the most common aneuploidy is trisomy 21 (89%) followed by trisomy 18 and 13 (4% each) and Turner syndrome (1%). Two percent of cardiac anomalies are associated with environmental factors. The recurrence risk after the birth of one affected child is to 2-5% and to 10% after the birth of two affected siblings[88]. Mother that are survivors of congenital heart disease have a 10% risk of having an affected fetus.

RELIABILITY OF PRENATAL DIAGNOSIS

The accuracy of prenatal diagnosis is difficult to establish[89]. In the literature, the accuracy of detailed fetal echocardiography has a wide range with sensitivities ranging between 5% to 91%. It is certain that numerous excellent diagnoses have been made prenatally; however, an exact match between the prenatal and the pathological diagnosis is very difficult to achieve since prenatal examination often misses some of the more subtle and accessory findings[90]. We are very suspicious of the accuracy reported in some series, and we consider that overall only about half of the anomalies are detected[91]. By including just a few differential diagnoses in the report, the likelihood of including the correct one easily reaches 75% , thus giving falsely good results.
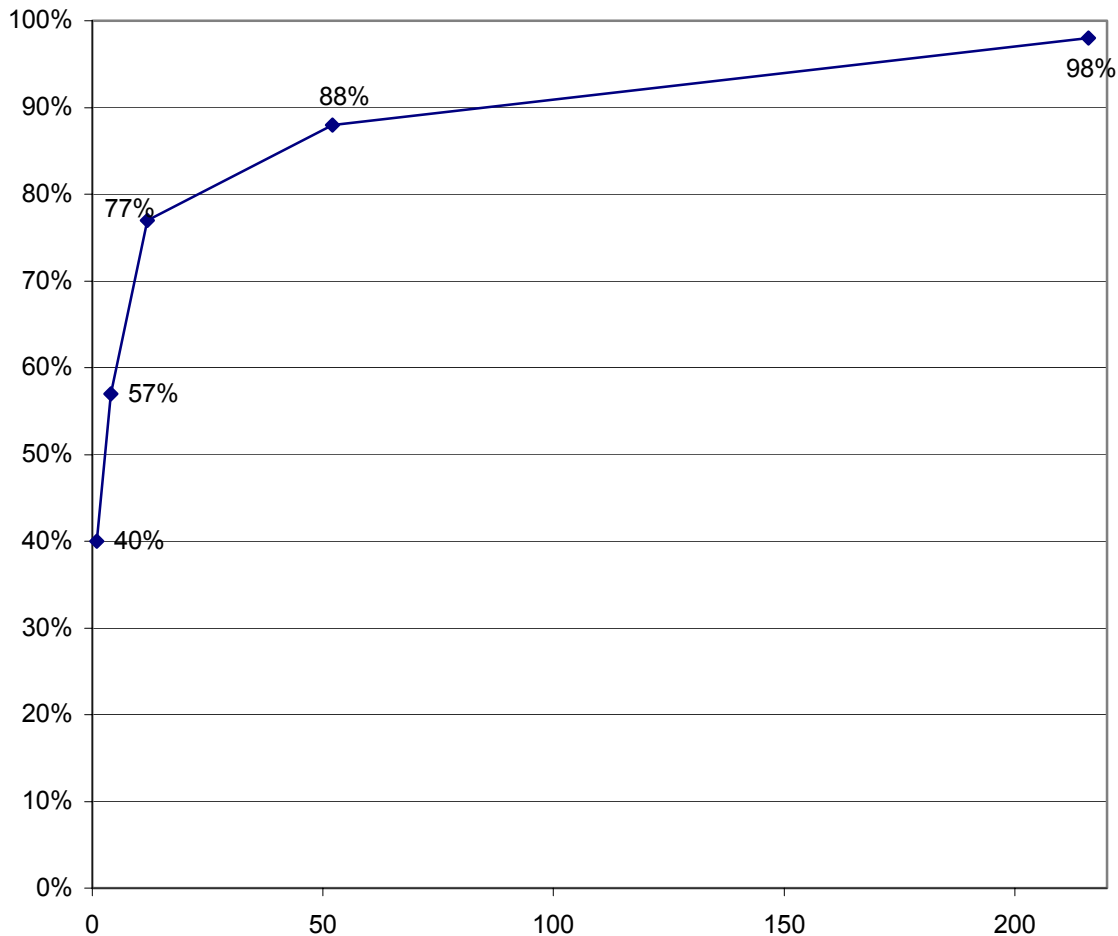
According to the Washington Baltimore study 40% of cardiac anomalies are detected at the end of the first year of life, 57% byt the end of the first month. It takes respectively 3 months, 1 years and 4 years to reach 77, 88 and 98%. These number of detections rates of children observed by qualified pediatricians are difficult to reconcile with the higher number of detection rates proposed by certain in utero series. A healthy dose of scepticism is in order when very high prenatal values are quoted.

The number of anomalies that are missed is even harder to estimate. Prenatal echocardiography has a tendency to detect the more severe anomalies (univentricular heart, tricuspid atresia, endocardial cushion defects) and miss the more benign anomalies (atrial septal defect, patent ductus arteriosus, etc.). Lesions that have commonly been missed include ventricular septal defect (membranous and muscular), secundum atrial septal defect, coarctation, supravalvar aortic stenosis and tetralogy of Fallot[92] among others. Lesions that are commonly overdiagnosed include dextrocardia (confused with dextroposition), transposition and secundum atrial septal defect. Lesions that affect the four-chamber view are more commonly detected than conotruncal lesions. Although this is frustrating it may not be very important clinically: infants with less severe anomalies may be easier to transport to a referral center than those with the more severe anomalies; thus, if their diagnosis is missed, it might bruise the ego of the sonologist more than endanger the newborn. This should not be interpreted as a license to miss anomalies but as a temporary consolation while we improve our technique and resolution. Finally, the natural evolution of some anomalies may be such that they only appear in the third trimester and be absent earlier. Examples of this include

premature occlusion of the foramen ovale[93], pulmonary stenosis with intact ventricular septum[94], and cardiac tumors[95] among others.

Table ACCURACY OF DETAILED ANTENATAL CARDIAC EXAMINATIONS

Population	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Number of Anomalies	Number of patients
High risk[96]	51	99	95	100	47	3223
High risk[97]	92	99	96	99	75	1022
High risk[98]	63	99	83	99	16	886
Low risk[99]	82	100	95	99	21	5347
High risk[100]	81	NA	99	NA	91	989
High risk[101]	62	100	100	96	13	124
High risk[102]	57	NA	100	NA	49	NA
High risk[103]	91	99	84	99	23	303

PROGNOSIS

There is little or no data concerning the prognosis of cardiac anomalies detected *in utero*. Survival data are always derived from studies of infants recognized postnatally. These series are biased since all the worst cases, which do not make it to the pediatric cardiologists, are not included in the assessment of the prognosis[104]. Unfortunately, a large number of the *in utero* detections are *ipso facto* the worse cases, and thus their prognoses are worse than those commonly quoted. Overall only about 32% of the fetuses detected survive in continuing pregnancies[105],[106]. Further, even if we detect the major findings, numerous accessory (but important) anomalies often escape prenatal detection. As the detection rate improves, we will probably detect anomalies that are subtler and the prognosis may improve. Since patient counselling has to be done, our rule of thumb is that when the defect appears small and no consequential anomalies (hydrops, growth retardation, polyhydramnios, arrhythmias, etc.) are noted, we tend to use the postnatal data, while when consequential anomalies are seen we explain that postnatal data are probably optimistic. Generalizations are rarely meaningful for individual patients when a complete assessment of the extent of the disease is not available. In spite of their often overly encouraging bias, pediatric cardiologists should be consulted for each case, and the parents encouraged discussing the future of their child with them.

The presence of a few findings carries an almost uniformly fatal prognosis. These include the association of a structural anomaly with 1) hydrops, 2) bradycardia, 3) tachyarrhythmia refractory to therapy, 4) cardiomegaly (heart greater than half of the chest), 5) Ebstein's anomaly with large right atrium, 6) chromosomal anomaly, 7) absent or reverse Doppler signal in the umbilical cord[107] and 8) growth retardation[108]. Bradycardia with a rate inferior to 50 bpm also carries a poor prognosis. When no structural anomaly is found, hydrops might represent a feto-maternal hemorrhage and the newborn may recover remarkably well.

OTHER TESTS TO PERFORM

Because approximately 30-40% of cardiac anomalies are associated with chromosomal disorders, a karyotype is indicated. Since extracardiac anomalies are present in 25-50%[109], a full scan is recommended. Consultation with others (sonographers, cardiologists, perinatologists, geneticists and the local guru) is highly recommended. We never scan these fetuses without involving the pediatric cardiologists, and we try to have multiple staffs' members do the examination. Pediatric cardiologists have a tendency to limit their examination to the heart, and it is not uncommon that they overlook simple anomalies that can pose as cardiac anomalies, the most common being a diaphragmatic hernia[110]. When time allows, we try to repeat the examination before 24 weeks to allow the parents to make their decision on the best possible grounds.

Whenever possible, outside consultations should be done by sending the patient, not a tape. It is often exceedingly difficult to follow the mental process of another investigator, and tapes are not as useful in cardiac evaluation as they are for other areas of congenital anomalies.

OBSTETRICAL MANAGEMENT

In view of the poor overall prognosis of cardiac anomalies detected *in utero*, parents should be informed that termination is an option when the lesion is recognized before the legal limit for termination. After the legal limit for termination, the obstetrical management depends on the nature of the anomaly. When a fatal prognosis is expected, a conservative management of fetal distress is advised (no cesarean section). When a salvageable infant is expected, there is usually no reason to deliver prematurely, since for most cardiac anomalies there is no deterioration of the cardiac function *in utero*. Obstetrical management will then aim at delivering to the cardiac surgeon an infant as stable as possible (prevent respiratory distress syndrome and stabilize arrhythmias). Premature delivery may be recommended in a few exceptions in which the lesion is treatable and the fetus presents signs of progressive degradation of the cardiac condition (decreased flow on Doppler, appearance of hydrops). Such conditions include aortic[111] or pulmonary stenosis and premature closure of the foramen ovale or ductus. Prenatal treatment of arrhythmias has been achieved successfully on numerous occasions and should be attempted.

NORMAL VARIANTS

CARDIAC ECHOGENIC FOCUS

The detection of fetal intracardiac echogenic focus by ultrasound was first described in the mid-1980s[112,113,114]. These echogenic foci have also been referred to as "golf balls" and were thought to be entirely benign, with no association with karyotypic abnormalities[114,115,116]. However, in the past decade many papers has suggested an increased association with fetal trisomies and in particular that it could be considered a sonographic marker for Down syndrome[117,118]. Although the literature remains controversial it is clear that the significance of the echogenic focus is different to high and low risk population. An estimation of an individual patient's prior risk of Down syndrome based on age and other sonographic markers is important to the assessment of the risk. In practice, if no other anomalies are detected and the

patient is less then 35 years of age and the triple screen is normal we do no further investigations.

PERICARDIAL FLUID

Normal pericardial fluid should not exceed a 2 mm layer and does not surround the whole heart[119]. Pericardial fluid usually accumulates in conditions that lead to hydrops: hypoplastic left heart[120], teratoma, rhabdomyoma, hemangioma, tachyarrhythmia, chorioangioma, saccrococcygeal teratoma with hemorrhage, endocardial cushion defect, cardiomyopathy, Rh disease, pericarditis associated with renal agenesis or posterior urethral valve and twin-to-twin transfusion[121].

ATRIAL SEPTAL ANEURYSM

An atrial septal aneurysm is a localized redundancy or bulging of the atrial septum into the left atrium that can be differentiated from the normal foramen ovale flap by its greater extension in the left atrium. The aneurysm may reach the free wall of the atrium or the mitral valve. It is more mobile than the normal flap but lacks the double closure normally associated with the normal motion of the foramen ovale flap[122]. In severe cases, there may by right-sided enlargement or even paradoxical motion of the septum[123]. The aneurysm does not prevent the normal right-to-left shunting. Atrial septal aneurysms are a common but often overlooked finding which might represent a normal variant. Occasionnally they may be associated with arrhythmias such as supraventricular tachycardia and premature atrial contractions.

Associated anomalies
include atrial septal defects, mitral and tricuspid valve prolapse, atrioventricular valve obstruction, pulmonary venous obstruction and arrhythmias.

Prognosis
Spontaneous closure is the rule (the pediatric cardiologist chuckles again), and the rare complications occur when the aneurysm is large enough to interfere with the mitral apparatus. Postnatal scans can be enhanced by contrast injection[124].

RIGHT SIDED PROMINENCE

Since the right atrium is the unique chamber to receive the entire cardiac output in the fetus, a mild predominance can occur. Sometimes in the four-chamber view the relative sizes of the chambers look abnormal, with a desproportion between right and left side. It is possible for a normal fetus to have not only the right atrium but also the right ventricle prominent, with no other pathological signs. In this situation, after we rule out congenital obstructive lesions such as pulmonary stenosis and restrictive ductus arteriosus, we cannot be a hundred percent sure that a "silent" coarctation isn't there[125].

TRICUSPID REGURGITATION

Fetal tricuspid regurgitation has been described in association with some pathological situations such as fetal cardiac tachyarrythmias, nonimmune hydrops, congenital heart diseases and fetal ductal constriction. Mild or trivial tricuspid regurgitation with normal heart

anatomy is more common after birth than in fetal life but usually does not affect clinical neonatal outcome[126].

Cardiac textbooks are usually organized by pathological entities. This is very useful for the clinician when he knows what disease is at hand. The challenge that we face is that we rarely know what disease is present and we have to establish it from rather incomplete data. We have a limited view of anatomy and, because of the size and motion of the fetal heart, a rather limited resolution. Further, structures that are easy to recognize in the newborn (such as the atrial appendage and the bronchus) are not visible in the fetus. Finally, since flow across shunts (ventricular septal defect for instance) is only partial because of the equal workload of both ventricle and the parallel circulation, the use of Doppler is more limited than in the newborn.

In this section we will attempt to review the most common abnormal findings in fetal echocardiography and suggest what diseases could cause them. The reader can then review the section concerning this disease for additional clues and possible findings. We realize that this approach is still in its infancy, since few diseases have been fully described in the fetus and their severity is variable.

As in other areas of prenatal diagnosis, the lesions recognized *in utero* are bound to be considerably more severe than those detected in the newborn or in the child: a fair proportion of those fetuses will die of cardiac failure before they ever have a chance to be seen by the pediatric cardiologist. Diagnostic criteria used in children or even in newborns are therefore not all applicable to the fetus. Another caveat is that a few structural anomalies in the newborn are normal conditions of the fetus. Of course, patent ductus arteriosus comes to mind first, but ostium secundum atrial septal defect is unlikely to be recognized as such in the fetus.

ENLARGEMENT OF THE HEART

We have lumped under this section diseases that present because *something is too big*. This may be due to a global or a focal enlargement. Many entities appear under different headings.

GLOBAL ENLARGEMENT

In this category, the architecture of the heart in the four-chamber view appears grossly normal, yet the overall size is too large. Global enlargement usually results from cardiomyopathy (endocardial fibroelastosis), regurgitation of an atrioventricular or semilunar valve, extracardiac shunts (chorioangioma) or obstructive lesions (either intracardiac such as aortic stenosis, premature closure of the ductus, truncus arteriosus, tumors, etc. or extracardiac such as true knot of the cord). A few other conditions such as some renal anomalies (bilateral multicystic kidney disease, renal agenesis) and skeletal dysplasia (thanatophoric dysplasia, achondrogenesis, short-rib-polydactyly, etc.) may also present with an apparent cardiac enlargement that results from hypoplastic lungs and/or chest.

INCREASED MYOCARDIAL THICKNESS

Increased myocardial thickness occurs in endocardial fibroelastosis, and univentricular hearts. Localized thickening of the interventricular septum (larger than either free wall) is characteristic of fetuses of diabetic mothers and of familial asymmetric septal hypertrophy.

This is essentially represented by the cardiac tumors and by prenatal myocardial infarction that presents as brightly echogenic masses.

ENLARGED CHAMBER

A large right atrium is present in tachyarrhythmias, Ebstein's anomaly, Uhl's anomaly, idiopathic right atrial enlargement[127], common atrium, pulmonary atresia with regurgitant tricuspid, pulmonary stenosis with intact interventricular septum and premature closure of the foramen ovale[128].

The right heart is enlarged in premature closure of the ductus, double outlet right ventricle, tetralogy of Fallot with congenital absence of the pulmonary valve, coarctation of the aorta and aneurysms of the vein of Galen. The left heart can be enlarged in dilated myocardiopathies, critical aortic stenosis and congenital mitral regurgitation. A cardiac tumor can obstruct the outflow of any chamber and create a massive dilatation[129] of the cavity upstream. Fetal hydrops is commonly associated with these.

ASYMMETRY OF THE HEART

The right chambers and the pulmonary artery should be about 10-20% larger than the left counterpart[130]. With a larger asymmetry (ratio of the right ventricle over the left ventricle greater than 1.3), a search for an associated anomaly should be carried out.
Although the asymmetry may result from overload of one side by a shunt such as a vein of Galen aneurysm[131], the cause will most commonly be attributable to an obstructive lesion. These include 1) coarctation of the aorta, 2) atresia of a semilunar valve or great vessel, 3) interruption of the aorta, 4) regurgitation at an atrioventricular valve, 5) tetralogy of Fallot, 6) premature closure of a shunting structure (ductus or foramen ovale) and 7) parachute mitral valve[132]. A few miscellaneous anomalies (such as trisomy 18[133] or diaphragmatic hernia[134]) can also produce asymmetry. Progressive enlargement of the right side indicates developing failure.
For marked asymmetry with one side barely visible, see the next section on "Incorrect number of chambers".

INCORRECT NUMBER OF CHAMBERS

TOO FEW

Less than four chambers results from assimilation of two cavities into one (common atrium, endocardial cushion defect, univentricular hearts, asplenia) or from the hypoplasia/aplasia of a cavity that is not perfused (atrioventricular or semilunar valve atresia).

TOO MANY

Normal structures such as the Eustachian valve or a Chiari network can mimic an extra chamber. An extra chamber exists in cor triatriatum where a membrane separates the pulmonary veins from the rest of the left atrium.
In anomalous pulmonary venous return with cardiac return, the distended coronary sinus may appear as an additional chamber in the back of the right atrium. A septal aneurysm can similarly pose as an additional chamber located between the two atria. Finally, an extra chamber (an ejection chamber) may coexist with a univentricular heart. This ejection chamber replaces the missing ventricle and the count of chamber is restored.

ANOMALIES OF POSITION

DEXTROCARDIA

Dextrocardia occurs in the cardiosplenic syndrome. Cardiac tumors may displace the heart into the right hemithorax. This would more properly be classified as a dextroposition (see below), if the tumor were not intrinsic to the heart.

DEXTROPOSITION

The heart can be on the right side of the chest because the left side is occupied by a diaphragmatic hernia, cystic adenomatoid malformation of the lung, congenital lobar emphysema, pleural effusion[135], and chylothorax or because the right side is empty in cases of right lung agenesis.

ECTOPIA CORDIS

When the heart is not entirely contained in the chest, it usually herniates through the chest wall, the diaphragm or into the cervical region. When associated with an omphalocele the condition is referred to as *pentalogy of Cantrell*.

ABNORMAL ECHOGENICITY

An increased echogenicity can be *focal* (fibrous changes in the tensil apparatus, air in fetal demise, dystrophic valves, usually atresia), *localized* (rhabdomyoma, fibroma, myocardial infarction) or *diffuse* (endocardial fibroelastosis). When outside, but adjacent to the heart, consider a teratoma, diaphragmatic hernia or a cystic adenomatoid malformation of the lung.

ABNORMAL VESSELS

The arteries and veins can be abnormal because of their number, size, shape, connections, position or echogenicity.

NUMBER

Too many vessels are seen in proximity of the heart in persistent left superior vena cava, double aortic arch and anomalous pulmonary venous return. Too few vessels are characteristic of single outlet hearts (semilunar valve atresia, some forms of atrioventricular atresia, and truncus).

SIZE OR SHAPE

Localized thinning of the aorta occurs in tubular hypoplasia, coarctation, calcinosis, and atresia[136]. A thin pulmonary artery should suggest pulmonic or mitral atresia.
An abnormally large great vessel is found 1) when the combined cardiac output exits through a single vessel such as in truncus, the aorta of fetuses with pulmonary atresia, and the pulmonary artery in aortic atresia, 2) in cases of overcirculation (vein of Galen aneurysm) and 3) with regurgitation (absence of the pulmonary valve results in a very large proximal pulmonary artery). Jet phenomenon rarely contributes to visible vessel enlargement in the fetus until late in the gestation and is best detected by Doppler[137].

CONNECTIONS

Abnormal connections are mainly represented by interrupted aortic arch and total anomalous pulmonary venous return. Discontinuity between the anterior aortic wall and the interventricular septum occurs in tetralogy of Fallot, truncus arteriosus and double outlet right ventricle. In the first two conditions the aorta is said to *override* the septum.

The aorta and pulmonary artery should cross each other. The pulmonary artery passes in front of the aorta and goes from left to right. When they arise from the heart side-by-side, search for double outlet right ventricle and corrected or uncorrected transposition of the great vessels. When the aortic arch is on the right side, there is a 65% chance of cardiac anomalies of which tetralogy of Fallot (90%), truncus and transposition are the most common. Double outlet right ventricle, atrial septal defect, ventricular septal defect, and coarctation can also be found. Another 34% will have vascular rings[138], which are probably not detectable by ultrasound yet.

ECHOGENICITY

A striking increase in echogenicity suggests aortic calcinosis.

ABNORMAL RHYTHMS

Should be divided into irregular rhythm within 100-160 bpm, tachyarrhythmias and bradycardia.

ABNORMAL VALVES

An atrioventricular valve that is not visible should suggest an Ebstein's anomaly or an endocardial cushion defect when two ventricles are present. When only one ventricle is visible and a bright band of echo replaces the valve, the likely diagnosis is atresia of the valve.

HYDROPS OF CARDIOVASCULAR ORIGIN

The global accumulation of fluid in the fetus (subcutaneous, ascites, pleural and pericardial effusion) is called hydrops and has numerous etiologies (see chapter Hydrops ***). In the past, immunological causes such as Rh disease were, by far, the most common. With improved prevention of Rh disease, non-immune causes have become more prevalent. Between 20 and 80% of non-immune hydrops are due to a cardiovascular cause (structural anomaly, arrhythmia or non-immune anemia)[139]. The present discussion will be limited to hydrops of cardiac etiology. Fetuses with hydrops will often present clinically with polyhydramnios, bradycardia, preterm labor or maternal preeclampsia.

MECHANISMS RESPONSIBLE FOR HYDROPS

Different mechanisms have been invoked to explain the hydrops in cardiovascular anomalies. In cases of anemia (Rh disease, alpha thalassemias, fetomaternal transfusion, etc.), the hepatic extramedullary hemopoiesis compresses the portal vessels and decreases albumin production. The low plasma colloid pressure is then responsible for the hydrops[140] and can be treated by albumin infusion[141]. Some Doppler studies have shown that in these fetuses the cardiac output is within normal limits, suggesting that the hydrops does not result from congestive heart failure alone [142]. Other studies of fetuses with congenital red cell anemia (and thus without hepatic hemopoiesis) have shown high output[143]. Increased capillary permeability has also been implicated. In most cardiac anomalies, however, the hydrops results from hemodynamic disturbances. The flow may be obstructed by a mechanical obstacle, either inside the heart (atresias, increased viscosity of the blood of the recipient twin) or outside (compression of the vascular pedicles by a mass, true knot of the cord), or it can be inefficient because the ejected fraction is too small (tachycardias) or because of regurgitation.

Differential diagnosis

When an immune or viral origin has been excluded, other causes such as fetomaternal hemorrhage should be investigated. The signs that evoke a cardiovascular etiology include: a dysrhythmia, a structural anomaly, and polyhydramnios. The association between polyhydramnios and hydrops is often a sign of cardiovascular anomaly.

SIGNS OF CARDIAC FAILURE

Signs of cardiac failure include dilatation of the right-sided cavities, fluid collections (ascites, pleural, pericardial, subcutaneous), polyhydramnios, growth retardation, decreased movements, bradycardia, decreased maximal velocity in the great vessels, hepatic and umbilical vein enlargement and hepatomegaly (highly subjective).

HYDROPS WITH A VISIBLE CARDIAC ANOMALY

Search for valvulopathy (atresia, stenosis, insufficiency) of either valve, tumors, endocardial fibroelastosis, myocarditis, truncus arteriosus with regurgitation, tachy- or bradycardia, Ebstein's anomaly, hypoplastic heart (right or left), ectopia cordis, premature closure of the foramen ovale or ductus, double outlet right ventricle, or tetralogy of Fallot.

HYDROPS WITH AN APPARENT NORMAL HEART

Think of shunt lesions (vein of Galen aneurysm, chorioangioma, hepatic arteriovenous fistulas) blood disorders such as anemias (fetomaternal transfusion, immune diseases, thalassemia, congenital red cell anemia, etc.) or congestive heart failure from obstruction to the flow, either by hyperviscosity (twin-to-twin transfusion syndrome) or by a mechanical obstruction (true knot of the cord, umbilical vein thrombosis, cardiac teratoma, cystic adenomatoid malformation of the lung, etc.).

FETAL ANEMIAS

Fetal anemias result from three distinct mechanisms: hemolysis, bleeds and impaired production. Hemolysis is usually of immune origin and due to incompatibility between the maternal and fetal antigens, in a sensitized mother. They include Rh antigens (D, c, E, C), ABO antigens (A, B) and Kell (K). Hemolysis can also result from toxic exposure such as glucose-6-phosphate dehydrogenase deficiency. Bleeding occurs in fetomaternal hemorrhage, twin-to-twin transfusion and sacrococcygeal teratomas[144]. Impaired production occurs in pure red cell anemia (Blackfan-Diamond syndrome) and thalassemia.

FUNCTIONAL ABNORMALITIES

PREMATURE CLOSURE OF THE FORAMEN OVALE

Premature closure of the foramen ovale may occur as early as the second trimester[145] but usually occurs late in the third trimester and presents as a progressive hydrops with dilatation of the right chambers and bulging of the interatrial septum into the left atrium. Other findings include: 1) an abnormal M-mode tracing[146] with absence of the two peaks of the normal motion of the foramen ovale, 2) failure to visualize the foramen ovale flap and 3) absence of transatrial flow on Doppler[147].

Although the postnatal echocardiographic diagnosis cannot be established (since the foramen ovale ought to be closed soon after birth), the diagnosis is known by pathologists who consider the diagnosis when the foramen ovale measures less than 2 mm[148]. A few cases have been

reported in association with atrial septal aneurysm [149],[150], supraventricular tachycardia[151] and congenital heart diseases [152][153]. Drug abuse such as crack and abortion attempt with misoprostol, a synthetic analogue of prostaglandin E2 has been described[154]. When supraventricular tachycardia is present, it can be converted to sinus rhythm by digitalis. Premature closure of the foramen ovale interrupts the flow of oxygenated blood to the left ventricle. Because of the separation of flow in the right atrium, the coronary flow is normally oxygenated blood. The replacement of this oxygenated blood by desaturated blood is one element that induces the cardiac failure. The second element is the right ventricular overload, which induces right heart failure and, presumably also the arrhythmia. The arrhythmia contributes to the cardiac failure.

Associated anomalies

The premature closure may be secondary to late aortic stenosis: the increase in left ventricular pressure produces mitral regurgitation, which, in turn, increases the left atrial pressure. This causes a functional closure of the foramen ovale which leads to the right heart overloading[155].

Prognosis

The condition resolves spontaneously at birth (the pediatric cardiologist chuckles at the sonologist). When the condition has been longstanding, the prognosis is poor[156], but when the onset is in the late gestation, the infants do well *ex-utero* and should be delivered as soon as lung maturity is documented. This is one of the rare cardiac anomalies where premature delivery may be indicated.

PREMATURE CLOSURE OF THE DUCTUS ARTERIOSUS

Patency in the ductus arteriosus is necessary to allow right-to-left shunting, bypassing the high-resistance pulmonary vascular bed. Prenatal diagnosis of ductus arteriosus constriction or closure is considered to be uncommon and usually results in congestive heart failure, hydrops fetalis, and perinatal death. In this situation fetal ductal waveform analysis show an increase in maximal and end-diastolic flow velocities. Premature closure of the ductus arteriosus could be related to a congenital heart defect[157] or maternal administration of indomethacin (a tocolytic agent)[158]. Other drugs have been related to ductus constriction such as diclofenac (antiinflamatory agent), sympathomimetic drugs for nasal decongestion and high dose aspirin [159]. Idiopathic ductal stenosis has also been reported[160]. The systolic flow velocity in the human fetal ductus is the highest detectable velocity in the normal fetal cardiovascular system, exceeding intracardiac velocities and umbilical flow velocities. The maximum systolic velocity ranges from 50 tp 140 cm/sec, with a mean of 80 cm/sec. Normal ductal diastolic velocity ranges from 6 to 30 cm/sec [161]. It is important to distinguish fetal ductal constriction (pulsatility index <2) from increased right ventricular output (pulsatility index >3, normal end-diastolic flow velocities[162]

CARDIAC HYPERTROPHY IN A FETUS OF A DIABETIC MOTHER

A transient and nonfamilial form of hypertrophic cardiomyopathy with a unneventfull outcome has been described in infants of diabetic mother. As in neonatal life, fetuses with a ratio of interventricular septal-to-left ventricular wall thickness of 1.3 or more were diagnosed as having asymetric septal hypertrophy[163].

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