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A Review: Newer, Noninvasive Cardiac Diagnostic Methods

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This review article will focus on the application of two noninvasive techniques that have become increasingly more useful in the diagnosis and management of infants and children with heart disease. In a general sense, noninvasive diagnostic techniques provide two types of information; first, one seeks anatomic information in order to more clearly describe the architectural details of the heart and circulation, and, second, one hopes to derive data allowing analysis of functional characteristics of the circulation. The ability to obtain important structure-function correlations by the use of both scintillation scanning and cardiac ultrasound forms the basis for their widespread applicability in noninvasive diagnosis. We will describe selected aspects of current applications of scintillation scanning of the lungs and heart and of echocardiography, and will attempt to indicate new and interesting directions that may be anticipated by continuing developments in these fields. We await, with interest, additions to the armamentarium of the diagnostician that may be expected in the future from electrocardiographic-gated, computerized axial tomograms of the heart and from flow velocity data provided by range-gated, pulsed Doppler technology.

It should be understood that noninvasive methods infrequently offer a substitute for invasive hemodynamic and angiographic studies performed in the cardiac catheterization laboratory. Rather, the former most often provide valuable ancillary data that assist the clinician appreciably in decisions concerning patient management.

SCINTILLATION SCANNING

Isotopes are employed to quantify the distribution of pulmonary blood flow in patients with a wide variety of acquired and

congenital heart disease in order to determine indirectly the levels of pulmonary venous and arterial pressures (12, 13) and to determine the patency of systemic arterial and systemic venous-pulmonary arterial anastomosis (9, 12). In addition to these lung scanning methods which employ radionuclide labeled macroaggregated human serum albumin, radionuclide angiography is utilized to view alterations in the anatomy of the heart and great vessels, and to detect and quantify left to right, intra-, or extra-cardiac shunts (2-4, 22, 33, 35). The latter studies are performed after intravenous infusion of ^{99m} technetium with a scintillation camera coupled to a computer tape storage system.

ALTERATIONS IN REGIONAL PULMONARY BLOOD FLOW

VERTICAL DISTRIBUTION OF FLOW

The distribution of pulmonary blood flow vertically or to either lung may be determined in an accurate and reproducible manner by scintillation scanning of the lungs (12). The rationale for evaluating the vertical distribution of pulmonary blood flow resides in the importance of distinguishing patients with both pulmonary arterial and venous hypertension from those with pulmonary arterial hypertension alone.

In this regard, more precise selection may be anticipated of patients requiring an accurate hemodynamic assessment of pulmonary flows and resistance. It is recognized that because of the influence of gravity on the low pressure vascular bed, normal erect subjects have greater blood flow to the lung bases than to the apices. In patients with pulmonary venous hypertension, there is a relative increase in blood flow to the apices and a decrease in perfusion to the lung bases. A linear relationship

exists between the magnitude of the shift of blood flow toward the apices and the level of mean left atrial pressure (12). When pulmonary blood flow increases, as it does in patients with left to right cardiac shunts, the normal difference in flow between the upper and lower pulmonary zones decreases, even if the pulmonary artery pressure remains normal (13). Patients with left to right shunts with pulmonary arterial hypertension and without pulmonary venous hypertension show a further reduction in the difference in flows between the apical and dependent zones of the lungs. When both pulmonary arterial and venous pressure rise, blood flow to the apices of the lung increases whereas flow to the bases diminishes, and the result is an inversion of the pattern observed in normal erect subjects.

Thus, the evaluation of the vertical distribution of pulmonary blood flow may be of especial aid in pre- and postoperative situations in which pulmonary venous hypertension may be a problem. In this regard, we have used this method to screen patients with pulmonary hypertension for potentially correctable lesions such as cor triatriatum and mitral stenosis, and to serially evaluate patients after mitral valve surgery for acquired or congenital lesions of the mitral valve in postoperative patients with endocardial cushion malformation, and most recently, after Mustard operation in those patients with transposition of the great arteries in whom pulmonary venous obstruction may result from the interatrial baffle.

DISTRIBUTION OF FLOW TO BOTH LUNGS

An analysis of the distribution of pulmonary blood flow to both lungs may also be of assistance in clinical management. In the normal subject, the distribution of blood flow to the right lung is $53 \pm 2.3\%$ (SD) (13). It has been noted recently that in some patients with transposition of the great arteries, pre- and/or post-Mustard operation scintillation scans of the lungs may show a remarkable reduction in isotope accumulation to the left lung (8, 42, 60). It is not yet known with certainty whether all postoperative patients with this finding show a similar abnormal preoperative distribution of pulmonary flow. The markedly asymmetric distribution of flow to both lungs likely results from the altered spatial orientation of the main pulmonary artery and elongation of the course of the left pulmonary artery favoring flow to the right lung (8).

The combination of xenon-133 lung ventilation-perfusion scan and technetium-99m radionuclide angiograms has been shown recently to be of importance to assess changes in pulmonary ventilation and perfusion pre- and postoperatively and to evaluate intracardiac shunting or atrial baffle obstruction postoperatively (42).

Studies of patients with tetralogy of Fallot pre- and postsystemic-pulmonary arterial shunting have demonstrated that, although total pulmonary blood flow is increased after a systemic-pulmonary anastomosis, the augmented flow to the lung on the side of the anastomosis may be largely composed of oxygenated shunted blood, whereas the flow to the opposite lung is largely unsaturated systemic venous blood (13). In addition, a patent shunt changes the distribution of blood entering the main pulmonary artery from the right ventricle, diverting most of the systemic venous return to the lung on the side opposite the anastomosis. Xenon-133 ventilation studies may be performed in these same patients (1). Since the distribution of ventilation most often remains symmetric, some patients are noted to have significant ventilation-perfusion imbalance. Moreover, subsequent operative correction of the tetralogy anomaly may not result in the restoration of normal ventilation-perfusion relationships (1). These observations lend support to the single stage surgical correction approach, rather than the palliative followed by repair approach to surgical management.

RADIONUCLIDE ANGIOGRAPHY

This technique utilizes an Anger scintillation camera that detects the passage through the heart and lungs of a radioactive

bolus of intravenously administered technetium-99m. Polaroid exposures are used to demonstrate flow through the central circulation. The camera output is also fed directly into a dedicated computer-controlled system and recorded on digital magnetic tape. This system allows review of the complete sequence so that Polaroid prints can be obtained at desired intervals and also permits selection of one or more anatomic areas of interest from which the analog tracings of changing count rate, which is equivalent to flow, may be plotted as a function of time. Upon replay of recorded data, these areas of interest may be positioned electronically to correspond to a cardiac chamber of great vessel or a portion of either lung. In the latter position, radionuclide pulmonary time activity, or vascular "dilution curves," may be inscribed (2, 3, 22, 35).

When radionuclide angiography is used to evaluate the anatomic details of cardiovascular malformations, the radioisotope images, in general, reflect the findings observed by standard contrast angiocardiology. Although the sequential radioisotope images do not provide the same degree of fine detail as x-ray angiocardiology, many altered intra- and extracardiac flow patterns can be identified and the compromise in image resolution may be acceptable since it is balanced by the simplicity, speed, and safety of the method (22, 33). In contrast to angiography, the isotope images do not provide the fine anatomic details required preoperatively to plan surgical repair of anomalies.

SHUNT DETECTION

Radionuclide angiography finds its widest application in the detection and quantification of left to right shunts. As mentioned above, the key to these analyses is provided by the inscription of pulmonary vascular isotope histograms. In our initial studies we employed a count ratio technique to analyze pulmonary vascular isotope dilution curves (22). It was clear that the absolute presence or absence of a shunt could be predicted with great accuracy with this technique, whereas the precise magnitude of the shunt was less well predicted in the absence of ancillary clinical data. Subsequently, two area ratio techniques have been employed to calculate shunt size from a ratio of areas under the pulmonary time activity curve. The areas are defined by fitting a mathematical function to the original data. One method uses a Steward-Hamilton extrapolation of the downslope of the curve (3), whereas the other employs γ function fitting of the pulmonary activity curve (35). A precise evaluation of the accuracy of the count ratio and two area ratio techniques have been performed (2). The count ratio technique did not adequately discriminate patients with shunts from those with either congestive heart failure or valvular regurgitation lesions in whom false positive results were obtained occasionally. Both area ratio techniques obviated this problem. Shunt quantification appears to be most accurate when the γ function algorithm is employed. Although the γ function method gives a higher correlation with oximetry than exponential fitting, the former requires a computer to extract the shunt recirculation curve from raw data. Thus, the γ function method seems desirable for those hospitals with appropriate computer facilities, whereas the exponential fitting method provides a useful alternative in other situations.

The applicability of a noninvasive technique to estimate shunt size in postoperative patients is self-evident. In patients who have undergone operative closure of their shunts, postoperative catheterizations may be avoided if the scanning method clearly indicates the absence of a residual shunt. Shunt detection and quantification is also of practical importance to screen and distinguish that large group of patients suspected of having left to right shunts from those patients with other forms of heart disease or insignificant functional murmurs. Moreover, the method may be employed to follow serially patients who may experience spontaneous closure of their shunts and those in whom a serial estimate of the magnitude of left to right shunting may detect the onset of pulmonary vascular obstructive disease.

It should be recognized that the scanning techniques described in the present report impose little risk or discomfort to the patient. Since radiation exposure to the patient is remarkably low when compared with cineangiocardiology, the techniques can be serially applied in patient management.

ECHOCARDIOGRAPHY

The most exciting new approach in the noninvasive evaluation of heart disease in infants and children is provided by ultrasound cardiography or echocardiography. This major advance has already had significant impact upon the practice of pediatric cardiology, and, indeed, it may be anticipated to substantially enhance diagnostic and management capabilities in the future.

SINGLE CRYSTAL ECHOCARDIOGRAPHY

Until recently, only single crystal echocardiographic techniques were used by pediatric cardiologists. With continuous recording techniques and high frequency transducers data have been collected defining the range of normal for the dimensions and motions of the great vessels and cardiac structures in infants and children (16, 20, 56), to evaluate cardiac performance by analyses of a host of indices of myocardial contractile and pump function (19, 25, 28, 43, 46, 62), detect and assess the magnitude of intercirculatory shunting (5, 7, 10, 29, 34, 39, 40, 41, 49, 50, 52, 53, 55, 58, 59, 64), to analyze the severity of left ventricular outflow tract obstructive lesions (15, 27, 54, 63) and the levels of pulmonary pressures (26), and, of course, to derive information concerning the anatomy of the heart, *per se* (16, 37, 38, 45, 57). The latter area especially has been the subject recently of comprehensive reviews and will not be dealt with in the current discussion. We have chosen to be selective and will focus our remarks upon the application of single crystal techniques to serial assessment of left to right shunts across a patent ductus arteriosus in the premature or newborn infant, to the combination of echocardiography and saline contrast techniques for the assessment of right to left and left to right intracardiac shunting, and to the derivation of systolic time intervals and their combination with ejection phase parameters of cardiac performance for the evaluation of cardiocirculatory function.

PATENT DUCTUS ARTERIOSUS IN PREMATURE OR NEWBORN INFANTS

Left atrial size, which may be measured accurately by echo, is increased in patients with left to right shunts distal to the atrioventricular valves. Serial analysis of the left atrium to aortic root dimension ratio (LA/Ao) was shown initially by Silverman *et al.* (55) to detect alterations in the magnitude of left to right shunting across a patent ductus arteriosus. Our laboratory (49, 50) and others (5, 7, 39, 64) have shown that appropriate directional changes in the LA/Ao ratio accompany both medical and surgical maneuvers that alter the magnitude of shunting and have established the fact that serial determinations of left atrial dimension are of major assistance in patient management. Most recently, for example, we have used the serial analysis of the LA/Ao ratio to confirm ductal closure induced by inhibition of prostaglandin synthesis in a group of respirator bound, premature babies with respiratory distress syndrome and clinical evidence of large volume, left to right shunting across the ductus (14).

Left atrial size determined in conjunction with simplified measures of alterations in left ventricular performance, either the mean velocity of circumferential fiber shortening (mean VCF) or fractional shortening of the left ventricle, have also proved of immense benefit in diagnostically separating infants without a congenital cardiocirculatory malformation but with signs of cardiac failure (hypoglycemia, sepsis, myocarditis, hypoxemia) from those with large left to right shunts (49, 50). Needless to say, the distinction between these two groups of

Fig. 1. The echocardiographically derived ratio between left atrium and aortic root dimension (LA/Ao) is significantly less in normal premature and full term newborns than in those with a large patent ductus arteriosus (PDA) ($P < 0.001$) or in those with nonstructural heart disease. The mean rate of left ventricular circumferential fiber (VCF) shortening is significantly higher than normal in infants with a large left to right shunt across a patent ductus arteriosus ($P < 0.001$), and significantly lower than normal or ductus infants in the presence of depressed myocardial function ($P < 0.001$). The numbers in brackets refer to the number of infants from whom values were obtained.

infants is often necessary in the management of ill newborns. The mean VCF is abnormally elevated in infants with a large ventricular or ductal shunt, even in the presence of cardiac failure (Fig. 1), and both mean VCF and the shortening fraction of the left ventricle are significantly lower than normal in infants with nonstructural heart disease (Fig. 1). The latter infants, however, have a substantial augmentation in left atrial volume and size when compared with normal infants and LA/Ao ratios comparable with newborns with large shunts (Fig. 1). Thus, the infants with cardiac dysfunction, but without a congenital cardiocirculatory malformation, have a high LA/Ao ratio and low mean VCF, or extent of ventricular shortening, whereas the infants with left to right shunts have elevations in all indices. Both groups can therefore be distinguished from each other and from normal subjects.

ECHOCARDIOGRAPHY AND SALINE CONTRAST

Initially, the echoes produced by injection of indocyanine green dye were used as markers to identify the source of intracardiac echoes (11, 17). For example, during cardiac catheterization the selective, rapid injection of indocyanine green dye produced ultrasonic opacification by microbubble formation and one could follow the passage of the ultrasound opaque stream as it traversed cardiac chambers. It has now been demonstrated that normal saline or the patient's own blood after injection into the peripheral or central venous system or into a great artery or cardiac chamber may identify a site of intercirculatory shunting (10, 29, 40, 41, 52, 53, 58, 59). For example, in the postoperative patient with tetralogy of Fallot, saline injected into the superior vena cava produces echoes in right atrium and right ventricle. If the echoes are seen to cross the ventricular septum and enter left ventricle, it is clear that a residual right to left ventricular shunt exists. Figure 2 is an illustration of how the principle of saline contrast opacification may be used in the newborn period. The technique will most likely have its widest application in the postoperative period in recognizing residual shunts at the bedside and may be of additional utility in differentiating cardiac from noncardiac causes of cyanosis in critically ill newborns.

ANALYSIS OF PULMONARY HEMODYNAMICS AND OBSTRUCTIVE LESIONS

Analysis of cardiac valve motions allows measurement of systolic phases of the cardiac cycle without the necessity of

Fig. 2. Echo opacification identifies a right to left atrial shunt after saline injection into the umbilical vein of an infant with a patent foramen ovale catheterized for exchange transfusion. In the upper panel, left ventricular (LV) opacification occurs initially from behind the mitral valve (arrow) just before opacification of the right ventricle (RV). Since the echoes appear from behind the mitral valve rather than across the ventricular septum directly, the shunt is at the atrial level. In the lower panel, imaging at the level of the aortic root (Ao) shows the early echo opacification of the left atrial cavity (LA) (arrow) and later fill of both the aorta and the right ventricular outflow tract (RVOT).

externally recording the carotid pulse and the apex cardiogram. Whereas the latter graphic methods to determine systolic time intervals were employed traditionally to assess left ventricular function, echocardiography has been employed recently to derive timing information relative to the pulmonary circuit, which is, of course, unavailable from external pulse recordings. A good correlation has been shown to exist between pulmonary artery pressure and the pre-ejection period and ejection time measurements derived by echoes from the pulmonary valve (26). Thus, a ratio of right ventricular pre-ejection period to right ventricular ejection time of less than 0.30 is almost always associated with low pulmonary vascular resistance and low pulmonary arterial pressure, whereas a ratio greater than 0.40 almost always indicates elevated mean pulmonary pressures and a pulmonary vascular resistance in excess of 5 units. The latter measurements in

association with loss of the A wave of the pulmonary valve echo trace and the presence of premature systolic closure of this valve appear to be accurate markers for the presence of pulmonary vascular obstructive disease (Fig. 3).

There are now several promising echo applications that aim to assess the severity of aortic stenosis. Thus, it has been shown that determination of left ventricular ejection time corrected for heart rate correlates with the peak systolic pressure difference across the left ventricular outflow tract (54). An excellent correlation has also been found with the severity of stenosis using echocardiographic measurements of end systolic wall thickness and left ventricular cavity transverse dimension, and utilizing a normalized value for left ventricular systolic wall stress (15). Of course, the measurement of left ventricular wall thickness in these patients provides an index of the degree of cardiac hypertrophy created by the obstructing lesion. Thus, it would appear that echocardiography offers a noninvasive method for estimating and predicting the severity of left ventricular outflow tract obstruction that is substantially more sensitive than other currently employed techniques.

CROSS-SECTIONAL ECHOCARDIOGRAPHY—ANATOMIC DIAGNOSIS

Despite the utility of single crystal techniques, they, nonetheless, provide only a "flashlight beam" section of the heart and may not allow an accurate assessment of the spatial orientation of intracardiac structures. Thus, the data provided by single crystal echocardiography in the presence of complex alterations in intra- and extracardiac architecture are often difficult to interpret objectively. Needless to say, it is precisely in those patients with the most complicated cardiac malformations that the pediatric cardiologist would value a reliable noninvasive means to assist in diagnosis.

Fig. 3. Pulmonary valve echogram from a patient with a ventricular septal defect and pulmonary vascular obstructive disease illustrates flattening of the diastolic slope, absence of a presystolic opening motion ("a" (atrial) wave) and premature systolic closure of the posterior pulmonary valve (PPV) cusp followed by a partial reopening. The right ventricular pre-ejection period (RPEP) and ejection time (ET) as well as the RPEP/ET ratio may be calculated from the pulmonary valve trace and the electrocardiogram (ECG). Beat to beat variability in cusp registration and in the duration of pulmonary valve opening (beats 1 and 3 vs. 2 and 4) may be observed occasionally, perhaps due to respiration. CW: chest wall; LA: left atrium.

Fig. 4. Normal multiscan sagittal cross-section. Transducer alignment and image orientation (top), and polaroid photo (bottom). The first element in the transducer (*) is superior. RV: right ventricle; SEPT: ventricular septum; Ao: aorta; LV: left ventricle; LA: left atrium; AML, aMVL: anterior mitral valve leaflet; PML, pMVL: posterior mitral valve leaflet; LVPW: left ventricular posterior wall; RVD: right ventricular dimension, the largest seen in field; LVD: left ventricular dimension, at the level of the leading edge of the AML. Reproduced by permission of American Heart Association, Inc., from Sahn *et al.* (59).

Recently, cross-sectional techniques have been developed that provide a real time, two dimensional format that allows a substantially enhanced appreciation of spatial intra- and extracardiac structural interrelationships. Cross-sectional methods include single crystal stop-action techniques (30, 31) and those that allow real time observations by single (18, 32, 61) or multiple crystal devices (6). Stop-action techniques are not particularly applicable to the study of infants and children who may not remain immobile during the course of study. Motion studies in real time using single crystal scanning methods provide excellent resolution of structures, although the angle of the scanning are limits the size of the cardiac cross-section. Linear array, multicrystal systems provide a large cross-section, but the size of the individual transducers restricts ultrasonic penetration and sharp resolution of deep structures. Technologic advances are occurring at a rapid rate and it has become clear that the cross-sectional approach, irrespective of the exact methodology utilized, greatly facilitates the noninvasive assessment of congenital heart disease since definition is enhanced of great vessel orientation, cardiac chamber position, and outflow tract anatomy.

MULTISCAN CROSS-SECTIONAL ECHOCARDIOGRAPHY

We have had extensive experience in the use of sagittal and transverse cross-sectional cardiac imaging with the multiple crystal (multiscan) method in evaluating the sites of left ventricular outflow tract obstruction (63), endocardial cushion defect (47), the common forms of cyanotic cardiac malformations (48), left to right shunt lesions (21), and tricuspid and mitral valve abnor-

malities (21, 44). Using a 4.5 MHz 20 element transducer, we have evaluated cardiac cross-sectional anatomy in a systematic manner using two sagittal and two transverse views (47). Figure 4 shows a long axis sagittal view of the heart of a normal subject. Four transducer positions are specifically designed to provide visualization of the relative sizes of the right and left ventricles in sagittal section, longitudinal visualization of the ascending aorta, visualization of tricuspid-pulmonary relationships, visualization of the size and course of the main pulmonary artery and visualization of the spatial orientation of the aorta and pulmonary artery in transverse and sagittal views. The echo identification of intra- and extracardiac structures in multiple cross-sectional planes has been validated by viewing catheter echoes and the passage of indocyanine green dye in patients with congenital heart disease during their hemodynamic study (51).

The multiscan technique is especially suitable for defining great artery and cardiac chamber orientation and position. In the normal individual, the great arteries have a spiral relationship to one another and in the transverse plane one observes the right ventricular outflow tract and pulmonary artery wrapping around the aorta from right to left so that the pulmonary artery lies to the left and anterior of the aorta (Fig. 5). Most importantly, in patients with D-transposition of the great arteries, the aorta may be observed to ascend retrosternally, in marked contrast to the normal posterior sweep of the pulmonary artery (48). In transverse cross-section in D-transposition patients the great arteries do not have the normal spiral relationship to one another and the anterior aorta may be seen to lie to the right of the posterior pulmonary artery (48) (Fig. 6).

In patients with tetralogy of Fallot the most important feature seen by multiscan is a disruption of aortic-septal continuity with preservation of mitral-aortic continuity. Moreover, one may almost always detect an enlarged ascending aorta which overrides the ventricular septum (48). The findings in patients with truncus arteriosus are quite similar to those in tetralogy, although a pulmonary artery may not be identified. In addition, in patients with truncus arteriosus, one may suspect the diagnosis by observing multiple and unusual cusp echoes within the truncal root, probably reflecting an abnormal number of cusps of the truncal valve (48). The distinctive findings in patients with endocardial cushion defect consist of multiple echoes in the mitral valve area, anterior mitral leaflet-septal apposition in diastole

Fig. 5. Normal great vessel orientation: transverse. Polaroid still frame from the multiple-crystal system illustrates the spiral relationship of the right ventricular outflow tract (RVOT) and main pulmonary artery (MPA) wrapping from right to left around the posterior aorta (Ao) in a transverse cardiac cross-section at the second intercostal space.

with reduced posterior motion in systole, and reduced excursion of the anterior mitral leaflet (47). In patients with the complete form of atrioventricular canal defect, the anterior leaflet may be observed passing across the plane of the ventricular septum into

the right ventricle during diastole, and, in some of these patients, the anterior mitral leaflet appears to be related to the tricuspid annulus.

Diagnostic findings are present in the various forms of left ventricular outflow tract obstruction (63). In patients with valvar aortic stenosis the aortic leaflets often appear thickened and display an unusual superior mobility with decreased lateral mobility. Poststenotic dilation of the ascending aorta is easily identified with the cross-sectional method. The findings in patients with discrete subvalvar aortic stenosis include a localized thickening in the ventricular septum at its insertion into the anterior wall of the ascending aorta just below the level of the valve. In patients with subaortic stenosis as a result of a parachute deformity of the mitral valve, one can visualize the anterior and posterior mitral leaflets related to one large papillary muscle. In the presence of supravalvar aortic stenosis, the ascending aorta shows an hourglass narrowing superior to the point at which aortic valve motion may be visualized. In patients with idiopathic hypertrophic subaortic stenosis, increased septal thickness and systolic apposition of the anterior mitral valve leaflet to the ventricular septum may be seen obstructing the left ventricular outflow tract.

SECTOR SCANNING CROSS-SECTIONAL ECHOCARDIOGRAPHY

High resolution ultrasound images of cardiac cross-sections are now being obtained utilizing either the mechanical motion of a single transducer to provide a real time sector scan (18, 36) or by systems employing phased array principles to rapidly steer the ultrasound beam through the structures under investigation in order to obtain a high quality tomograph image in real time (32, 61). Electronically steered phased array sector scanning has not yet been applied to problems in pediatric cardiology.

Recently, mechanical sector scanning in the transverse plane has been shown to aid greatly in the evaluation of atrioventricular valve morphology (24). Earlier studies reported a "fish mouth" shape of the mitral valve orifice in transverse sections and suggested further that the size of the mitral orifice could be assessed accurately (23). An extension of these studies in patients with cardiac malformations has shown that transverse plane cross-sectional imaging at the level of the junction of the atrial and ventricular septa allows analysis of complex morpho-

Fig. 6. Altered spatial relationship between aorta (*Ao*) and pulmonary artery (*PA*) in an infant with D-transposition. The aorta lies to the right and anterior and the spiral relationship between the vessels is absent.

Fig. 7. Normal atrioventricular valve (A-V) morphology imaged with the sector scanning system. Imaging is in the transverse plane of the heart. The images are oriented differently from the multiscan illustrations (*i.e.*, chest wall is at the top, right-sided structures are at the left side of each image, and left-sided structures are at the right). The left panel shows A-V valves at the level of the atrioventricular septum. The insertions of the anterior (*ALT V*) and posterior leaflets (*PLTV*) of the tricuspid valve (*TV*) are shown relative to the insertion of the mitral valve (*MV*). *RVOT*: right ventricular outflow tract; *LVOT*: left ventricular outflow tract. An electrocardiogram artifact is seen anteriorly on this image. In the panel the normal fish mouth appearance of the mitral valve is shown in transverse section at the level of the valve orifice.

logic changes involving both the mitral and tricuspid valves, and may, indeed, allow the determination of ventricular situs. This is of especial advantage since conventional single crystal echo techniques have not heretofore allowed the examiner to distinguish the morphologic characteristics of mitral from tricuspid valve. Thus, the technique promises to be of great value in patients with ventricular inversion and L-transposition of the great arteries in whom the mitral valve guards the right-sided ventricle, and in patients with various forms of endocardial cushion defect. Figure 7 provides an illustration of normal atrioventricular valve morphology as imaged by the mechanical sector scanning system.

Cross-sectional echo by sector scanning may not only allow the determination of the actual size of the mitral valve orifice, but may also prove of value in the assessment of the severity of aortic stenosis. The measurement of maximum aortic cusp separation during long axis cross-sectional scanning of the aortic valve, related to the echocardiographically determined diameter of the aortic root at the valve level, appears to provide an index that correlates well with the severity of obstruction (27).

It seems clear that single crystal, and especially cross-sectional echocardiographic approaches, irrespective of the exact method employed, will enjoy their widest application as initial tests to establish diagnosis, as precatheterization studies to more appropriately plan the course of subsequent hemodynamic investigation, and as methods for serially evaluating patients in whom anatomic findings and their functional consequences may change with time. Furthermore, it is evident that echocardiography is applicable to large numbers of patients and provides clinically important information to assist in the diagnosis and management of infants and children with diverse forms of heart disease.

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Alveolar macrophages surfactant
differentiation tubular myelin
lamellar myelin ultrastructure
lysosomes

Maturation of the Rabbit Alveolar Macrophage during Animal Development. I. Perinatal Influx into Alveoli and Ultrastructural Differentiation

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Summary

Rabbit alveolar macrophages (AM's) were collected by tracheobronchial lavage at sequential times during animal development. The total number of cells recovered by this technique was found to increase markedly shortly before birth (Fig. 4). This apparent influx of macrophages into the alveoli continued during the first postnatal week, and, at a reduced rate, throughout the first postnatal month of life (Fig. 3).

Ultrastructurally, AM's of the prenatal period resembled their monocyte precursors, and contained modest numbers of lysosomes and mitochondria, scant lamellae of ribosome-studded endoplasmic reticulum (RER), and a small Golgi apparatus (Fig. 12). A considerable amount of phagocytosed material was observed in these AM's, and consisted largely of cellular debris and

two forms of surfactant-related phospholipids, termed tubular and lamellar myelin (Figs. 12-15). The quantity of these ingested phospholipids increased dramatically shortly after birth, in correlation with the known release of similar material from type II pneumocytes at this time. (Figs. 16 and 19).

During the first postnatal week AM's showed a considerable increase in number of mitochondria and in the development of the RER and Golgi apparatus (Fig. 22). Increased accumulations of lipid droplets were also noted during this period. Ingested material continued to consist largely of surfactant-related phospholipids, but was less abundant at this time.

By 28 days after birth, AM's were nearly morphologically mature (Fig. 25). They showed large numbers of lysosomes and mitochondria, and well developed RER and Golgi apparatuses. Ingested phospholipid material was still visualized, and the in-