Magnification Pulmonary Wedge Angiography in the Evaluation of Children with Congenital Heart Disease and Pulmonary Hypertension

MICHAEL R. NIHILL, M.D., M.R.C.P. AND DAN G. MCNAMARA, M.D.

SUMMARY In order to determine the presence and extent of obstructive pulmonary vascular disease in patients with congenital heart disease, magnified cineangiograms were obtained with a catheter in the pulmonary artery wedge position in 155 infants and children undergoing cardiac catheterization. The wedge angiograms (WA) were analyzed in groups according to the pulmonary hemodynamics: group A — normal pulmonary blood flow (PBF) and pulmonary artery pressure (PAP) (31 patients; 53 WA); group B — increased PBF and normal PAP (46 patients; 69 WA); group C: increased PBF and PAP but a pulmonary vascular resistance (PVR) < 6 u/m² (19 patients; 33 WA); group D — increased PAP and PVR > 6 u/m² (30 patients; 66 WA); group E — pulmonary venous hypertension (15 patients; 27 WA); and group F: infants < 3 months old with a variety of congenital heart defects (14 patients; 19 WA).

WA from group A patients defined the microcirculation of the secondary pulmonary lobule with an evenly tapered, orderly arborization of muscular pulmonary arteries and numerous supernumerary vessels as small as 100 μ in diameter with a full, even granular capillary blush surrounding each small, muscular artery. Increased PBF produced dilatation of the elastic and muscular vessels with engorgement of the lobule, while increased PAP produced tortuosity of the vessels. An elevated PVR was manifest by dilatation and tortuosity of the elastic vessels and a more abrupt tapering of the muscular arteries. Patients with a PVR > 12 u/m² and those with obstructive vascular disease by histological examination (eight patients) showed marked reduction or absence of supernumerary vessels and decreased arborization of the distal muscular pulmonary arteries as well as the other hypertensive changes, and the capillary blush was incomplete, patchy and reticular. Obstructive signs were distributed randomly within the lobules and the lung lobes.

Pulmonary venous hypertension was associated with dilatation of the paralobular veins with a vein-central artery ratio of > 1.3:1. WA in the infants showed no obstructive pattern, and the microvascular morphology reflected the pulmonary hemodynamics seen in groups A, B and C.

We conclude that the presence of obstructive pulmonary vascular disease can be determined in patients with pulmonary hypertension and elevated PVR by magnification wedge angiography. The degree and extent of obstructive vascular lesions can be assessed more readily by this method than by histologic examination or random lung biopsy specimens.

THE CLINICAL USE of magnification pulmonary wedge angiography was first described by Loomis Bell in 1958, to study the morphology of the small pulmonary arteries in patients with pulmonary hypertension. These studies developed from work of Evans and Short, who studied magnified post-mortem angiograms of lungs from patients with various forms of pulmonary hypertension. These workers compared the angiographic morphology with histological data and were able to identify specific angiographic patterns which corresponded with various stages of pulmonary vascular obstructive disease (PVOD).

Since the first publications of Bell, there have been several studies in patients and in experimental animals with varying degrees of pulmonary vascular disease, demonstrating a correlation between the morphological pattern in the wedge angiogram and the stage of pulmonary vascular disease described by Heath and Edwards.

This technique, however, has not had wide clinical application because of technical factors. Until recently, in order to obtain high resolution pictures, it was necessary to construct special equipment with fine focal spot x-ray tubes; large cut films which were used in previous studies limited the number of exposures, and magnification for small vessel visualization was limited. Lung parenchymal damage frequently occurred when powered injections were used, and repeated injections were often necessary to obtain adequate visualization of all vessels. In recent years, fine focal spot x-ray tubes and high-resolution cesium iodide image intensifiers with variable magnification have become available. These factors, together with fine grain cine x-ray film, have made good quality magnification wedge angiography possible in most modern catheterization laboratories.

This paper describes a simplified technique for obtaining magnified pulmonary wedge angiograms in infants and children with congenital heart disease, both those with normal vessels and those with various degrees of PVOD. The purpose of this study was to compare the angiographic morphology in the pulmonary microcirculation with hemodynamic data,
and histological findings in a few instances, to determine if the pulmonary wedge angiogram is a reliable indicator of the presence and extent of PVOD.

Material and Methods

There were 267 wedge angiograms performed in 155 infants and children undergoing diagnostic cardiac catheterization at Texas Children’s Hospital (table 1). Pulmonary blood flow was calculated by the indirect Fick method, using the oxygen consumption data from the tables of LaFarge and Miettinen. Pulmonary vascular resistance index (PVR-units/m²) was calculated by subtracting the mean pulmonary wedge pressure from the mean pulmonary artery pressure and dividing by the pulmonary blood flow (1/min/m²). The ratio of pulmonary-to-systemic blood flow (Qp/Qs) was calculated using measured left atrial saturation (assumed to be 95% if not measured), pulmonary artery saturation, aortic or femoral artery saturation, and superior vena cava saturation. The data from these patients were classified into six groups according to the hemodynamics of the pulmonary circulation determined at the same catheterization (table 1).

Hemodynamic data for all patient groups are listed in table 2.

The 31 patients in group A (normal hemodynamics) included some patients who had repair of tetralogy of Fallot (11 patients), ventricular septal defect (two patients) or pulmonary valve stenosis (six patients). Each of these patients was catheterized at least one year after operation and each had normal pulmonary artery pressure and no left-to-right shunt. All of the patients who had ventricular septal defect repair had normal PVR before surgery. The morphology of the wedge angiogram in these postoperative patients subsequently was identical to that of the patients with a normal pulmonary circulation; thus, we felt justified in including the data from these patients with data from patients with a normal pulmonary circulation. There were seven patients with normal cardiac anatomy and hemodynamics catheterized for electrophysiological studies.

Group B consisted of patients with ventricular septal defect (18 patients), atrial septal defect (10 patients), transposition, patent ductus arteriosus and systemic-to-pulmonary shunts (six patients each). The lesions in group C consisted of ventricular septal defect (10 patients), systemic-to-pulmonary shunts (four patients), atrioventricular canal (three patients) and transposition (two patients).

Increased PVR (group D) was due to transposition (14 patients), ventricular septal defect (eight patients), atrioventricular canal (six patients) and anomalous pulmonary venous drainage and truncus arteriosus (one patient each).

Group E included patients with pulmonary venous hypertension. These patients were grouped together because of various congenital or acquired heart defects which caused pulmonary venous hypertension; pulmonary hypertension was due to left ventricular failure secondary to cardiomyopathy or early postoperative noncompliance with high left ventricular end-diastolic pressures in five patients. Three patients had congenital mitral regurgitation and one had prosthetic mitral valve replacement with obstruction. Three patients had cor triatriatum, two of whom had a large left-to-right shunt; two patients had unilateral pulmonary vein obstruction after a Mustard procedure and one had congenital pulmonary vein atresia on the right side.
Fourteen patients less than 3 months of age were grouped separately (group F); this group included patients with a variety of congenital heart defects and pulmonary hemodynamics, and we assumed that these infants were likely to have grade I and were very unlikely to have greater than grade II pulmonary vascular changes.

The angiograms were performed during cardiac catheterization in a standard laboratory equipped with an untiletable x-ray tube with an 0.6 mm focal spot (Siemens) and a 6/10-inch cesium iodide image intensifier which produces a magnification of 1.3 when in the 6-inch mode, 9 inches from the table top. This was determined by filming a radiopaque grid of 1 cm².

When the end- and sidehole catheter (Goodale-Lubin) was placed in the desired wedge position, the image intensifier was raised 21 inches from the catheter tip, and a 6/10-inch cesium iodide image intensifier which produces a magnification of 1.3 when in the 6-inch mode, 9 inches from the table top. This was determined by filming a radiopaque grid of 1 cm².

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technique was necessary when the endhole catheter could not be wedged because of large dilated elastic pulmonary arteries. Only well-filled, muscular pulmonary arteries < 2 mm in diameter were studied.

An angiographic catheter was used on seven occasions, and satisfactory wedge angiograms of several small pulmonary lobules were obtained, since the dye extruded from the sideholes into small pulmonary arteries.

Recordings of phasic and mean pulmonary artery wedge pressure were made immediately before and after the wedge angiogram. Any contrast remaining in the radiographic field after flushing and withdrawing the catheter was recorded as a stain.

One to five separate wedge angiograms in different positions were performed in each patient; a greater number of injections were made in different areas of the lungs in patients with pulmonary hypertension.

The most easily analyzed angiograms were obtained from the peripheral or cortical areas of the right lower lobe, right upper lobe and left upper lobe, in that order. In the cortical areas of the lung the secondary pulmonary lobules are aligned horizontally along radii from the hilus.19 Angiograms near the hilus were sometimes difficult to interpret because the orientation of the lobule may be parallel to the direction of the x-ray beam.

A Tagarno 35 mm projector was used to project the films onto a matte white wall 6–8 feet away, producing an average magnification of 7.5 times actual size. The projected catheter diameter was used as the reference diameter for calculating the magnification factor and absolute arterial diameter. Although there was some degradation in the edge definition at this magnification, projected arterial images of 1.5–2 mm (220–270 μ actual size) could be measured with reproducible accuracy.

Measurements were made of: 1) the catheter diameter, 2) the diameter of the artery just distal to the catheter tip, and 3) the paralobular vein at the same level as the arterial measurement (fig. 1). The ratio of the vein diameter to the arterial diameter was then calculated. When the pulmonary artery branched dichotomously (branching angle less than 90°), the diameter of the branches was measured and compared to the diameter of the parent artery. Branches of the small pulmonary arteries which subtended a 90° angle (monopedial branching) were also measured and this diameter was compared to the parent branch. A note was made about the uniformity and completeness of the background capillary blush and graded a) sparse, b) patchy, c) incomplete, d) full. Reflux of contrast around the catheter back into the pulmonary arteries was graded from none (0) to minimal (+) to gross (++).

Biopsies were taken at cardiac surgery from the same lung as the angiogram in 19 patients within one week of catheterization. Lung histology was obtained in three of the patients who died after open heart surgery. Pulmonary vascular pathology was examined by Dr. Harvey Rosenberg, who reported the findings in relation to Heath and Edwards' grading of pulmonary vascular disease.21

Results

Two hundred sixty-seven wedge angiograms were obtained in 155 patients without serious side effects or complications. Seventeen (6%) were unsatisfactory for analysis because of poor exposure. Extravasation of contrast (stain) occurred in two infants under 3 months of age and in 10 of 66 patients with pulmonary hypertension. Any residual contrast remaining in the lung field after flushing and withdrawing the catheter from the wedge position disappeared within 5 minutes. One or two coughs occurred in 23 patients (14.8%) during the injection (30 of 267 angiograms, 11.2%), but paroxysmal coughing occurred only twice and no patient had hemoptysis, pneumothorax or pulmonary infarction. There was no change in the phasic or mean wedge pressure after the angiogram. Respiratory movement did not alter the angiographic morphology of the vessels, which became more crowded in expiration, but measurement of vessel size could still be made.

Group A — Normal Hemodynamics

Fifty-three angiograms were obtained in 31 patients, and 51 were suitable for analysis.

In the normal lung, a catheter with an outside diameter of 1.7–2 mm (#5–6 French gauge) in the wedge position, produces an angiogram which represents the vascular anatomy of the secondary pulmonary lobule. The centrally placed muscular or transitional pulmonary artery was 1–2 mm in diameter (average 1.64 ± 0.48 mm), which branched dichotomously in a uniform, evenly tapering arborization. (fig. 1A) The diameter of the branches was 68–79% (mean 72 ± 3.4%) of the parent artery, while more numerous monopedial or supernumerary branches arose at right angles to the parent branch, and their diameter was 20–60% (mean 42.1 ± 12%) of the parent branch. The dichotomous branches follow the respiratory bronchiolar branching, while the monopedial branches represent the supernumerary and terminal branches which give off precapillary arterioles at right angles and supply the alveolar capillary network.15, 16 The monopedial branches were also seen to arise from the larger muscular, transitional and elastic arteries along the course of the major bronchi where respiratory alveoli occur.17, 18

With a film speed of 30 frames/sec, we could see sequential filling of all arterial branches followed by a dense, granular, uniform blush which represented the capillary phase (fig. 1B). With continued injection of contrast, the peripheral veins of the secondary pulmonary lobule started to fill and usually coalesced to a single vein which ran in the septa of the lobules, parallel to the central artery. Sometimes several small veins were filled and drained to other lobar veins. It was possible to measure accurately vessels 250–400 μ
Figure 1. Wedge angiogram from the right lower lobe. Group A morphology, normal hemodynamics. A) Arterial phase with early filling of the paralobular vein. B) Mid-flush phase showing a complete capillary blush surrounding all of the small arteries and better filling of the pulmonary veins. C) Venous phase showing clearing of the capillary blush and complete filling of the paralobular veins draining to the left atrium. D) A line drawing of the flush phase (B). A = catheter diameter (2 mm); B = diameter of artery measured distal to the catheter tip; C = diameter of the vein measured at same level as the arterial diameter; D = capillary background blush; E = paralobular vein; F = monopedial muscular artery 600 μ in diameter.
in diameter, and vessels of 100 μ were clearly seen in most angiograms.

The flush phase of the angiogram produces even greater filling of the small pulmonary arteries and a more uniform capillary blush and greater filling of the pulmonary veins (fig. 1C). Incomplete filling of the small pulmonary vessels during the initial injection of contrast was probably due to the high viscosity of the contrast medium, and the flush phase is an important step in the complete evaluation of the vascular morphology.

**Group B — Increased Pulmonary Blood Flow and Normal Pressure**

The 69 wedge angiograms were almost identical to the normal group, except that the proximal arteries and veins were larger (1.9 ± 0.5 mm; P < 0.02) and there was a more dense and diffuse capillary blush (fig. 2).

**Group C — Increased Pulmonary Flow and Pressure**

Although the mean Qp/Qs ratio for this group was not significantly different from that in group B, the added component of increased pulmonary artery pressure was associated with an increased arterial tortuosity (fig. 3A). The degree of tortuosity was more pronounced in patients with the highest pulmonary artery pressures. The mean proximal pulmonary artery diameter was 1.93 mm (range 0.99–3.97 mm), similar to group B; the proximal vein to arterial ratio was smaller because of the larger size of the artery rather than a small venous size. For this same reason, small arteries arising at right angles appeared to be smaller because of the parent artery dilation.

The capillary blush remained full when there was a direct injection into the lobular artery (fig. 3B), but reflux of contrast was more common (27.3% of the angiograms), and more extensive in this group, and there was often incomplete filling of adjacent lobular arteries.

The effect of increased blood flow on the wedge angiogram morphology is to produce generalized dilation of all vessels and an engorged lobe; an increase in pulmonary artery pressure leads to further dilation of the elastic and transitional vessels together with tortuosity and dilation of all vessels, including the muscular arteries.

Seven patients with group C hemodynamics had a lung biopsy at the time of corrective surgery, and each showed medial hypertrophy in the small muscular arteries (grade I); three patients had isolated areas of intimal fibrosis in a few larger muscular arteries (early grade III).

**Group D — Increased Pulmonary Arterial Resistance**

These 30 patients were grouped together because they had pulmonary hypertension with an increase in pulmonary resistance of greater than 6 μm², with an average pulmonary-to-systemic resistance ratio (Rp/Rs) of 0.86 ± 0.28 (range 0.42–2.36). Nine of the 66 angiograms (13.6%) were unsuitable for analysis because of poor x-ray exposure. The appearance of the wedge angiograms ranged from very similar to group C angiograms to the classical “pruned tree” appearance of PVOD.

There was a more abrupt termination of dilated tor-
tuous arteries and the number of supernumerary (monopedial) branches was markedly decreased or absent. The capillary blush was incomplete or patchy in random areas of the lobule and absent around many well filled larger vessels during the flush phase. There was a reticular consistency rather than the granular blush seen in normal lungs (fig. 4). There was an increased resistance to injection and contrast refluxed back around the catheter in 63.6% of the angiograms, especially during the flush phase, rather than passing through the high-resistance lobule.

Beading and irregularity of the lumen of the arteries less than 600 μ in diameter was seen in patients whose pulmonary vascular resistance was greater than 12 u/m². Lower lobe arteries showed a greater degree of pathology than upper lobe arteries in five patients whose pulmonary resistance was equal to or greater than systemic resistance and with right-to-left shunting (Eisenmenger's syndrome). There was the typical “pruned tree” appearance in the lower lobe, while the upper lobe in the same patient showed changes consistent with group C hemodynamics.

It was impossible to wedge the catheter in six patients and pre-wedge angiograms were obtained; these were not as satisfactory as the wedge angiograms, since more contrast material was required to adequately fill the smaller vessels, and we could not be sure that the lack of filling was due to high resistance and vascular disease or to inadequate opacification with contrast material. If a Goodale-Lubin catheter could not be wedged, better filling of the smaller vessels was obtained when a pre-wedge angiogram was performed with an inflated balloon catheter.

The five patients with Eisenmenger's syndrome had severe pruning of the peripheral vessels and only an occasional vessel less than 500 μ was seen (fig. 5). There was delayed filling of the pulmonary veins and some contrast material would linger in abruptly terminating tortuous vessels, producing a streaked residual picture quite different from an iatrogenic stain.

**Group E — Pulmonary Venous Hypertension**

If pulmonary hypertension was entirely due to pulmonary venous obstruction, the wedge angiogram demonstrated the typical vasoconstrictive pattern in the lower lobes as described by Evans and Short with long, slowly tapering proximal arteries and a decreased number of monopedial branches (figs. 6A and B). There was a faint but uniform capillary blush with no gaps, but the concentration of contrast was decreased with a rather weblike reticular pattern to the small arteries. The paralobular veins were normal, but the vein running parallel to the proximal injected artery was dilated; when the vein and artery were measured at the same level, the average ratio was significantly greater than normal (1.43 vs 1.04, P < 0.001).

When angiograms were taken in both the upper and the lower lobes in the same patient, a distinctly
different pattern was seen in the morphology of the microvasculature: the upper lobes showed dilated arteries and a full capillary blush, while the bases showed generalized vasoconstriction and oligemia as described by Doyle et al.\textsuperscript{18} Using wedge angiography, in two patients we found pulmonary varices which were not observed by conventional main pulmonary artery angiograms. Both patients had anomalies of pulmonary venous return, one with cor triatriatum and the other with single ventricle with partial anomalous pulmonary venous return with obstruction.

**Group F — Less Than 3 Months of Age**

These 14 patients were all less than 3 months of age, with a variety of congenital heart defects; only three had no left-to-right shunt and all but three had elevated pulmonary artery pressure. It is assumed that
there was medial hypertrophy (grade I changes) in those patients who had some degree of pulmonary hypertension.

The morphology of the microcirculation in each patient corresponded to the hemodynamics of the congenital heart lesion; no patient had pulmonary resistance of greater than 5.5 u/m² or an Rp/Rs > 0.22. Some dilation and mild tortuosity was seen in the patient with the highest pulmonary artery pressure and highest resistance (group C...
Table 3. Histological-Angiographic Correlations

<table>
<thead>
<tr>
<th>Histological grade</th>
<th>Age (years)</th>
<th>Diagnosis</th>
<th>Group</th>
<th>PAP: AoP</th>
<th>Qp/Qs</th>
<th>PVR (u/m²)</th>
<th>Reflux</th>
<th>Muscular arteries</th>
<th>Monopodial vessels</th>
<th>Capillary blush</th>
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<td>Normal</td>
<td>1-4</td>
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<td>-</td>
<td>Dilated</td>
<td>Numerous</td>
<td>Full</td>
</tr>
<tr>
<td></td>
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<td>C</td>
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<td>+</td>
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<td>Full</td>
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<td>-</td>
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<td>Numerous</td>
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<td>1.4</td>
<td>TGA, VSD</td>
<td>C</td>
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Abbreviations: TGA = transposition of the great arteries; VSD = ventricular septal defect; PS = pulmonary stenosis; PDA = patent ductus arteriosus; AV canal = atrioventricular canal; Cor Triat. = Cor Triatriatum; ASD = atrial septal defect; PO VSD = postoperative VSD closure; Band = main pulmonary artery banding; PO Truncus = postoperative Rastelli repair of truncus arteriosus; Pseudotrunc. = pseudotruncus arteriosus. Other abbreviations same as in table 1.

morphology); the wedge angiograms obtained in the other 13 patients were indistinguishable from those of groups A and B.

Histological Correlations

Lung histology was available from autopsy material in three patients and from lung biopsies taken at operation in 19 patients (table 3).

PVR was $\geq 6.7$ u/m² (range 6.7–17 u/m²) in those with late grade III PVOD or greater, but the level of PVR was not a good indicator of the degree or extent of PVOD, either angiographically or histologically. With lesser degrees of PVOD histologically, there was a wide range of values for PVR. One patient with a ventricular septal defect and coarctation had normal vessels histologically and angiographically and had a PVR of 5.5 u/m², while another with cor triatriatum had a PVR of 11.9 u/m² and only grade II changes histologically.

Intimal fibrosis was observed histologically in 10 patients ranging from slight fibrosis in the hyperplastic intima (early grade III) to diffuse, irregular, dense fibrous plaques, almost occluding the vessel lumen in some of the vessels. Four patients had extensive grade III changes, short of occlusion, and were labelled “late grade III” changes. There were three patients with early grade IV changes, with occlusive intimal lesions and one with an isolated angiomatoid lesion (grade V).

Patients with either normal, grade I or grade II changes were from hemodynamic groups B, C, E and F. All patients with grade III changes or greater were from groups C and D. The patients with late grade III changes or obstructive vascular disease were from the group with elevated PVR (group D).

The angiograms of patients with late grade III changes were almost identical to those of patients with grade IV or greater pulmonary vascular disease. The common feature in those patients with advanced obstructive vascular disease was incomplete filling of the capillary background blush; when there was fill-
ing, there tended to be a coarse, reticular pattern rather than a fine, granular blush as seen in unobstructed vessels. The degree of filling varied from lobe to lobe and was random in distribution in the lobules; pulmonary hypertension and obstructive vascular disease (Eisenmenger’s syndrome) had a more pruned appearance to the lobules, especially in the lower lobes.

There were nine patients with less than complete capillary filling, and each of these had a pulmonary resistance > 6 u/m². Only one of the nine patients had early grade III vascular disease and the others had late grade III or greater.

All grades of severity of pulmonary vascular disease by histology were associated with a wide range of pulmonary artery pressures, resistance ratios and flow ratios, so these factors were not predictive of the degree of histological pulmonary vascular disease. When the vascular disease was obstructive by histological findings (late grade III to grade IV changes) the most consistent and specific angiographic finding was a patchy or incomplete capillary blush in one or more lobular angiograms. If a patient had a PVR ≥ 6 u/m² or greater and an incomplete capillary blush, then there was an 89% chance that he had diffuse, late grade III changes or better.

The hemodynamic, angiographic and histological findings are compared in table 4.

**Table 4. Wedge Angiographic Features and Hemodynamics**

<table>
<thead>
<tr>
<th>Angiographic features</th>
<th>Group A Normal hemodynamics</th>
<th>Group B ↑ Flow Normal pressure</th>
<th>Group C ↑ Flow ↑ Pressure</th>
<th>Group D ↑ PVR</th>
<th>Group E Pulmonary venous hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistance to hand injection</td>
<td>Low</td>
<td>Low to moderate</td>
<td>Increased</td>
<td>Variable</td>
<td></td>
</tr>
<tr>
<td>Reflux of contrast</td>
<td>Rare</td>
<td>Rare</td>
<td>Frequent 27%</td>
<td>Usual 63%</td>
<td>Occasional 10%</td>
</tr>
<tr>
<td>Proximal muscular arteries (1-2 mm)</td>
<td>Straight</td>
<td>Dilated</td>
<td>Dilated, tortuous</td>
<td>Dilated, tortuous</td>
<td></td>
</tr>
<tr>
<td>Tapering of muscular arteries</td>
<td>Even, gradual</td>
<td>Even, rapid</td>
<td>Uneven, rapid</td>
<td>Uneven, rapid, Beading</td>
<td></td>
</tr>
<tr>
<td>Supernumerary vessels (monopodial branching)</td>
<td>Numerous from elastic and muscular arteries</td>
<td>Numerious, dilated</td>
<td>Reduced, especially from elastic arteries</td>
<td>Reduced to sparse or absent</td>
<td></td>
</tr>
<tr>
<td>Capillary blush</td>
<td>Full, granular blush around each artery</td>
<td>Full, granular</td>
<td>Full reticular-granular (18%)</td>
<td>Sparse, patchy 94%</td>
<td></td>
</tr>
<tr>
<td>Small veins (1-2 mm) vein artery</td>
<td>Narrow, orderly aborisation</td>
<td>Dilated</td>
<td>Normal</td>
<td>Dilated</td>
<td></td>
</tr>
<tr>
<td>Diameter ratio</td>
<td>V/A = 1.04 ±0.28</td>
<td>V/A = 0.99 ±0.23</td>
<td>V/A = 0.87 ±0.18</td>
<td>V/A = 0.93 ±0.22</td>
<td>V/A = 1.43 ±0.33 (P &lt; 0.001)</td>
</tr>
<tr>
<td>Histology grade (22 patients)</td>
<td>Normal to I</td>
<td>Normal to II</td>
<td>Normal to early III</td>
<td>Early III, late III II to early III</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ↑ = increased; PVR = pulmonary vascular resistance.

Discussion

The difficulties in evaluating the state of the pulmonary vascular bed in children with congenital heart disease have been analyzed in great detail by Hoffman.19

The measurement of pulmonary blood flow and calculations of PVR are only approximations, at best, using standard techniques,20-22 and the finding of an elevated PVR poses the question of interpretation of this value. There have been some empirical correlations between pulmonary resistance calculations and the degree of pulmonary vascular disease and its reversibility,23 but in any patient, one cannot rely too heavily on the calculated resistance value because of the many sources of possible error in the calculations.22 Even if reactivity of the pulmonary vascular bed is demonstrated by administering vasodilator drugs, it is still possible that 50% of the small vessels have occlusive pulmonary vascular disease.19 Conventional examination of lung biopsies may not present an accurate picture of the extent of the vessel pathology, since vascular lesions are not uniformly distributed over the whole lung or even along the length of a single vessel.3, 10, 11

Studying the morphology of the intact pulmonary lobular circulation allows a better overall evaluation of the degree and extent of pulmonary vascular changes in a patient with pulmonary hypertension. Detailed studies of the normal peripheral pulmonary vascular bed have clearly defined the size, structure and morphology of the vessels of the primary and secondary pulmonary lobules,15-17 and it is at this level that the early stage of obstructive pulmonary vascular disease occurs.11, 24, 25 Since Bell’s first report of the clinical use of magnification pulmonary wedge angiography,1 many investigators have been able to
reproduce detailed angiograms of the secondary pulmonary lobe and of vessels as small as 100–300 μ in diameter.\textsuperscript{5–9} Previous studies in animals,\textsuperscript{9} patients with mitral stenosis\textsuperscript{1} and children with congenital heart disease\textsuperscript{4·6–10} have shown a correlation between changes in the magnified wedge angiogram or postmortem magnification angiograms with histological changes in the pulmonary arteries.

Increased tortuosity, dilation and abrupt tapering of muscular arteries was noted to be associated with an increase in PVR\textsuperscript{4·6–8} in children with congenital heart defects. These changes were also noted by Friedman\textsuperscript{9} in serial studies of experimental animals with left-to-right shunts and pulmonary hypertension. Reduced small vessel arborization and a patchy capillary blush were associated with intimal fibrosis and luminal occlusion in histological specimens from these studies\textsuperscript{4·8–9} (grades III–IV of Heath and Edwards).

Using a quantitative structural analysis of necropsy and lung biopsy specimens, Reid and colleagues\textsuperscript{24–25} described changes in the pulmonary microcirculation associated with pulmonary hypertension. They found abnormal extension of medial musculature into arteries less than 250 μ, together with abnormal thickening in the larger muscular arteries. There was also a decrease in the number and size of smaller intra-acinar arteries which was indicated by reduction in the background blush in the postmortem angiograms and a decrease in the number of small arteries per unit area of the lung histologically. This latter observation corresponds with our finding of a decreased number of supernumerary vessels and the incomplete or patchy capillary blush in the magnified wedge angiograms.

Until recently, however, the equipment necessary to obtain high-quality, high-definition angiograms was not available in all catheterization laboratories; the introduction of very high resolution cesium iodide image intensifiers, coupled with fine-grain 35 mm cineangiographic film and fine focal spot x-ray tubes, has made it possible to obtain high-quality magnification wedge angiograms in any patient undergoing routine cardiac catheterization. Manual injection of contrast, with video monitoring, allows the operator to evaluate the technical quality of the image as it is formed, and a complete study of all phases of the microcirculation is obtained without excessive use of contrast material or force. With a little experience, this technique can be performed without serious complication. Repeated wedge angiograms should be performed in several areas of the lung, since the distribution of vascular disease is not uniform.

The findings in this study are in general agreement with previously published reports in that there are identifiable angiographic features of the peripheral pulmonary vasculature with different degrees of PVOD. There is a distinct difference in the wedge angiogram of the patient with elevated pulmonary artery pressure and low vascular resistance compared with that of the patient with high resistance and PVOD. The primary features of pulmonary hypertension with increased pulmonary blood flow are dilation and tortuosity of the elastic pulmonary arteries, with rapid tapering of arteries less than 1 mm in diameter to the peripheral vasculature of the secondary pulmonary lobe. The diameter of the monopedial branches which arise at right angles remains constant, but the ratio of the branch to the parent artery becomes smaller because of proximal dilation. With high pulmonary artery pressure and flow, tortuosity increases and the morphology of the secondary lobule becomes distorted; there is still a complete granular background blush and supernumerary vessels are reduced in number, but still present on the elastic arteries if there is no obstructive vascular disease or late grade III changes.

As pulmonary resistance rises with intimal fibrosis and occlusion, tortuosity of the elastic and muscular arteries becomes more prominent and there is an increased resistance to manual injection while the amount of reflux increases; there is also slower filling of pulmonary veins and slower clearing of the capillary bed and small muscular arteries due to reduction in the lumen.

When intimal fibrosis encroaches upon the lumen of the vessel and becomes occlusive, particularly at the right angle on supernumerary branches, fewer small vessels are filled, together there is a lack of filling of the surrounding capillary bed. Supernumerary vessels are among the first vessels affected by occlusive pulmonary vascular disease, and these become sparse and finally are not seen on the angiogram. Failure to demonstrate any of these vessels suggests late grade III or grade IV changes. Vascular occlusion occurs in a random fashion, and not all vessels are affected simultaneously or to the same degree. The capillary blush will look patchy and incomplete until progressive occlusive vascular disease obstructs all capillary filling and the bare, pruned “tree-in-winter” appearance is seen. This morphology is seen in the lower lobes more frequently, but may be seen in other lobes next to lobules with less severe changes.

Clinical examination, chest radiography and routine ventriculography will easily identify the patients with pulmonary hypertension who have increased pulmonary blood flow and a low PVR and those who have a high fixed resistance or Eisenmenger syndrome. If, however, a patient has pulmonary hypertension with a moderate-to-high pulmonary resistance (6–10 u/m²) and a modest left-to-right shunt (Qp/Qs < 2:1), pulmonary wedge angiography will identify the presence of irreversible intimal sclerosis by the presence of abrupt tapering of the 1–2 mm muscular arteries and a reduction in the small vessel arborization, together with an incomplete capillary blush. The extent of this obstructive vascular disease can be determined by wedge angiograms in several areas of the lung. If these changes are not present, then it can be assumed that there may be up to grade II changes or, at most, scattered, slight intimal sclerosis in larger elastic arteries, and that these changes are reversible after corrective surgery. The angiographic signs of diffuse intimal obstructive dis-
ease means that pulmonary resistance will not fall even after successful corrective surgery, and progressive vascular disease may continue in these patients.

It may be useful to observe directly any changes in vascular caliber and capillary filling by repeating the wedge angiogram after administering vasodilator drugs directly into the peripheral vascular bed.

Magnification wedge angiography of the pulmonary lobular vascular bed from several areas of the lung provides a comprehensive and accurate assessment of the presence and degree of pulmonary vascular disease in children with congenital heart disease.

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