Pulmonary Vascular Lesions Occurring in Patients With Chronic Major Vessel Thromboembolic Pulmonary Hypertension*

Kenneth M. Moser, M.D., F.C.C.P.; and Colin M. Bloor, M.D.

The status of small pulmonary arteries may influence diagnosis, surgical selection and postoperative outcome of patients with chronic major vessel thromboembolic pulmonary hypertension (CTEPH). Therefore, in patients with the established diagnosis of CTEPH, lung tissue was obtained by biopsy (15 patients) or at autopsy (16 patients) to assess the histopathologic composition of small pulmonary arteries. Pathologic examination disclosed the full range of pulmonary hypertensive lesions in the small arteries, including plexogenic lesions. The type and extent of hypertensive lesions did not relate to preoperative hemodynamic values, to patient age, or to symptom duration. The findings indicate that primary pulmonary hypertension cannot be differentiated from potentially correctable CTEPH on the basis of histopathologic findings in small pulmonary arteries. Furthermore, none of the histologic findings preclude a positive hemodynamic and clinical result from pulmonary thromboendarterectomy. However, development of these hypertensive changes may explain the deterioration which these patients experience preoperatively over time.

Methods

Biopsies

Patients who agreed to lung biopsy had this procedure performed at the time of thromboendarterectomy. The site was chosen on the basis of the absence of pleural adhesions as determined by preoperative chest x-ray films, chest computed tomography scans, and inspection at the time of surgery. The status of flow to the biopsy site, as assessed by preoperative perfusion scan and angiogram, was confirmed at the time of surgical pulmonary thromboendarterectomy. These samples were placed in 10 percent buffered formalin for fixation.

Thirty-five tissue blocks from these 15 patients had samples of lung tissue available for complete analysis including morphometry of the small muscular arteries and arterioles. Histologic sections of lung, 6 μm thick, were stained with hematoxylin-eosin and Verhoeff-van Gieson elastic stains. The initial readings of the slides were done by the attending surgical pathologists at the University of California, San Diego, Medical Center or the San Diego VA Medical Center. After their preliminary reports were filed, the slides were submitted to one of us (C. M. B.) for additional review. These same sections were submitted for morphometric analysis of the small muscular arteries and arterioles. The pathologic features catalogued in Tables 1 and 2 list lesions that two or more of the reviewing pathologists identified as being present and agreed upon as to classification.
### Table 1 — Pathologic Findings in Lung Biopsy Specimens

<table>
<thead>
<tr>
<th>Case</th>
<th>Site</th>
<th>EIF</th>
<th>CIF, IFP</th>
<th>Thrombus</th>
<th>Arteritis</th>
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*Flow: 0 = no flow; P = partial flow; NL = normal flow as assessed by preoperative perfusion scan and pulmonary angiogram.

### Table 2 — Pathologic Findings in Autopsy Specimens

<table>
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<tr>
<th>Case</th>
<th>Site</th>
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<th>CIF, IFP Lesions</th>
<th>Thrombotic Lesions</th>
<th>Plexogenic</th>
<th>Flow$</th>
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$\dagger$ Died 3 years after operation.

$\dagger$ Died 5 years after operation.

$\dagger$ Died 17 years after operation.

$\dagger$ Flow: 0 = no flow; P = partial flow; NL = normal flow as assessed by preoperative perfusion scan and pulmonary angiogram.
Autopsies

Autopsy specimens were obtained from 16 patients who died after surgery. Thirteen died in the perioperative period at 12 h to 12 d after surgery; the others died of unrelated causes at 3, 5, and 17 years after a successful thromboendarterectomy. Two autopsied patients, both of whom died within 48 h of surgery, also had had a lung biopsy at the time of surgery.

Sixty-one tissue blocks from these 16 patients had samples of lung tissue available for complete analysis. These tissue sections were taken by the prosectors at the time of autopsy in a random fashion, with the site of the sample recorded by the prosector. In all cases, samples were obtained from at least two different lobes of the lung. The lungs were inflated by inserting a cannula into the main bronchus and perfusing with 10 percent buffered formalin solution with a water pressure of 25 to 30 cm. The lungs were fixed in the distended state for a minimum of 24 h before the tissue samples were obtained.

These sections were processed and analyzed in the same manner as were the biopsy samples. Before our examination of the material, the slides were reviewed by the autopsy prosector and the Director of the Autopsy Service at either the University of California, San Diego, Medical Center or the San Diego VA Medical Center. These same sections were submitted for morphometric analysis of the small muscular arteries and arterioles.

Control Specimens

We obtained lung tissue samples from ten autopsy patients (15 to 42 years old) who died from nonpulmonary causes and did not have gross or microscopic evidence of pulmonary disease at the time of autopsy. Twenty-three tissue blocks from these ten patients had samples of lung tissue available for complete analysis. These tissue sections were taken by the prosectors at the time of autopsy in a random fashion. In all cases, samples were obtained from at least two different lobes of the lung.

These sections were processed and analyzed in the same manner as were the other autopsy samples, ie, the lungs were inflated by inserting a cannula into the main bronchus and perfusing with 10 percent buffered formalin solution with a water pressure of 25 to 30 cm H2O. The lungs were fixed in the distended state for a minimum of 24 h before the tissue samples were obtained. Before our examination of the material, the slides were reviewed by the autopsy prosector and the Director of the Autopsy Service at either the University of California, San Diego, Medical Center or the San Diego VA Medical Center. These same sections were submitted for morphometric analysis of the small muscular arteries and arterioles and served as controls. We conducted morphometry on 98 vessels (25 to 100 μm in diameter) from the tissue blocks on these control patients. The mean muscle mass averaged 0.368 (SD ± 0.086), a value similar to control values obtained in our laboratory previously.26

Morphometric Measurements and Analysis

Tissue samples were obtained from either surgical pathology specimens or autopsy specimens as described before. Six-micrometer-thick sections were prepared from these tissue blocks and stained with hematoxylin-eosin and elastic tissue stains for microscopic examination. The histologic slides were coded so that their origins were unknown to the grading observer.

To determine if isolated medial hypertrophy was present, we measured vessels that did not have intimal changes, luminal changes, or evidence of arteritis. Morphometric measurements were performed as previously described from this laboratory.29,31 In the absence of pulmonary venous hypertension, pulmonary arteries can be distinguished from pulmonary veins in general because they accompany the bronchi and bronchioles and possess a medial coat of circular smooth muscle bounded by an internal elastic lamina and an external elastic lamina. The small pulmonary veins are located in the interlobular fibrous septa. Other criteria used were those described by Meyrick and Reid;32 ie, pulmonary arteries were distinguished from pulmonary veins as follows: (1) for a given diameter, veins have less muscle and more connective tissue than arteries; (2) in a muscular vein, there is no internal elastic lamina; (3) the larger veins run at the edge of an acinus and (4) in a given length, small veins have more tributaries than the arteries. All sections were stained with hematoxylin-eosin and the Verhoeff-von Gieson elastic stain for morphometry.

Using a Microtech Model 100 automated image analysis system, we projected the histologic slides at ×400 magnification. The components of the vessel walls were outlined on the video screen. The measurements obtained included total vessel area, lumen area, and medial area. Since intimal area is negligible in vessels without intimal injury,26,28,34 we included intimal area with lumen area for convenience in making accurate measurements. Medial muscle mass was expressed as a ratio of medial area (MMA) divided by total vessel area (EA) or MMA/EA. Only vessels which could be clearly distinguished as arteries or arterioles with an internal elastic lamina were analyzed. The analyzed vessels’ external diameters ranged from 25 to 100 μm. We quantified the magnitude of medial muscle mass per vessel in each patient, determined the average value for each patient, and then averaged individual patient values for the surgical pathology and autopsy groups separately. Only vessels free of lesions other than muscular hypertrophy were submitted for morphometric analysis.

In addition to the quantitative measurements, all sections were surveyed to detect if any additional pathologic changes were present in the lungs that were not listed in the surgical pathology or autopsy reports.

Classification of Pulmonary Arterial Lesions

Pulmonary arterial lesions, when present, were categorized by the reviewing surgical pathologists, autopsy pathologists, and us according to the classification of the World Health Organization as adopted by the Pathology Core of the National Institutes of Health-sponsored Registry for Primary Pulmonary Hypertension.35 This system classifies vessels as normal or as having isolated medial hypertrophy, eccentric intimal fibrosis (EIF), concentric laminar intimal fibroelastosis (CIF), organized thrombus, arteritis, or plexiform lesions. We used the measurements of medial muscle mass described previously to determine if isolated medial hypertrophy was present. Criteria for the presence of the other lesions were similar to those described by Lloyd et al29 and Pietra et al.34 Namely, EIF is a patchy, asymmetric or eccentric intimal fibroelastosis. Concentric intimal fibroelastosis consists of multiple, well-defined onionskin layers of cellular or fibroelastic intimal proliferations which are deposited concentrically. Internal fibromuscular proliferation (IFP) comprises longitudinal internal fibromuscular tissue involving the circumference of a muscular artery. Organized thrombi are fibrotic obstructing lesions within the vessel lumen which have recanalized with one or more channels. Plexiform lesions are thin-walled multichanneled vascular lesions within the involved vessel. They may have a central sclerotic region. Often they occur in small muscular pulmonary arteries with partially or totally destroyed media. Angiomatoid lesions comprise discrete conglomerations of thin-walled, blood-filled vessels adjacent to a muscular pulmonary artery. In our cataloguing the observed lesions in our patients, we have grouped plexiform and angiomatoid lesions as plexogenic lesions.17 Arteritis was defined as the presence of inflammatory cells within the vessel wall. Fibrinoid necrosis also may accompany this change.

Other Data

Hemodynamic data were obtained in each patient preoperatively, as were perfusion lung scans and angiograms. The angiograms,
FIGURE 1. Eccentric intimal fibrosis. Biopsy specimen, case 12. A muscular pulmonary artery shows asymmetric fibroelastosis of the intima. Fibroelastotic changes are present in the intima inside of a relatively intact internal elastin (Verhoeff-von Gieson elastic stain). scans, and operative findings were used to determine whether the biopsy and autopsy specimens were obtained from lung regions served by proximal pulmonary arteries which, preoperatively, were normal, partially occluded, or totally occluded.

Postoperative hemodynamic data also were obtained in 14 of 15 patients on whom biopsies were done while in the intensive care unit just before removal of the Swan-Ganz catheter; one patient, who died 12 h after surgery, was too unstable to allow reliable measurements. Postoperative hemodynamics were available in 12 of 16 autopsied patients; four died within 36 h of surgery while hemodynamically unstable.

Statistical Analyses

For mean muscle mass, the values in patients versus controls on whom biopsies were done and autopsied patients versus controls were compared using Student's unpaired t test. The clinical and hemodynamic data in biopsied versus control patients were compared by this same method and correlation coefficients by standard techniques.

RESULTS

Biopsy Patients

Clinical Features: The mean age of patients on whom biopsies were performed was 46 years (range: 20 to 70 years). Thirteen were male and two, female. The duration of symptoms prior to surgery averaged 3.5 ± 4.0 (SD) years. Preoperative hemodynamic data disclosed (Table 3) that the mean pulmonary artery pressure was 48 ± 12 (SD) mm Hg, and the calculated pulmonary vascular resistance was 913 ± 395 (SD) dynes·sec·cm⁻⁵. Postoperatively, in the 14 patients in whom valid postoperative hemodynamic values were available, highly significant (p<0.001) decreases occurred in both mean pulmonary artery pressure (48 to 28 mm Hg) and pulmonary vascular resistance (911 to 270 dynes·sec·cm⁻⁵).

Table 1 shows the status of the flow in the major elastic pulmonary arteries proximal to the biopsy site, as defined by findings on the preoperative perfusion scan and pulmonary angiogram.

Pathology Results: We conducted morphometry on 194 vessels (25 to 100 μm in diameter) from the tissue blocks of these patients. Only vessels without other lesions were subjected to morphometry. The number of vessels examined per patient ranged from 5 to 24. Morphometry confirmed the presence of medial hypertrophy. The mean muscle mass of the muscular arteries and arterioles in this group was 55 percent greater than the value for the control group (0.569 ± 0.141 [SD] vs 0.368 ± 0.086; p<0.05).

The other arterial lesions associated with pulmonary hypertension are listed in Table 1. The most prevalent lesions were EIF, CIF, and IFP. We observed EIF (Fig 1) in ten (67 percent) and CIF or IFP (Fig 2) in 12 (80 percent) of the 15 cases. Organized thrombi (Fig 3) were present in small pulmonary arteries in 8 (53 percent) of the 15 cases. Three cases (20 percent) had at least one small muscular artery present with inflammatory cells within the medial muscle layer.

FIGURE 2. Intimal fibromuscular proliferation. Biopsy specimen, case 12. This muscular pulmonary artery shows marked proliferation of longitudinal intimal fibromuscular tissue involving the entire circumference of the vessel (hematoxylin-eosin, original magnification ×250).

FIGURE 3. Autopsy specimen, case 4. Organized thromboembolus. A fibrotic lesion obstructs the lumen of this muscular pulmonary artery. Recanalization has occurred resulting in several small vascular channels within the thromboembolus (hematoxylin-eosin, original magnification ×100).
Focal fibrinoid necrosis sometimes accompanied this change. In 9 (60 percent) of the 15 cases, we observed one or more plexogenic lesions (Fig 4) in the tissue sections examined.

Autopsy Patients

Clinical Features: The mean age of the autopsied patients was 55 years (range: 33 to 73 years) (Table 3). This age was significantly older than that of the patients who had biopsies (p<0.03). The average duration of symptoms preoperatively in autopsied patients (4.5 SD ± 4.1 years) was longer, but not significantly different from patients who had biopsies.

The preoperative hemodynamic values in the autopsied patients were not significantly different from those in patients who had biopsies, with the pulmonary artery mean pressure averaging 48 ± 12 mm Hg and the pulmonary vascular resistance 940 ± 323 dynes-sec-cm⁻² (Table 3).

As in the patients who had biopsies, the mean pulmonary artery pressure fell significantly after thromboendarterectomy in the 12 patients with reliable postoperative data, from 46 to 31 mm Hg (p<0.001) as did the pulmonary vascular resistance (928 to 324 dynes-sec-cm⁻²; p<0.001).

Pathology Results: We conducted morphometry on 234 vessels (25 to 100 μm in diameter) from the tissue blocks on these patients. The mean muscle mass of the muscular arteries and arterioles in the autopsy group was 41 percent greater than the value for the control group (0.519 ± 0.319 vs 0.368 ± 0.086; p<0.05). Of the other vascular lesions associated with pulmonary hypertension, the most prevalent lesions were EIF and CIF. We observed EIF in ten (63 percent) and CIF or IFP in eight (50 percent) of the 16 cases. Organized thrombi were present in small pulmonary arteries in eight (50 percent). We did not observe any lesions diagnostic of arteritis in the 16 autopsy cases. In 11 (69 percent) of the 16 cases we observed one or more plexogenic lesions in the tissue sections examined. Also, we observed a different plexogenic lesion suggestive of an angiomatoid lesion in seven (44 percent) of the 16 autopsy cases (Fig 5).

Relationship Between Clinical and Physiologic Parameters and Pathology Findings: There were no significant correlations between mean muscle mass in cases in which autopsies or biopsies were done and preoperative values of mean pulmonary artery pressure, pulmonary vascular resistance, patient age, or duration of symptoms prior to surgery. Of the 244 small arteries analyzed in the patients who had biopsies, the 194 submitted to morphometric analysis were free of other lesions; thus approximately 21 percent of vessels inspected did contain one of the other hypertensive lesions. In autopsied patients, 18 percent of

Table 3—Hemodynamic Data in Cases in Which Biopsies and Autopsies Were Done*

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<thead>
<tr>
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<th>Pulmonary Artery Mean Pressure, mm Hg</th>
<th>Pulmonary Vascular Resistance, dynes-sec-cm⁻²</th>
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<tr>
<td></td>
<td>Pre-operative</td>
<td>Post-operative</td>
</tr>
<tr>
<td>Biopsies done</td>
<td>48 ± 12</td>
<td>28 ± 8.0†</td>
</tr>
<tr>
<td>Autopsies done</td>
<td>48 ± 12</td>
<td>31 ± 8.1‡</td>
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*There were no statistically significant differences between any preoperative or postoperative values between those patients who had biopsies and those who had autopsies.
†In 14 preoperative vs postoperative patients, p<0.001.
‡In 12 preoperative vs postoperative patients, p<0.001.
FIGURE 5. Plexogenic lesion. Top, autopsy specimen, case 16. This muscular pulmonary artery has multiple thin-walled vascular channels within its wall and in the surrounding adventitia (Verhoeff-van Gieson elastic stain, original magnification ×100). Bottom, autopsy specimen, case 16. This small arteriole contains several thin-walled vascular channels within its wall. Distended capillaries are present in the adjacent tissue (Verhoeff-van Gieson elastic stain, original magnification ×250).

the 331 vessels analyzed contained these other hypertensive lesions. Because only two patients who had biopsies and three cases that had autopsies failed to demonstrate one or more of the hypertensive lesions, we did not attempt to relate the type and number of hypertensive lesions to the preoperative hemodynamic data.

In cases in which biopsies were done, there was no obvious relationship between the flow to the lobes from which the biopsy specimen was taken (absent, partial, or normal, as assessed by the preoperative angiogram or scan) and the pathologic lesions (Tables 1, 2). For example, of the 12 specimens with no pulmonary arterial flow to the area from which a biopsy specimen was removed, 9 had plexogenic lesions; of the five with partial flow, none had plexogenic lesions; the one patient with normal flow had both plexogenic and angiomatoid lesions.

In the autopsied cases, there was a similar lack of relationship between preoperative angiogram or scan assessment of flow to the lung zones from which sections were taken and the pathologic characteristics observed. Plexogenic and other lesions were found when proximal vessels demonstrated no, partial, or normal flow preoperatively. Conversely, these lesions were absent in some patients with each type of flow.

Other Data: In two cases, both biopsy and autopsy specimens were available for review. In one, a right upper lobe (RUL) biopsy disclosed EIF, CIF, and thrombotic lesions but no plexogenic lesions. The RUL autopsy specimen showed these same findings, but other lobes, at the time of autopsy, disclosed plexogenic lesions.

The other patient had EIF, CIF, and thrombotic lesions in an RUL biopsy specimen; the RUL autopsy findings were the same except that CIF was absent. Plexogenic lesions were absent in both the biopsy and autopsy specimens.

In the three autopsied patients who died of other causes after hospital discharge, one (No. 13, Table 2) who died 17 years later had no pulmonary hypertensive lesions; one (No. 1, Table 2) who died 3 years later had only EIF; and one (No. 11) who died 5 years later, had EIF, CIF, thrombotic, and plexogenic lesions.

Of the 12 patients who had biopsies who survived the perioperative period, all are still alive at an average 7.3 years (range: 6 to 9 years) after surgery. Of these survivors, eight had plexogenic lesions at the time of biopsy.

DISCUSSION

Chronic major vessel thromboembolic pulmonary hypertension is a more common condition than previously recognized.1,2 Correct diagnosis of CTEPH has assumed greater importance because it has become potentially remediable by surgical thromboendarterectomy.3,4 However, long diagnostic delays have been characteristic, averaging more than three years; and, often, the patients have been considered to have primary pulmonary hypertension. Indeed, lung biopsies, performed elsewhere, led to apparent confirmation of the diagnosis of primary pulmonary hypertension (PPH) in eight patients operated on at our institution, causing significant diagnostic delay. Furthermore, the natural history of CTEPH suggests that, over time, right ventricular dysfunction progresses and pulmonary hypertension increases, even though recurrent embolism has not occurred.5 This sequence suggested to us a role for progressive lesions in the small pulmonary arteries in these patients and focused our attention upon the status of these small arteries. Furthermore, the relative infrequency of the confirmed diagnosis of this condition has provided little information about the status of the nonelastic arteries. Indeed, the only comparable observations were those reported by Anderson et al in 1972.6 They described detailed microscopic findings at the time of autopsy in two patients with confirmed CTEPH of five and six
years' duration. They found an increase in medial thickness and fibrous intimal thickening and stated that "dilatation lesions were as common as in the cases of advanced PPH." They did note that dilatation lesions were less common in "uninjected" (proximally obstructed) regions than in "injected" (nonobstructed regions), but were present in both types of regions. They concluded that the "close similarity of the end stages of PPH and T-EPH [suggests that] many of the pathologic findings represent the non-specific effect of long-standing pulmonary hypertension." Our observations, in this much larger series of patients with proven CTEPH, confirm these previous findings.

Other reports dealing with histopathology of the lung vasculature in pulmonary hypertensive patients do not provide data that allow comparison with ours. For example, Goodwin et al.¹⁰ in 1963 reviewed a series in which some patients had PPH while others apparently had large vessel thromboembolic hypertension. Unfortunately, no microscopic descriptions of small pulmonary arteries in patients with the latter condition are provided. Presti et al.²⁰ reported a study of 68 patients with chronic emboli discovered at autopsy. This retrospective study covered a period of 37 years (1948 to 1985). No hemodynamic or angiographic data were provided, and the limited historical and clinical data were obtained by retrospective chart review. Thus, whether these patients had pulmonary hypertension is unknown. Without such information, the histopathologic findings in that series cannot be related to those we have described.

Previous reports regarding pulmonary hypertension associated with congenital and acquired cardiac conditions have documented that a variety of pulmonary hypertensive lesions occur in these states in the small pulmonary arteries. These lesions include muscular hypertrophy, intimal proliferation-fibrosis and plexogenic lesions.¹⁴,²¹,²² Clearly, then, none of these lesions has pathogenetic significance or infers a specific diagnosis. Instead, they are accepted as consequences of the hypertensive state. The precise mechanisms which lead to their development remain to be elucidated.

Similar lesions also are encountered in pulmonary hypertensive patients without coincident cardiac disease; that is, in patients with so-called primary or idiopathic pulmonary hypertension.¹⁷,²⁵,²⁶ In such patients, certain of these lesions have been suggested as having pathogenetic significance.⁶ Furthermore, and of more direct clinical importance, has been the impression that the finding of plexogenic lesions in lung biopsy specimens is pathognomonic of PPH so long as coincident cardiac or parenchymal pulmonary disease has been excluded. The data reported here indicate that such a use of lung biopsy data may lead, unfortunately, to an erroneous diagnosis; that is, a diagnosis of PPH instead of CTEPH. Furthermore, the identification of plexogenic lesions is likely conditioned by the extent to which lung sampling is possible, as Lloyd et al.¹⁶ have indicated. Thus, identification of such lesions is likely to be more frequent at the time of autopsy than via lung biopsy, as was the case in our series.

These histopathologic issues have a direct bearing upon the diagnosis and management of patients in whom the differential diagnosis lies between PPH and CTEPH. Clinically, PPH and CTEPH can mimic each other quite closely.¹,² Further, while the diagnosis can be distinguished by lung scan and pulmonary angiography, instances might occur in which a lung biopsy is done first, with a presumptive diagnosis of PPH. If, in such patients, the finding of pulmonary hypertensive lesions were accepted as confirming the diagnosis of PPH, diagnostic evaluation might cease. As we have indicated, such instances have been encountered in our series. These patients have encountered substantial delay in consideration of a potentially curable pulmonary thromboendarterectomy. Our data indicate, to the contrary, that PPH cannot be differentiated from CTEPH on the basis of lung biopsy findings.

Several other aspects of the findings reported here are intriguing. First, the finding of plexogenic lesions in CTEPH does not have adverse prognostic implications regarding the outcome of thromboendarterectomy. Specifically, patients with such lesions had positive postsurgical hemodynamic and functional improvements which paralleled those seen in the remainder of the patients in our series. Second, it is interesting that the pulmonary hypertensive lesions, including plexogenic lesions, occurred not only in lung regions served by open proximal vessels—and therefore exposed to pulmonary hypertension—but also in lung regions distal to completely obstructed and partially obstructed proximal vessels, as previously noted by others.¹⁸ Data from experimental animals have documented that similar lesions develop distal to ligated pulmonary arteries.²⁵ The mechanisms responsible remain obscure but lead us to speculate that production/release of mediators from endothelial cells or platelets, or both, is somehow stimulated by the pulmonary hypertensive state. The role of such mediators in human vascular disease is an object of intense investigation in many laboratories.²⁶

The time course over which such lesions develop in CTEPH is unknown. However, their development in the open vascular bed may well play a role in the deterioration which many of these patients experience over time. Also, such changes in the open bed may explain the vascular steal phenomenon we have described in the postoperative period.²⁷ In this phenomenon, flow increases to the lung zones from which proximal thrombi have been removed but sharply
decreases (is stolen from) zones supplied by elastic arteries free of thromboemboli by scan, angiogram, and surgical observation. We have speculated that such stealing may reflect more severe, diffuse hypertensive lesions in the open versus the closed vascular bed, a speculation we are currently studying.

However, it is important to note that survivorship and hemodynamic improvement after surgery were not conditioned by the preoperative hemodynamic values nor by the histologic findings at biopsy or autopsy. While thirteen of the autopsied patients died in the postoperative period, the causes of death were variable, including myocardial infarction, reperfusion lung edema, sepsis, and other postoperative complications. Three of the biopsied patients died postoperatively from complications of reperfusion edema or bleeding. The causes of death in the cases in which biopsies and autopsies were done were not different from those in the entire series of patients who had operations.

From the clinical viewpoint, however, the most critical finding was that pulmonary hypertensive lesions, including plexogenic lesions, at the time of lung biopsy do not exclude the diagnosis of CTEPH, nor do they preclude an excellent short- and long-term result from surgical pulmonary thromboendarterectomy.

REFERENCES

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