Pathology of the Pulmonary Vascular Tree

II. The Occurrence in Mitral Insufficiency of Occlusive Pulmonary Vascular Lesions

By Donald L. Becker, M.D., Howard B. BurcheLL, M.D., and Jesse E. Edwards, M.D.

Two cases of mitral insufficiency are reported. In 1 case the lesion was produced by rupture of the chordae tendineae of the posterior leaflet of the mitral valve. In the other case it was produced by fibrous adhesion of the posterior leaflet of the mitral valve to the underlying left ventricular wall, which occurred during healing of subacute bacterial endocarditis. Changes occurred in the pulmonary vascular bed which are essentially identical with those found in mitral stenosis.

In 1936 Parker and Weiss described certain changes which occurred in the pulmonary arteries and arterioles and in the alveolar walls in cases of severe mitral stenosis. These changes consisted of intimal thickening of arteries, hyperplastic arteriolosclerosis, arteriolonecrosis, collagenous thickening of alveolar walls, alveolar capillary dilatation, thickened capillary basement membranes, pericapillary edema and the presence of cuboidal epithelial cells lining the alveoli. In 1949 Larrabee, Parker and Edwards confirmed these observations and stressed that medial muscular hypertrophy preceded intimal fibrous thickening of the involved vessels.

It is our purpose to present and discuss data on 2 cases of mitral insufficiency with pulmonary vascular changes identical with those seen in cases of mitral stenosis.

REPORT OF CASES

Case 1.

Clinical Features. A man aged 52 years entered the Mayo Clinic on Nov. 16, 1948, with chief complaints of weakness and dyspnea of 12 months' duration. In November, 1947, following a day's work on a harvesting combine, and while he was at rest, acute shortness of breath developed. For this he was confined to a hospital for one week. His condition improved slightly during the next two weeks, but he noted some weakness and returned to the hospital at the end of this time with "fluid in the lungs." He improved, but weakness continued. Subsequently palpitation and intermittent orthopnea developed. In April, 1948, edema of the lower extremities appeared. From September until the time of admission on Nov. 16 the symptoms became progressively more pronounced. One week before admission cough with blood-streaked sputum appeared. The patient had had frequent attacks of tonsillitis since childhood but had no other history suggestive of rheumatic fever or scarlatina.

Examination revealed a white man, appearing chronically ill. He was dyspneic and was coughing. The apical beat of the heart was in the left axillary line. There was a loud, harsh systolic murmur with a presystolic component loudest at the apex. The murmurs were transmitted toward the left axilla. There were dry rales over the lower portion of the right lung, marked hepatomegaly and moderate pitting edema of the ankles. The blood pressure was 105 mm. Hg systolic, and 85 diastolic. The pulse rate was 106 beats per minute. Erythrocytes numbered 4,150,000 per cu. mm. of blood and leukocytes 14,100. The differential blood count was normal. The hemoglobin concentration was 12.2 Gm. per 100 cc. of blood.

The patient was treated with digitalis, diuretics and a diet low in sodium content. This resulted in an immediate loss of about 12 pounds (about 5 Kg.), with considerable improvement of his respiratory distress.

On December 1, 1948, a severe pain in the right flank suddenly developed, followed in five hours by a chill, a temperature of 104 F. and a friction rub in the right axilla. Roentgenograms of the thorax on the following day revealed evidence of consolidation in the right lower pulmonary field consistent with pulmonary infarction. A blood culture taken on December 2 was positive for hemolytic streptococcus. The patient's condition became rapidly more serious, with "spiking" fever, cyanosis, weakness and falling blood pressure. A regimen of penicillin, dicumarol and oxygen was instituted, but he did not respond. He died on Dec. 8, 1948.

Necropsy Features. The heart was enlarged, weighing 555 Gm. Both ventricles appeared slightly di-
Fig. 1 (case 1). a. The left atrium from above. The posterior leaflet of the mitral valve has a dome-shaped deformity. The probe points to the endocardial "jet lesions" resulting from mitral insufficiency. b. The left atrium and left ventricle. The majority of the chordae tendineae of the posterior leaflet of the mitral valve (at the left side of the photograph) are ruptured. The endocardial "jet lesions" are seen on the left atrial wall. The left ventricular wall is hypertrophied. c. Posterior mitral leaflet showing details of ruptured chordae tendineae.

lated, and the ventricular walls were thickened, the left averaging 1.8 cm. and the right 1.0 cm. in thickness. The posterior leaflet of the mitral valve was distorted, bulging upward toward the left atrial cavity, and all of the chordae tendineae of this leaflet except three attached near the medial commissure were discontinuous (fig. la and b). The free ends of the disrupted chordae tendineae were
rounded and smooth (fig. 1c). Attempted approximation of the ends of the divided chordae revealed a deficiency of length averaging several millimeters. There was no apparent thickening of the involved chordae nor of the chordae tendineae of the anterior leaflet of the mitral valve. There were no vegetations on either mitral leaflet and the endocardial surfaces appeared normal. The circumference of the mitral valve was abnormally great (15.0 cm.), equaling that of the tricuspid valve. The endocardium of the inferior portion of the septal wall of the left atrium over an area 3 cm. in diameter was roughened and irregular and contained innumerable small elevations giving it a corrugated appearance (fig. 1a). There were multiple friable, thrombotic masses attached loosely to the wall of the right auricular appendage. The tricuspid, aortic and pulmonary valves were normal. The coronary arteries showed only minimal degrees of atherosclerosis.

The left lung weighed 430 Gm. It was crepitant and appeared slightly darker than normal, having a faint brownish hue. The right lung weighed 810 Gm. Deep within the substance of its upper lobe was a dark red circumscribed area of consolidation 2 cm. in diameter; a small pulmonary artery adjacent to this area was occluded by a dark red, moderately soft thrombus. The surrounding substance of the upper lobe of the right lung and the entire middle lobe appeared grossly normal. The central part of the lower lobe of the right lung was occupied by a firm, grayish, consolidated lesion 11 by 3 by 4 cm. in dimension. In the center it was softened as though necrotic. Two of the larger arteries supplying the region of the lesion were occluded by a yellow-brown adherent thrombus.

The main branches of both pulmonary arteries contained scattered yellow atheromatous lesions from 1 to 5 mm. in diameter.

The liver and spleen presented the gross picture of mild chronic passive congestion, weighing respectively 1,845 Gm. and 295 Gm. At the lower pole of the right kidney there was a pyramidal scar 0.5 cm. wide at its cortical base representing a healed infarct. The remaining organs appeared essentially normal.

Microscopically, sections of the myocardium from all chambers showed changes only in the left posterior papillary muscle. Here there were scattered tiny collagenous scars, each of a diameter only slightly more than the diameter of a muscle fiber.

Sections of two of the ruptured chordae tendineae revealed no cellular infiltration, vascularity or other recognizable abnormality. This supported the opinion that the chordae had ruptured long before death and probably at the same time as the onset of the patient's illness about a year before his death. A section of the left atrium through the area of roughened endocardium revealed rather marked irregular endocardial thickening by collagen and scattered fibroblasts. This change was interpreted as a "jet lesion" or an "endocardial pocket," that is, a lesion resulting from the trauma of regurgitant blood.

Whereas the lesions observed in the major pulmonary arteries and in intrapulmonary elastic arteries were atheromatous in nature, the lesions within the smaller pulmonary vessels were nonatheromatous. They were similar to those seen in the lung in cases of mitral stenosis.

For descriptive purposes the changes in the pulmonary vascular tree will be divided into those of the capillaries, the arterioles, the muscular arteries, elastic arteries and the veins. The alveolar capillaries, particularly in the upper lobes, were dilated and tortuous and appeared to have slightly thickened
basement membranes. Here and there the capillary dilatation was marked to the extent that there was protrusion of the capillary into the alveolar space, with the production of so-called capillary aneurysms. In general there were fewer visibly patent capillaries in the lower lobes than in the upper; some areas in others by concentric layers of fibroblasts (fig. 2c). These changes were often extreme, resulting in marked narrowing of the lumen. No vessels showed hyaline or necrotic changes.

The smaller muscular arteries showed medial hypertrophy causing mild or moderate degrees of

![Figure 3](http://circ.ahajournals.org/)

**Fig. 3** (case 1). Pulmonary muscular arteries (Verhoeff's elastic tissue stain counterstained with van Gieson's connective tissue stain). *a.* Small artery showing hypertrophy of the medial musculature with slight narrowing of the lumen. The intima is not thickened (×335). *b.* Medial hypertrophy and a moderate degree of intimal thickening (×330). *c.* Greatly narrowed lumen. The intimal thickening here overshadows the medial hypertrophy. Toward the right the media appears atrophic (×225). *d.* In this artery the intimal tissue is relatively acellular, dense and composed predominantly of collagen (×340).

the lower lobes were, in fact, noticeably deficient in patent capillaries.

The arterioles showed, in virtually all areas of all lobes, some degree of fibrous intimal thickening. This was caused in some instances by relatively acellular and collagenous tissue (fig. 2a and b), in luminal narrowing (fig. 3a). Many of the smaller muscular arteries showed, as well, intimal nonatheromatous fibrous thickening (fig. 3b, c and d). When this change was present the luminal narrowing was accentuated. A few of the small muscular arteries presented split and reduplicated internal
elastic membranes. In some with pronounced intimal change, there was focal atrophy of the media (fig. 3c). In the larger muscular arteries the predominant change was muscular hypertrophy of the media. In a few vessels there were collagenous strands among the muscle cells. In nearly every vessel there was some degree of intimal thickening, although this was usually not a marked change. Almost every one of these vessels had some degree of narrowing of the lumen, usually slight in degree. The elastic arteries showed small focal intimal atheromas. The veins showed intimal thickening by bundles of smooth muscle and connective tissue (fig. 4).

In addition to the vascular changes described there were scattered pulmonary arteries of varying size containing organizing thrombi. The thrombi were interpreted as being emboli from the mural thrombus of the right auricular appendage.

In all lobes there were varying degrees of patchy alveolar collapse; the upper lobe of the left lung presented, in addition, areas of emphysema. The basement membranes of the alveolar capillaries appeared to be slightly thickened in the sections stained by the Masson trichrome stain, but this was by no means a marked change. In scattered areas in the lower lobes the alveolar epithelium was cuboidal in character; this change was seen only in the areas adjacent to infarcted pulmonary tissue. The alveolar spaces contained no precipitate resembling edema fluid. In all lobes there were scattered small extravasations of blood into the alveoli, and in every section numbers of macrophages laden with hemosiderin were seen. All of these changes were more marked in the lower lobes than in the upper lobes. The lumina of scattered bronchioles were filled with exudate, mainly neutrophils, accompanied by neutrophilic infiltration in the adjacent alveoli and connective tissue.

Case 2.

Clinical Features. A woman aged 43 years entered the clinic on Nov. 25, 1948, because of subacute bacterial endocarditis. Over a period of 20 years she had been repeatedly examined and treated at the clinic for rheumatic heart disease characterized by an apical systolic murmur and slight cardiac enlargement. Since childhood she had had a rather marked kyphoscoliosis. For eight years she had had intermittent episodes of mild congestive failure which responded well to the usual therapy. At the time of her admission she had a low-grade fever, splenomegaly, intermittent microscopic hematuria and recurrent tender red spots on the fingers. On November 29 an episode of abdominal pain developed, which was interpreted as resulting from splenic infarction. Blood cultures yielded Streptococcus mitis. Starting on Nov. 29, the patient was treated with penicillin in doses of 1,000,000 units daily for a period of 35 days. A blood culture taken two days after the beginning of therapy was negative. Many subsequent blood cultures were also consistently negative.

On Jan. 23, 1949, while the patient was at home after having felt quite well for a period of several weeks, acute severe right hemi-cranial headache suddenly developed, followed in a few moments by complete left-sided hemiplegia. During the following seven weeks the hemiplegia improved gradually to the point at which she was able to walk with assistance and to care for her own needs. Between June, 1949, and January, 1950, her condition remained stable. Her cardiac status seemed essentially the same as before her attack of subacute bacterial endocarditis.

Early in January, 1950, a cough developed, with mild dyspnea and orthopnea and edema of the feet. The patient's symptoms became gradually more severe. At the time of final admission on Jan. 27, 1950, the cardiac findings on physical examination were essentially like those of previous examinations. There were rales over the lower portions of both lungs. The liver was palpably enlarged and slightly tender. There were residual neurologic changes from the old left-sided hemiplegia. The patient was maintained on a regimen of digitalis, low sodium diet, mercurial diuretics and oxygen.

Necropsy Findings. The heart was enlarged, weighing 450 Gm. Both ventricles appeared dilated and the ventricular walls were thickened, the left averaging 1.7 cm. and the right 1.0 cm. in thickness. The central two thirds of the posterior leaflet of the mitral valve was firmly adherent to the underlying posterior wall of the left ventricle. This portion of the leaflet was completely immobilized and so had lost any ability to function as a valve flap. The anterior (aortic) leaflet of the mitral valve was slightly and uniformly thickened and contained a small calcified vegetation at the line of closure near the medial commissure. All of the chordae tendineae of the mitral valve were thickened and shortened. The circumference of the mitral valve was 12.5 cm. The endocardium of the inferior portion of the septal and posterior walls of the left atrium was roughened and irregular, presenting a corrugated appearance. The aortic, pulmonary and tricuspid valves appeared normal.

The right lung weighed 290 Gm. and the left, 255 Gm. The dependent portions of both lower lobes were firm, noncrepitant and dark red. The remaining portions of the lungs appeared normal.

The lining of the main branches of both pulmonary arteries contained a few scattered yellowish atheromatous plaques. The liver weighed 1,130 Gm. and presented the gross picture of mild chronic passive congestion. The right renal artery was completely occluded by a dark red thrombotic mass, and the right kidney was infarcted. There was marked kyphoscoliosis with rotation of thoracic and upper lumbar vertebrae to the left. Examination of the brain revealed an old cystic infarct in the right motor area.

On microscopic examination the posterior leaflet of the mitral valve was applied closely to the surface of the underlying left ventricular wall and was bound so closely to it by bundles of collagenous connective tissue that it was difficult to distinguish ventricular endocardium from the valve proper (fig. 5a). Within the valve substance there were many small capillaries, and immediately adjacent to several of these were minute focal collections of neu-
trophilic leukocytes. At several points along the atrial aspect of the valve there was ulceration and small nodular excrescences of acellular fibrinous material.

At the line of closure of the anterior mitral leaflet there were scattered small scars, consistent with healed small infarcts. No Aschoff bodies were identified in any of the sections.

Sections of the left atrium in the region of the corrugated patch revealed the irregular endocardial

Fig. 6 (case 2). Pulmonary vessels (Verhoeff's elastic tissue stain counterstained with van Gieson's connective tissue stain). a. An arteriole showing marked intimal thickening by relatively acellular connective tissue. The lumen is very narrow (×515). b. A muscular artery showing muscular hypertrophy of the media and eccentric proliferation of the intima (×380). c. A muscular artery showing very marked luminal narrowing. The intimal proliferative change here overshadows the hypertrophy of the media. The intimal tissue is dense and acellular (×400). d. In this muscular artery the intimal tissue is cellular. The media is irregular in thickness and contains strands of proliferated elastic tissue. The adventitia is somewhat thickened by fibrous tissue (×250). e. A small vein. There is marked intimal thickening by fibrous tissue (×175).

there was a small nodular mass of relatively acellular collagenous connective tissue (fig. 5b). No infiltrating cells were present in the leaflet.

Representative sections of the myocardium revealed a small interstitial collection of lymphocytes in the ventricular septum. In the left anterior papillary muscle there were scattered small scars, consistent with healed small infarcts. No Aschoff bodies were identified in any of the sections.

The lungs presented a picture almost identical to that of case 1 save that in case 2 there were neither major arterial occlusions nor infarcts. The capillaries were engorged and dilated in scattered areas of
all sections and there were many minute alveolar hemorrhages. The capillary basement membranes did not appear to be greatly, if at all, thickened.

The intimas of the arterioles were greatly thickened, in part by concentric cellular proliferation, but predominantly by collagenous fibers (fig. 6a).

The predominant change in the muscular arteries, present in virtually every vessel, was muscular hypertrophy of the medine (fig. 6b). In some vessels there were collagen strands among the muscle cells. The smaller muscular arteries presented, in addition, varying degrees of cellular intimal thickening (fig. 6c and d). This change tended to occur much less frequently in the larger arteries of this type than in the smaller arteries.

The intrapulmonary veins showed intimal thickening with bundles of fibrous tissue (fig. 6e). Focal small atheromas were present in the elastic arteries.

Occasional small muscular arteries were partially or completely occluded by small organizing or organized thrombi. Throughout all areas of the lungs the alveoli contained numbers of hemosiderin-laden macrophages. Sections from the consolidated dependent portions of the lower lobes of both lungs revealed the picture of atelectasia. There was no evidence of alveolar edema fluid nor of acute inflammation. We were unable to find any areas in which the alveolar lining cells appeared cuboidal.

The spleen and liver presented moderate degrees of passive congestion. The right renal artery was completely occluded by a bland thrombus. No local or embolic source for this could be determined. Scattered glomeruli in the left kidney contained small adhesions between the capillary loops and Bowman's capsule. The blood vessels of the left kidney appeared normal; there was no evidence of hypertensive vascular changes in the vessels of the left kidney nor of any other area.

**Comment**

These 2 cases have in common a functional cardiac defect in the form of mitral insufficiency. The cause of each lesion is different; yet the end result has been almost complete inadequacy of the posterior leaflet of the mitral valve.

In case 1 mitral insufficiency resulted from rupture of the majority of the chordae tendineae of the posterior leaflet of the mitral valve. It is probable that rupture occurred immediately before the onset of symptoms about one year before the patient's death. Cause of the rupture has not been settled, but there is no evidence to support an inflammatory basis for it.

In case 2 there is evidence in the history and in the necropsy findings of chronic rheumatic mitral endocarditis without stenosis. As a complication of this in November, 1948, subacute bacterial endocarditis involving the mitral valve developed. Our interpretation is that with chemotherapy the mitral lesions healed and part of the posterior mitral leaflet became fused to the left ventricle, making it ineffective as a valve leaflet. This led to mitral insufficiency which probably existed for about thirteen months immediately before the patient's death. It was not felt that the kyphoscoliosis had had any significant adverse effect on her condition since it had existed since childhood.

It is to be emphasized that in our case 1 there was no evidence of valvular disease other than the rupture of chordae tendineae of the posterior mitral leaflet and the attendant effects of mitral insufficiency.

Bailey and Hickam described 7 cases of ruptured chordae tendineae of the mitral valve. In 2 there was definite evidence of pre-existing rheumatic fever while in the remainder the changes suggested quiescent rheumatic fever but were not pathognomonic.

In our second case the rheumatic residue did not cause mitral stenosis. Mitral insufficiency therefore was the only functional valvular abnormality in each case.

We wish to focus attention on the fact that in each of our 2 cases of mitral insufficiency the hypertrophic and occlusive lesions in the pulmonary arteries, arterioles and veins were indistinguishable from those occurring in mitral stenosis.

Minor differences between our 2 cases of mitral insufficiency on one hand and the reported cases of mitral stenosis on the other were observed in the basement membranes of the alveolar capillaries and in the lining of the alveoli. We observed little, if any, thickening of the basement membranes of the alveolar capillaries; in mitral stenosis they may be thickened. We observed cuboid cells lining the alveolar walls only in relation to infarcts of the lung. In mitral stenosis these cellular changes need have no such localization.

With interest in surgical therapy of mitral stenosis becoming progressively greater and more widespread our cases seem to support the
concept that operative procedures on the stenotic mitral valve must be directed in such a way as to avoid significant mitral insufficiency. Otherwise secondary effects upon the pulmonary vascular tree and upon the right side of the heart may be caused or accentuated by the very operative procedures designed to prevent their occurrence.

SUMMARY

Two cases of mitral insufficiency are reported. In one case the lesion was produced by rupture of the chordae tendineae of the posterior leaflet of the mitral valve. In the other case it was produced by fibrous adhesion of the posterior leaflet of the mitral valve to the underlying left ventricular wall, which occurred during healing of subacute bacterial endocarditis. Changes occurred in the pulmonary vascular bed which are essentially identical with those found in mitral stenosis.

REFERENCES

3 Bailey, O. T., and Hickam, J. B.: Rupture of the mitral chordae tendineae; clinical and pathologic observations on 7 cases in which there was no bacterial endocarditis. Am. Heart J. 28: 578, 1944.
Pathology of the Pulmonary Vascular Tree: II. The Occurrence in Mitral Insufficiency of Occlusive Pulmonary Vascular Lesions

DONALD L. BECKER, HOWARD B. BURCHELL and JESSE E. EDWARDS

Circulation. 1951;3:230-238
doi: 10.1161/01.CIR.3.2.230

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1951 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/3/2/230