The Anatomical Factor in Pulmonary Heart Disease

Michiyoshi Harasawa, M.D., Seiichi Yoshida, M.D., Yasunobu Fukushima, M.D., Hiroshi Murao, M.D., and Satoshi Kitamura, M.D.

Pulmonary heart disease was found in 6.9% among 450 autopsies of an aged population. Pulmonary emphysema was much commoner in men, but pulmonary heart disease occurred in about 20% of the cases of pulmonary emphysema, regardless of the sex. In the cases of pulmonary tuberculosis, pulmonary heart disease was seen only in far advanced cases with long standing history. In the cases of pulmonary tumor emboli, primary pulmonary hypertension, pulmonary scleroderma and pulmonary tuberculosis, marked reduction was observed in the vascular cross section due to obliteration or narrowing in a sufficient extent to raise the pulmonary arterial pressure. A marked difference was found in the arteriographic findings between the centrilobular emphysema and the panacinar emphysema, however, no difference was found in the rate of the development of pulmonary heart disease between these 2 types of emphysema. The most important organic changes to reduce the large reserve of the pulmonary vascular bed in emphysema appears to be the loss of the pulmonary vascular bed.

The term pulmonary heart disease is generally defined as “hypertrophy of the right ventricle resulting from diseases affecting the function and/or the structure of the lung, except when these pulmonary alterations are the result of diseases that primarily affect the left side of the heart or of congenital heart disease.” The mechanism of the development of pulmonary heart disease, however, is not completely understood, except for the important role played by the pulmonary hypertension.

There are 2 basic mechanisms, that lead to pulmonary hypertension: 1) Anatomical changes of the pulmonary vascular bed or 2) functional factor, or a combination of these factors.

The present investigation is conducted to examine the morphological changes of the pulmonary arterial system in pulmonary heart disease in an attempt to clarify the anatomical factor in the pathogenesis of pulmonary hypertension in several diseases of the lung.

From the Department of Geriatrics, and the Third Department of Internal Medicine, Faculty of Medicine, University of Tokyo, Tokyo.
MATERIALS AND METHODS

The pulmonary arteries were examined in 28 cases which had been given the pathological diagnosis of pulmonary heart disease in the Yokufukai Hospital for the aged during last 4 years, with conventional histological technique and by post-mortem arteriography.

The morphological diagnosis of the chronic pulmonary heart disease in Yokufukai Hospital was based on following criteria, 1) presence of right ventricular hypertrophy, 2) presence of pulmonary atherosclerosis, 3) greater total blood volume at autopsy in the right side of the heart, and 4) absence of diseases of the left side of the heart, which are responsible for these changes.

Pulmonary arteries with an external diameter ranging from 100 μ. to over 1,000 μ. are divided into 5 sections; small artery, muscular arteries I, II, III and elastic artery. The thickness of the arterial wall and of its components, and the external diameter of the vessels were measured in each section. The calculated media-to-diameter ratio and media-intima-to-diameter ratio in each section of the pulmonary arteries were compared between the cases of pulmonary heart disease and those without pulmonary or heart disease.

The histological changes of intima and media were also studied in each sections of the pulmonary arteries. In some cases of pulmonary emphysema, post-mortem arteriography has been employed. Barium mixed with gelatin sulfate in aqueous solution was injected with a pressure of 15 mm.Hg.

In order to clarify the anatomical factor responsible for the pathogenesis of pulmonary hypertension, the morphological aspects of pulmonary arterial system were also studied in 12 cases of pulmonary tumor emboli, a case of primary pulmonary hypertension, a case of pulmonary scleroderma and 59 cases of pulmonary tuberculosis.

RESULTS

1. Incidence of pulmonary heart disease among the aged and the underlying primary lung diseases

Out of 415 autopsied cases in Yokufukai Hospital during the last 4 years, 28 cases (6.7%) were given the pathological diagnosis of pulmonary heart disease.

Table I. Incidence of pulmonary Heart Disease among the Aged, and Their Underlying Pulmonary Conditions

<table>
<thead>
<tr>
<th>Autopsied cases (1959~1963)</th>
<th>415</th>
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<tbody>
<tr>
<td>Pulmonary heart disease</td>
<td>28  (6.7%)</td>
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<tr>
<td>Underlying pulmonary condition</td>
<td></td>
</tr>
<tr>
<td>Pulmonary emphysema</td>
<td>23</td>
</tr>
<tr>
<td>Pulmonary tuberculosis with pleural scar</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1</td>
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The underlying pulmonary conditions consist of pulmonary emphysema in 23 cases, pulmonary tuberculosis with marked pleural scar in 3, pulmonary fibrosis in one and pulmonary embolism in one (Table I).

2. Vascular changes in pulmonary heart disease

1) Pulmonary atherosclerosis

Atheroma and fatty streak in the pulmonary trunk and the major pulmonary arteries were seen in all of 28 cases with pulmonary heart disease but only in 37% of 108 cases without pulmonary and heart disease.

The incidence and grade of pulmonary atherosclerosis showed a correlation with neither the age nor the atherosclerosis in other arteries such as the aorta, cerebral and coronary arteries (Fig. 1).

2) Anatomical changes of the pulmonary arterial wall

Fig. 2 and Fig. 3 show the changes of media-to-diameter ratio and the

![Graph 1](image1)

**Fig. 1.** Correlation of the grade of atherosclerosis between pulmonary artery and systemic vessels, such as the aorta, cerebral and coronary arteries. The grade of sclerosis is classified into 4 degrees from none (−) to the most severe (+++).

![Graph 2](image2)

**Fig. 2.** Media-to-diameter ratio at various levels of pulmonary arterial system in cases of pulmonary heart disease and controls.
Fig. 3. Media+intima-to-diameter ratio at various levels of pulmonary arterial system.

Table II. Anatomical Changes of the Pulmonary Arterial Wall

<table>
<thead>
<tr>
<th>External diameter</th>
<th>S</th>
<th>M₁</th>
<th>M₂</th>
<th>M₃</th>
<th>E</th>
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**Table II** shows the morphological changes of the pulmonary arterial wall in these cases. Intimal fibrosis and increase of elastica in media were fairly common in the muscular pulmonary arteries in these cases.
3. Anatomical factors in response to the pathogenesis of pulmonary hypertension in several pulmonary diseases

Pulmonary heart disease is generally classified into 2 major categories; 1) diseases of pulmonary vascular bed, 2) disorders of the lung parenchyma. The anatomical factors which might be directly responsible for the production of pulmonary hypertension were studied by standard histological methods and by post-mortem pulmonary arteriography in several diseases of the lung.

1) Diseases of the pulmonary vascular bed
   (i) Pulmonary tumor embolism
   A 26-year-old woman complained of cough with sputum for 11 months. The electrocardiogram showed a right heart loading 1 week before death. At necropsy, the pulmonary arteries were filled with numerous tumor cells and thrombi at various stages of organization (Fig. 4).

   (ii) Primary pulmonary hypertension
   A 32-year-old woman was admitted to the Hospital because of a pro-

Fig. 4. Muscular pulmonary arteries in a woman with pulmonary tumor emboli. The pulmonary arteries were filled with numerous tumor cells and thrombi at various stages of organization ($\times 25$).

Fig. 5. Pulmonary arteries in a woman aged 32 years with primary pulmonary hypertension. Obliteration and narrowing of the lumen due to reactive intimal proliferation was found ($\times 100$).
gressive exertional dyspnea and palpitation. For the last one and a half year she had noted cyanosis and edema herself. A right side cardiac enlargement was demonstrated in the chest X-ray film and electrocardiogram. Cardiac catheterization revealed a marked elevation of the pulmonary arterial pressure. In the post-mortem study, obliteration and narrowing of the lumen due to reactive intimal proliferation was found throughout the pulmonary arteries (Fig. 5).

2) Disorders of the lung parenchyma
(i) Pulmonary scleroderma

A 34-year-old woman suffered from scleroderma for 3 and a half years. For the last 2 years she showed the signs of pulmonary insufficiency. The chest X-ray film showed fine nodular densities throughout both lungfields, and a right heart enlargement was suggested from the electrocardiogram. A marked perivascular fibrosis and intimal proliferation with narrowing of the pulmonary artery was demonstrated by the histological examination with an extensive distribution (Fig. 6).

Fig. 6. Muscular pulmonary arteries in a woman aged 34 years with scleroderma. There is perivascular fibrosis and intimal proliferation with narrowing of the pulmonary arteries (×100).

(ii) Pulmonary tuberculosis

Fig. 7 shows the relationship between the incidence of right ventricular hypertrophy and chest X-ray findings in 59 cases of pulmonary tuberculosis in advanced age. The incidence of right ventricular hypertrophy was the highest in the far advanced group. As the clinical course was prolonged, moreover, the incidence of right ventricular hypertrophy was further increased in far advanced cases.

Fig. 8 shows the small pulmonary arteries in the tuberculous caseous foci. Narrowing of the lumen due to reactive intimal fibrosis is obvious with infiltration of round cells. In some places, only the elastic laminae remain to show the previous structure of the vessel.
Fig. 7. Correlation of right ventricular hypertrophy and chest X-ray findings in 59 cases of pulmonary tuberculosis.

Fig. 8. Small pulmonary artery in tuberculous caseous foci. Narrowing of the lumen due to reactive intimal fibrosis with infiltration of round cells is seen. Also there is the elastic laminae remain to show the previous structure of the vessel (×100).

Fig. 9. Muscular pulmonary artery in tuberculous fibrous foci. The vessel is almost occluded by the intimal fibrosis and the increase in elastic fibers in the media (×100).
In the fibrous foci, the vessel is almost occluded by the intimal fibrosis and the increase in elastic fibers in the media. These changes are seen only in the tuberculous foci or in the neighboring area (Fig. 9).

(iii) Pulmonary emphysema

Our study has apparently confirmed the general concept of male preponderance in the incidence of pulmonary emphysema (Fig. 10). Out of 415 cases, the pulmonary emphysema was found in 47% in males and in 17% in females. However, no marked sex differences were seen in the incidence of

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Fig. 10. Incidence of pulmonary emphysema among the aged, and incidence of cor pulmonale among patients with pulmonary emphysema. Discussed in the text.

Fig. 11. Post-mortem pulmonary arteriograms in various types of pulmonary emphysema. Discussed in the text.
the development of pulmonary heart disease from the preexisting emphysema.

Fig. 11 shows the arteriograms of the pulmonary arteries in cases of different types of pulmonary emphysema. A marked decrease in the number of the small branches of the pulmonary arteries is seen in every type of pulmonary emphysema. The mode of destruction of the pulmonary arteries, however, is different in the 2 types of emphysema; panacinar and centrilobular varieties. In the centrilobular emphysema the central part of the lobule is preferentially destroyed, while the destruction takes place more in the peripheral part of the lobule in the panacinar type.

No marked difference was observed in the rate of the development of pulmonary heart disease between these 2 types of emphysema; the right heart enlargement was found in 9 of 23 cases of the centrilobular type and in 9 of 20 cases of panacinar type.

**DISCUSSION**

The task of the estimation of the frequency of pulmonary heart disease is a difficult one. White and Brenner considered it a rare disease, giving the figures of 1% among patients with heart disease. Wood concluded that a conservative estimate of its frequency would be 5 to 10% of all cases of organic heart disease. Flint, analysing 500 consecutive cases of heart failure, found pulmonary heart disease in 75 cases or 15%. In the autopsy data, McMichel found 114 cases (2.4%) with right heart hypertrophy out of 4,700 cases. McKeown encountered 114 instances (1.6%) of chronic pulmonary heart disease among 6,770 autopsies.

The slightly higher value obtained in our studies might be due to the age difference in the research materials. Results obtained from the studies of an aged population are apt to be higher in view of the high prevalence of emphysema which definitely favours the development of pulmonary heart disease.

Despite numerous primary pulmonary diseases that affect the pulmonary vascular bed, pulmonary emphysema has remained the most important cause of pulmonary heart disease in both absolute and relative estimations. Pulmonary emphysema also accounted for the majority of the cases in our study. The current opinion of the male preponderance in the incidence of pulmonary emphysema was also supported in our study, 47% in males and 17% in females. Pulmonary heart disease occurred in 20% of the cases of pulmonary emphysema, regardless of the sex.

Pulmonary atherosclerosis is a common finding, especially above the age of 40. Brenner pointed out the increase in the frequency of atherosclerosis
with age. Heath and associates studied the incidence and severity of atherosclerosis in the pulmonary arteries in relation to age, the pulmonary arterial mean blood pressure, the pulmonary blood flow and the grade of structural changes in the small pulmonary arteries in congenital and acquired heart disease. The results indicated the importance of pulmonary hypertension and high pulmonary blood flow in the etiology of pulmonary atheroma. The high incidence of pulmonary atheroma in pulmonary heart disease and the absence of a correlation between the atherosclerosis of the lung and that of systemic vessels such as aorta, cerebral and coronary arteries in our study, suggested the importance of pulmonary hypertension in the development of pulmonary atherosclerosis over against the role played by the age.

The thickening of the intima and media with a uniform distribution throughout the pulmonary vessels, intimal fibrosis and the increase of elastica in the media of muscular pulmonary arteries were the main histological findings in the small pulmonary artery. The changes in the medial muscle were not marked as compared with controls. In view of the fact that the development of pulmonary hypertension can hardly be explained by these changes in the walls of the pulmonary artery, these atherosclerotic changes probably represent the result rather than the cause of the persistent pulmonary hypertension.

The effect of pulmonary hypertension on the pulmonary vasculature had been studied intensively in acquired and congenital heart disease. The histological changes in pulmonary heart disease were extremely mild when compared with these reports. This is probably related to the fact that the degree of pulmonary hypertension in pulmonary heart disease was only slight except during periods of respiratory infection with congestive cardiac failure.

Although numerous factors and agents of various nature appear to be responsible in the production of pulmonary hypertension in several diseases of the lung, only 2 pathophysiologic mechanisms are basically important: 1) disturbances in physiological regulation, such as anoxia, carbon dioxide retention and increase of intra-alveolar air pressure, 2) disturbances in the anatomic structure of the lung and pulmonary circulation. Normal lungs have been reported to be able to accommodate at least a doubling of cardiac output without any significant increment of the pulmonary arterial pressure. The removal of one lung therefore does not increase the pulmonary arterial pressure. It follows that the loss of more than 50% of the lung is required before pulmonary hypertension is induced solely by the reduction of the capacity of the pulmonary vascular bed.

In the cases of pulmonary tumor embolism, primary pulmonary hyper-
tension, pulmonary scleroderma and pulmonary tuberculosis, a marked reduction was observed in the number of pulmonary vessels as the result of obliteration or narrowing of the vessels. It seems, therefore, likely that anatomic lesions are primarily responsible for the development of cardiac complications in these cases. The fact that the right heart enlargement in pulmonary tuberculosis was usually seen only in far advanced cases with long history also suggested the important role played by the anatomical factor.

In pulmonary emphysema, on the other hand, the importance of the functional factors is indicated by the reversibility of the pulmonary hypertension upon appropriate treatment and also by the failure of anatomical changes alone to raise the pulmonary arterial pressure. Irreversible organic changes, however, can reduce the large reserve of the vascular bed of the lung in emphysema. Upon the occurrence of the anatomic restriction, and superimposed physiologic factors tending to produce hypertension would more likely exert a significant effect.

Different organic changes have been referred by several authors as the most important vascular lesions to raise the pulmonary vascular resistance; loss of the capillaries, decreased distensibility of the vasculature resulting from the intimal fibrosis in arterioles, destruction of the capillary bed and parenchymal fibrosis, vascular obliteration or the narrowing of the vessels in areas of pulmonary fibrosis, organic stenosis of the small pulmonary arteries and arterioles near a chronically inflamed bronchiole, thromboembolic phenomena and precapillary bronchopulmonary arterial anastomoses in the areas of localized bronchiectasis. In general, these changes in emphysema are not sufficiently widespread or advanced to cause pulmonary hypertension by themselves.

In our study, a marked difference was found in the angiographic findings between the centrilobular emphysema in which the pulmonary destruction is confined to the central part of the lobules, the alveoli at periphery being relatively normal, and the panacinar emphysema in which the destruction takes place more in the peripheral part of the lobule. Based on similar observations, Dunnill emphasized the significance of the centrilobular emphysematous spaces in the centre of the secondary lobule, concluding that the most important factors in raising in these cases were vascular deformity and pressure by the emphysematous spaces on the adjacent branches of the pulmonary artery.

These changes could hardly be the main cause of pulmonary hypertension in every case of pulmonary emphysema in view of the absence of the difference in the incidence of right ventricular hypertrophy between the centrilobular and panacinar types of emphysema. In addition, it should be remembered that
the pulmonary capillaries are more easily affected by the elevated intra-alveolar air pressure than the small pulmonary arteries or arterioles. These results would point out to the importance of the loss of the pulmonary vascular bed as an irreversible organic changes in pulmonary emphysema.

**Summary**

1. Out of 415 autopsied cases in Yokufukai Hospital (old people's home) during last 4 years, 28 cases were given the pathological diagnosis of pulmonary heart diseases: 23 cases of pulmonary emphysema, 3 cases of pulmonary tuberculosis, 1 case of pulmonary fibrosis and 1 case of pulmonary embolism. Although the incidence of pulmonary emphysema is much greater in men than in women, no marked sex difference was found in the incidence of pulmonary heart disease among patients with pulmonary emphysema, pulmonary heart disease occurring in about 20% regardless of the sex. In pulmonary tuberculosis, pulmonary heart disease is seen only in far advanced cases with long standing history.

2. Pulmonary atherosclerosis in the major arteries and thickening of the intima and media throughout the arterioles, muscular arteries and elastic arteries of the pulmonary vessels were very common in pulmonary heart disease. Histological examination of the pulmonary arterial wall in these cases revealed intimal fibrosis and increase of elastica in the media in the muscular pulmonary arteries. These changes probably represent secondary manifestations of the disturbances in pulmonary circulation.

3. The aetiologic factors in the production of right heart hypertrophy in several lung diseases have been studied by standard histological methods and by post-mortem pulmonary arteriography. In the cases of pulmonary tumor emboli, primary pulmonary hypertension, pulmonary scleroderma and pulmonary tuberculosis, a marked reduction was observed in the vascular cross section due to obliteration or narrowing in a sufficient extent to raise the pulmonary arterial pressure.

4. Marked decrease in the number of the small branches of pulmonary arteries was found in the arteriograms in every type of pulmonary emphysema, although the mode of destruction of the arteries is different between the centrilobular and panacinar types of emphysema; in the centrilobular emphysema the central part of the lobule is destroyed while in the panacinar emphysema the destruction is mainly seen in the peripheral part of the lobule. No marked difference, however, was found in the rate of the development of pulmonary heart disease between these 2 types of emphysema. The most important or-
ganic changes to reduce the large reserve of the vascular bed of the lung in emphysema appears to be the loss of the pulmonary vascular bed.

**References**