CARDIOVASCULAR PATHOLOGY

Volume 2

Edited by

Malcolm D. Silver

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PREFACE

The idea for this book came from the continued success of the Core Curriculum Course in Acquired Heart Disease sponsored by the American College of Cardiology and arranged by Drs. Jesse E. Edwards and Maurice Lev and, lately, with the help of Dr. Saroja Bharati. Indeed, several authors of chapters have been participants in those courses.

The need for a comprehensive pathology text dealing with acquired cardiovascular disease in adults is self-evident. A discussion of congenital heart diseases, with the exception of those encountered in, or allowing survival to adulthood, has been omitted. This is a deliberate choice because congenital heart disease has its own excellent texts. Also, few individuals combine both pediatric and adult age groups in a cardiology, cardiovascular surgery, or pathology practice. In considering chapters that are included, the surgical correction or palliation of congenital heart lesions has allowed affected children to survive to adulthood and prompted a need to understand the morphological effects of such treatments. Also, new diagnostic methods (cardiac biopsies) are available and new methods of treatment have created a pathology of their own.

The book is designed to be useful to pathologists, cardiologists, and cardiovascular surgeons. It is also for clinicians, residents, and paramedical personnel who must maintain familiarity with the topics presented. For the pathologist, this book will be useful in both the surgical pathology and autopsy suites.

I wish to thank my co-authors for their contributions and my clinician colleagues in both Toronto and London, Ontario, for their enthusiasm and interest. Such enthusiasm makes the current practice of cardiology, cardiovascular surgery, and cardiovascular pathology as exciting as it is. My thanks too, to many colleagues in pathology who have allowed me to examine their interesting and often instructive cases.

It is a pleasure to acknowledge financial assistance, in the form of research grants, from the Ontario Heart Foundation. Grants from that body supported, in part, investigative studies that are reported in my chapters.

Ruth Asselin, Susan Budlovsky, Sophia Duda, and Maria Lorber at the University of Toronto and the staff of the photographic unit at Toronto General Hospital all greatly assisted me in the past and, at the University of Western Ontario Dr. Hani Dick, Neil Falconer, Dr. Sally Ford, Hannah Koppenhoefer and Sharon Wilton have had a similar role there. I owe an especial debt to Sheila Collard for her excellent secretarial work and to my wife, Dr. Meredith M. Silver, for her ability to be, at the appropriate time, critic, inquisitor, helpmate, and goad.

I am grateful to the staff of Churchill Livingstone for their interest, cooperation, and helpfulness at all phases of the development of this book, especially Donna Balopole, Brooke Dramer, and William Schmitt.

Malcolm D. Silver

CONTENTS

VOLUME 2

18

Diseases of the Pulmonary Circulation

C.A. Wagenvoort and Noeke Wagenvoort

INTRODUCTION

The pulmonary circulation is essentially separate from the systemic circulation. It has a different function, different hemodynamics, a different reaction to humoral, pharmacological or other vasomotor influences, and a different morphology of the vasculature.

The function of the pulmonary circulation is primarily gas exchange, and as such it serves the whole body. Moreover, lung tissue is involved in the metabolization, production, and destruction of various substances, while it may also filter particulate matter from the blood. The nutrition of large parts of the lungs, on the other hand, is provided by the systemic circulation by way of the bronchial arteries.

The differences in morphology between systemic and pulmonary vessels are no doubt closely related to their underlying hemodynamic characteristics. The thin wall, particularly the thin media, and the relatively wide lumen of the intrapulmonary arteries reflect the low pressure and resistance and the large flow in the pulmonary circulation. This is in contrast to the much thicker wall and more narrow lumen of comparable systemic arteries. In the presence of disease, the reactions and adaptations of the pulmonary vessels toward abnormal stimuli or changes in hemodynamics resemble, in part, those found in systemic vessels in comparable conditions. Even so, the frequency and severity of many of these lesions, as well as their significance for the circulation as a whole, are often much more pronounced in the pulmonary than in the systemic circulation. Moreover, some types of vascular alterations are limited to the pulmonary vasculature and have not been described in systemic vessels.

ANATOMY OF PULMONARY VASCULATURE

Blood passing through the pulmonary circulation is carried from the right cardiac ventricle to the lungs and from there to the left atrium to enter the systemic circulation. The orifice of the pulmonary trunk with its valve, supplied with three cusps, is localized anteriorly to the orifice of the aorta. From here the pulmonary trunk runs upward at the left side of the aorta, somewhat to the left and dorsally, before it divides at the bifurcation into right and left main pulmonary arteries. The length of the pulmonary trunk is approximately 4.5 cm. Its internal diameter ranges from 2 to 3 cm, while the thickness of the media is between 600 and 900 μm. Both the caliber and the medial thickness increase somewhat with age.[36]

The right main pulmonary artery forms a right angle with the pulmonary trunk and follows a horizontal course posterior to the hilus of the right lung. The left main pulmonary artery is more or less a continuation of the trunk. It curves in a cranio-dorsal direction, ventrally to the thoracic aorta and left main bronchus to reach the hilus of the left lung. A small scar at the luminal side of the left pulmonary artery close to the bifurca-

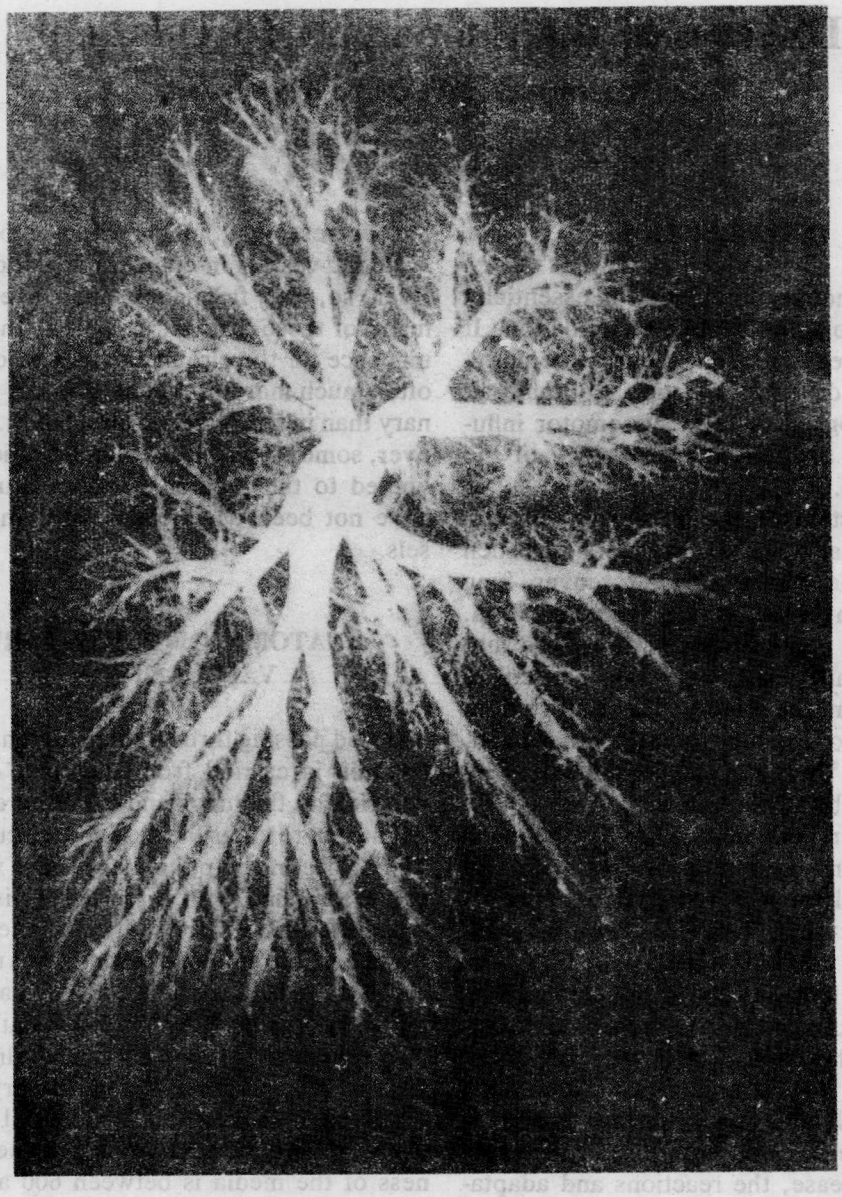

Fig. 18.1. Normal pulmonary arteriogram of right lung in a 75-year-old man. There is a regular dichotomous distribution of the branches.

tion represents the remnant of the orifice of the ductus arteriosus of which the ligament connects the wall of this artery with that of the aorta.

At the hilus of each lung the main pulmonary arteries divide into one or two, sometimes more, lobar arteries which in turn give rise to varying numbers of segmental arteries and subsequently to the smaller muscular pulmonary arteries. The course of the pulmonary arterial tree, which is closely associated to the bronchial tree, can be best demonstrated in a postmortem arteriogram (Fig. 18.1)

From the lung tissue small pulmonary veins unite to larger ones lying in the interlobular fibrous septa. Eventually two venous trunks emerge at each hilus to enter, after a short extrapulmonary course, the upper part of the left atrium. There are no valves in the pulmonary veins.

HISTOLOGY OF PULMONARY VASCULATURE

Pulmonary Trunk and Main Pulmonary Arteries

The pulmonary trunk and its two main branches are essentially elastic arteries. The structural resemblance of the pulmonary trunk to the aorta is very striking at the time of birth, when both vessels have approximately the same medial thickness and the same dense configuration of elastic tissue in their media. Within the first year of life, the ratio in thickness of the media of pulmonary trunk to that of aorta decreases to approximately 0.6. In that same period occurs the transition to a different elastic configuration such as exists in the adult.[23] In the adult pulmonary trunk, the amount of elastic tissue per unit of medial surface area in a histologic section is only 50 to 60 percent of that in the aorta.[36] This implies that, while in the aorta the elastic laminae are fairly regular, parallel, and densely arranged (Fig. 18.2), in the pulmonary trunk these laminae are usually interrupted and fragmented (Fig. 18.3). These fragments often appear swollen with clubbed terminations. In individual cases there may be considerable variation in the amount of elastic tissue. The elastic laminae, together with smooth muscle cells and collagen fibers, are embedded in an intercellular ground substance.

The intima of the pulmonary trunk and main arteries is very thin in young individuals, consisting of a single layer of endothelial cells resting on a basement mem-

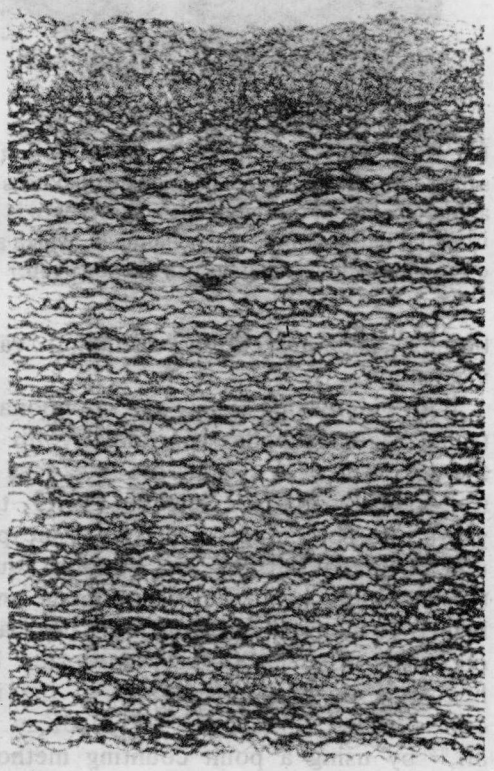

Fig. 18.2. Wall of normal aorta in a woman aged 59 years. The parallel elastic laminae in the media form a regular pattern (Elastic van Gieson ×50.)

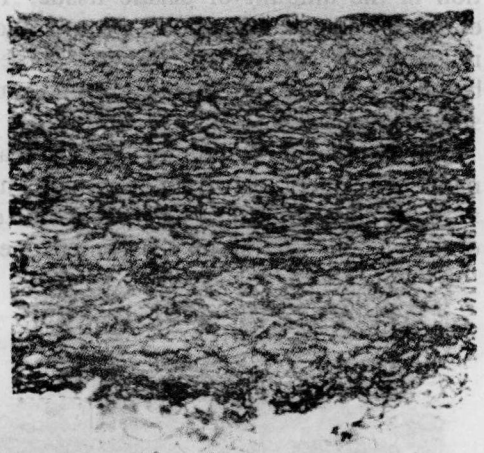

Fig. 18.3. Wall of pulmonary trunk from the same case as figure 1. The medial thickness is about 60 percent of that of the aorta. There is an irregular pattern of the elastic laminae, which are often interrupted. (Elastic van Gieson × 50.)

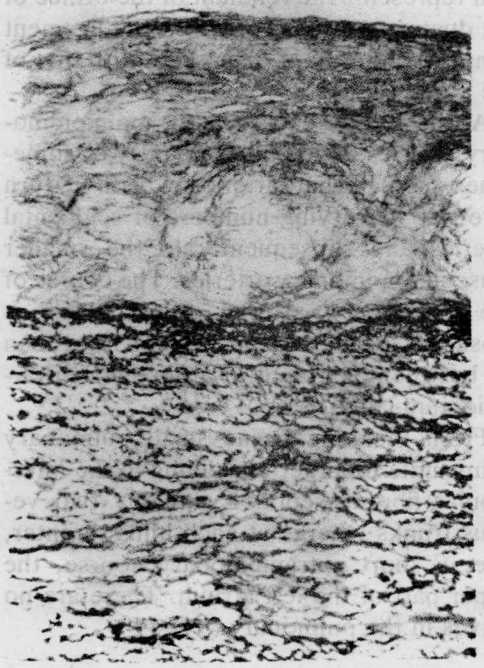

Fig. 18.4. Pulmonary trunk with mild atherosclerotic patch in the intima in a 64-year-old woman. (Elastic van Gieson × 140.)

brane. The adventitia contains vasa vasorum.

With increasing age, the pulmonary trunk becomes wider, particularly up to the age of 50 years, while the thickness of the media increases slightly. Over the years, the percentage of elastic tissue per unit of medial surface area remains equal (as assessed by a television-image-analyzer).[36] This is in contrast to the decrease of elastic tissue with age, suggested by histologic evaluation,[20, 23] and to the increase found chemically.[3, 29] MacKay et al.,[32] by using a point counting method, found some tendency for elastin to fall with age.

The intima tends to become thickened with advancing years. Mild patches of atherosclerosis are common, particularly at the bifurcation (Fig. 18.4).

Elastic Pulmonary Arteries

Within the lung, the lobar and segmental pulmonary arteries accompany the ramifications of the bronchial tree. They are all of the elastic type with a regular arrangement of the elastic laminae (Fig. 18.5). This also applies to their branches down to a caliber of approximately one millimeter, so that here we deal with the smallest elastic arteries found in the body. The structure of the media is little influenced by age, but the intima very often shows patches of atherosclerosis particu-

Fig. 18.5. Normal elastic pulmonary artery in a 2-year-old girl. Regular arrangement of elastic laminae. (Elastic van Gieson ×230.)

larly within lobar arteries. In smaller branches there is often some intimal fibrosis.

Muscular Pulmonary Arteries and Arterioles

As a continuation of the elastic arteries, the muscular pulmonary arteries closely follow the smaller bronchi and bronchioli, gradually diminishing in caliber. Approximately at the transition of respiratory bronchioles to alveolar ducts, the arterioles usually dissolve into the capillary networks of the lung, but some continue over some distance in the lung tissue and are not associated with bronchioles. While part of the ramifications of the pulmonary arteries are dichotomous, there are also numerous branches that, instead of following the bronchial tree, arise at an approximately perpendicular angle from elastic as well as from muscular pulmonary arteries.[12, 41] These so-called supernumerary arteries cause the branching pattern of the pulmonary arterial tree to be asymmetrical rather than consistently dichotomous, although this is not usually evident in an arteriogram.

The structure of all muscular pulmonary arteries is essentially the same, whether conventional or supernumerary branches and whether large or small. At the transition of an elastic to a muscular pulmonary artery—that is, at a caliber from approximately 1000 to 500 μm—the elastic laminae in the media become discontinuous and gradually disappear, with the exception of the internal and external laminae that remain present in all muscular arteries.

The media of the muscular artery therefore contains no or hardly any elastic fibers but consists of smooth muscle fibers that have an approximately circular orientation, with very little collagen in between (Fig. 18.6). The thickness of the media depends somewhat on the way the lung tissue is treated. In collapsed lung tissue, the medial thickness, expressed as a percentage of the external diameter of the vessel in cross-section, averages about 5 percent, with a range of 3.5 to 8.2 percent.[50] If the lungs are expanded at autopsy by instillation of fixative in the bronchial

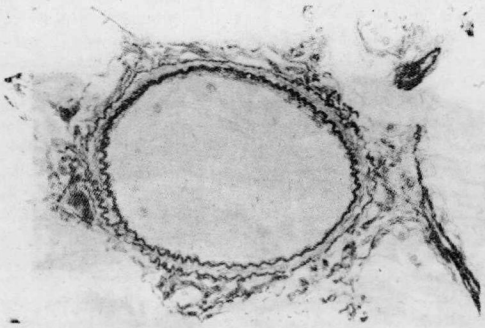

Fig. 18.6. Normal muscular pulmonary artery in a 28-year-old woman. The media is bounded by internal and external elastic laminae (Elastic van Gieson ×350.)

tree, either while the lungs are in situ or after removal from the thorax, their vessels dilate so that the relative medial thickness decreases. Dilatation is also produced if the pulmonary arteries are injected with fixative or contrast material for arteriography. The degree of dilatation, however, depends not only on the injection pressure but also on the reactivity of the vascular wall, so that it may differ according to the elapsed period between death and injection. This makes this method somewhat unpredictable.

The transition of a muscular pulmonary artery to an arteriole is gradual rather than abrupt. Peripheral arterioles (Fig. 18.7) have been defined as branches that have a complete circular muscular coat in their initial segment followed by an incomplete, discontinuous media with spiral smooth muscle fibers and terminating in a nonmuscular segment.[9] This transition of pulmonary arterial branches that in cross-section have a complete muscular coat to those with a discontinuous media, takes place at an external vascular caliber in the range of 70 μ.[58]

The small pulmonary arteries and arterioles are in close contact with the alveolar spaces so that alveolar hypoxia may directly exert its vasoconstrictive influence on their walls. Reid[38] assumed that

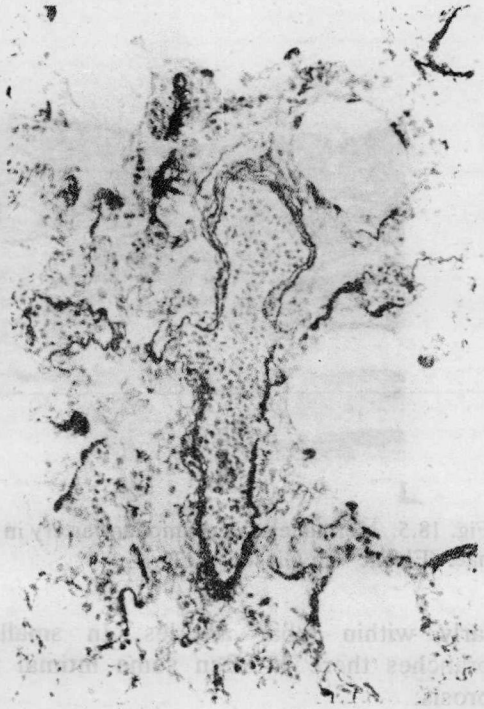

Fig. 18.7. Normal pulmonary arteriole in a girl aged 4 years. Muscular portions alternate with non-muscular portions of its wall. (Elastic van Gieson ×230.)

this is particularly true for the intermediate segments of the arterioles in which muscular and nonmuscular portions alternate and that the stimulus for medial muscle contraction is transmitted along the spiral-smooth muscle fibers.

The adventitia is much thicker than the media in the larger muscular pulmonary arteries but somewhat thinner in the smaller ones. The intima normally consists of a single layer of endothelial cells resting on a basement membrane.

As in the pulmonary trunk and elastic arteries, the media of the muscular pulmonary arteries is little affected by age—in contrast to the intima, which tends to become thickened and fibrotic, particularly after the age of 40 years[50].

Alveolar Capillaries

Thin-walled precapillary branches without a muscular coat arise from the pulmonary arterioles and in turn break up into the networks of alveolar capillaries. These networks lie in the alveolar walls in such a way that their capillaries penetrate the fibrous core of the alveolar wall and thus are in close contact with the spaces of adjacent alveoli.[62]

The alveolar wall consists essentially of five layers. From capillary lumen to alveolar space they are, respectively: endothelial layer; basement membrane; interstitial space containing some collagen; another basement membrane; and epithelial layer. The thickness of the whole free part of the capillary wall is in the range of 1.6 to 1.8 μm.[61] The interstital space is much thicker and contains much more collagen and also some elastic fibers where the capillary borders the central core of the alveolar wall. With increasing age the capillary wall, including its free part, becomes slightly thicker.[47]

Pulmonary Venules and Veins

From the capillary networks arise postcapillary collecting venules. These have very thin walls, consisting of an endothelial layer over an elastic lamina, and cannot be distinguished from the precapillary arteriolar branches. They merge to larger pulmonary venules and veins to form, eventually, the large lobar veins. Usually two large venous trunks emerge at the hilus of each lung to join the left atrium. The pulmonary venules follow a course through the lung tissue, small pulmonary veins enter the interlobular fibrous septa, and subsequent larger veins follow the septa so that they are as far removed as possible from the pulmonary arteries of comparable caliber.

While the smallest venules are indistinguishable from nonmuscular arterioles, having the same structure as well as localization, the larger pulmonary veins generally have a clearly recognizable structure. The pulmonary venous wall is even thinner than that of an artery. In contrast to the regular configuration of the arterial wall with its muscular media wedged between two elastic laminae, the venous wall has an irregular arrangement of elastic membranes and fibers alternating with collagen and smooth muscle fibers[52] (Fig. 18.8); as a result of this irregular pattern, there is no sharp demarcation between venous media and adventitia. The latter is thinner, particularly in the smaller veins, and consists of collagen with some elastic fibers. At the luminal side of the venous wall, often, but not always, a single elastic membrane, comparable to the arterial internal elastic lamina, may be recognized. The intima consists normally of a single endothelial layer. There are no valves in the pulmonary veins.

Age changes in the pulmonary veins are particularly observed in the intima, which shows fibrotic thickening with hyalinization. In the media there is fragmentation of elastic laminae with loss of elasticity.

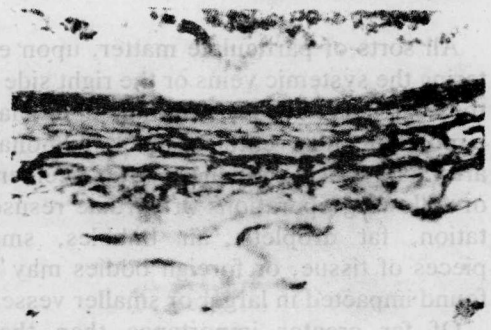

Fig. 18.8. Wall of normal pulmonary vein in a woman aged 50 years. There is an irregular pattern of elastic and collagenous fibers. (Elastic van Gieson $\times$ 230.)

DISEASES AFFECTING THE LUNG VESSELS

If the pulmonary arteries and veins are affected by alterations other than age changes, these are most commonly associated with an elevation of pulmonary arterial pressure. However, hypertensive pulmonary vascular disease is not an entity. The causes of pulmonary hypertension are many and diverse, and with each the pattern of pulmonary vascular lesions tends to differ considerably. Even so, the type of pulmonary hypertension may be deduced from these patterns. This has practical implications because, if lung tissue becomes available either from autopsy or by lung biopsy, the pathologist may indicate at least the broad category of cause for the increased pressure in the pulmonary circulation.[59]

Pulmonary arteries and arterioles rarely escape being affected in pulmonary hypertension, irrespective of its cause. The pulmonary veins and venules are particularly involved when there is obstruction to the pulmonary venous flow. The most striking changes are observed in the arterial and venous media and intima, rather than in the adventitia.

Pulmonary Embolism

All sorts of particulate matter, upon entering the systemic veins or the right side of the heart, may be swept into the pulmonary circulation and eventually block pulmonary arteries or their branches. After accidents or following operations or cardiac resuscitation, fat droplets, air bubbles, small pieces of tissue, or foreign bodies may be found impacted in larger or smaller vessels.

Of far greater importance than these forms of pulmonary embolism is thromboembolism. A massive pulmonary embolism, obstructing the main pulmonary arteries and sometimes filling the pulmonary trunk and part of the right ventricle as well, is a common cause of death. Survival is possible if enough blood is forced beyond the embolus and into the pulmonary circulation. The embolus may then become organized, causing a considerable fibrotic obstruction in the lumen of the main pulmonary arteries, but such cases are uncommon.

Emboli obstructing medium-sized branches such as segmental arteries often cause only limited damage to the areas of lung tissue supplied by them. This depends largely on the effectiveness of the circula-

Fig. 18.9. Cut surface of lung in a woman aged 68 years with recurrent pulmonary thromboembolism. Bands and webs in lobar arteries. Entrapped in these webs is a later embolus (*bottom*) with subsequent organization.