PROGRESS IN RESEARCH IN EMPHYSEMA AND CHRONIC BRONCHITIS

NORMAL AND ABNORMAL PULMONARY CIRCULATION

EDITED BY

ROBERT F. GROVER, DENVER, COLO.

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Progress in Research in
Emphysema and Chronic Bronchitis
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Normal and Abnormal Pulmonary Circulation

Fifth Annual Conference on Research in Emphysema, Aspen, Colo.,
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Edited by
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I. The Peripheral Pulmonary Circulation

Moderator: GILES F. FILLEY

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Perspective

By GILES F. FILLEY, Denver

We will focus on the pulmonary circulation, but as in past conferences, we will concentrate on a part of the respiratory system only to make it clearer in its relationship to the whole. In accord with the basic fact that the pulmonary arteries follow the course of the airways, we have for our conference brought together in potentially congenial juxtaposition experts in both the blood and gas transport systems. This morning it will be our particular purpose to show the morphologic and mechanical relationships between the blood vessels and the airspaces of the lung. Before I introduce our speakers, I would like you to be prepared to deal with the two chief types of informational entities which will be communicated, namely concepts and models. We will hear from anatomists who will directly or indirectly imply physiological concepts. We will also hear from physiologists who will build anatomical and mathematical models.

What is the difference between a concept and a model? Basically they are very similar. The model is in many ways a concept made explicit, laid bare, exposed with all its assumptions showing. Furthermore, a model is a concept you can experiment with, a great advantage over something you can only discuss. Models, however, tend to be arbitrary, whether because of human prejudice or fallibility, or because of the action of formaldehyde or Zenker's. Concept formation, if created by the humbly receptive observer, even though fuzzy and nonquantitative, may well be the process touching closest to reality. In the end, however, concepts and models are of the same stuff, not only the stuff that dreams are made of, but the fabric of science itself.

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Baltimore, Md.

Relationships of Peripheral Pulmonary Vessels to the Respiratory Areas of the Lung[1]

By VERNON E. KRAHL

From the time the lung makes its appearance in the early embryo it becomes intimately associated with the primitive pulmonary arteries and as the advancing lung buds begin to ramify the vessels keep pace with their growth. Accordingly, at the completion of lung development each of the myriad airways is accompanied by a corresponding ramification of the pulmonary arteries. While the pulmonary arteries closely follow the airways out to their tips and are centrally located in the pulmonary lobules, the veins begin peripherally and descend through connective tissue septa which vary in size and completeness and which form boundaries of the secondary lobules in many species. The septa conduct the veins toward the hilus of the lung where the veins at last come to lie along the large airways. This, then, is the basic vascular pattern of the definitive lung:—the pulmonary arteries follow the airways toward the periphery; the veins follow connective tissue septa toward the hilus at the greatest possible distance from the airway.

Fig. 1 (photomicrograph of a section from the lung of a five-month fetus) confirms that the characteristic relationship of vessels to airways is established very early in the development of the lung. The figure shows a bronchiole passing through the center of a secondary lobule of lung tissue. Its accompanying artery lies close by, but the veins are found (above, below) in the connective tissue septa where they are receiving tributaries (venules) from the adjacent lobules of lung tissue. The lymphatics take a similar course. At the time of birth

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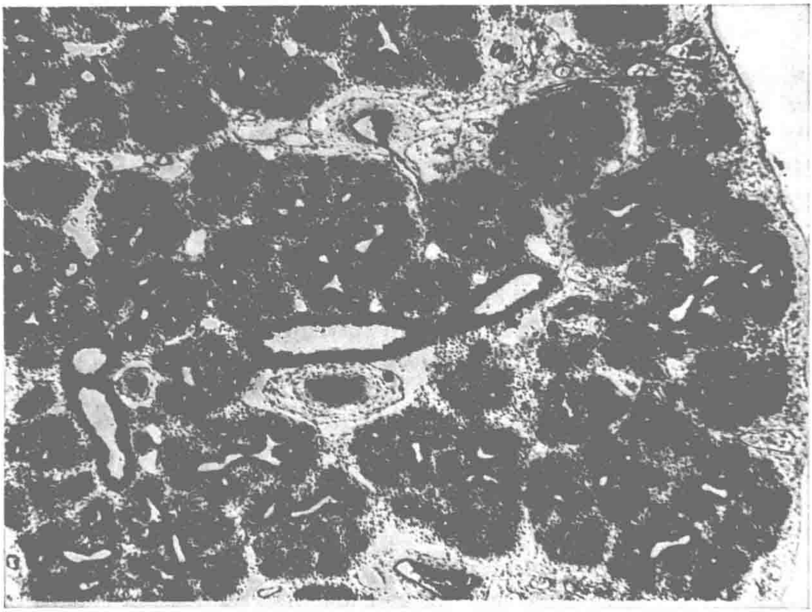

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Fig. 1. **Subpleural secondary lobule in the fetal human lung at 5 months. The principal bronchiole and its accompanying branch of the pulmonary artery are centrally located in the lobule, while the veins (above and below, center) lie in the interlobular septa. Lymphatic vessels are also present in the septa. c. 35 × (from a slide prepared in 1923 by *M. Heidenhain*, Susa, Azan, 6μ).**

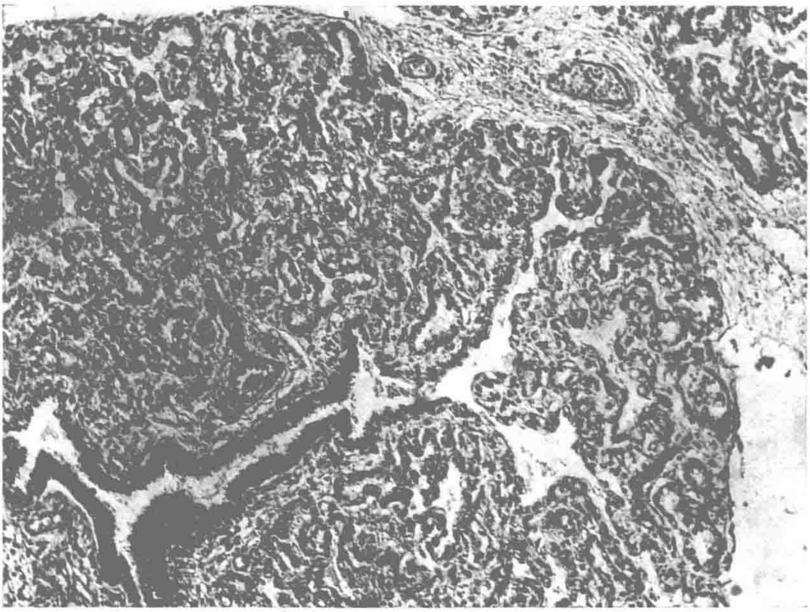

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Fig. 2. **Human fetus at term, again showing the fundamental arrangement of the centrally placed bronchiole (its accompanying artery is not in the plane of section) and the veins at the periphery of the lobule, lying in the interlobular septum. ca. 120 × (from the U. of Md. Histological collection).**

(fig. 2) the vascular arrangement is quite the same. This illustration of a peripheral area of the newborn lung is strictly comparable to the preceding one. Subpleural connective tissue is continuous with that of an interlobular septum. Veins are present within the septum and some lymphatic vessels can be distinguished as well. As the bronchiole approaches the center of the lobule it gives rise to more peripheral airways that are still somewhat atelectatic. Unfortunately, the accompanying artery is not seen here, for it does not lie in the plane of section.

Thin sections such as those seen in the preceding figures are essentially two-dimensional preparations, for the dimension of depth is virtually absent. However, there are several excellent methods of preparing thicker lung sections [1, 3–5] so that we can appreciate (particularly with the dissecting microscope) the third dimension—depth.

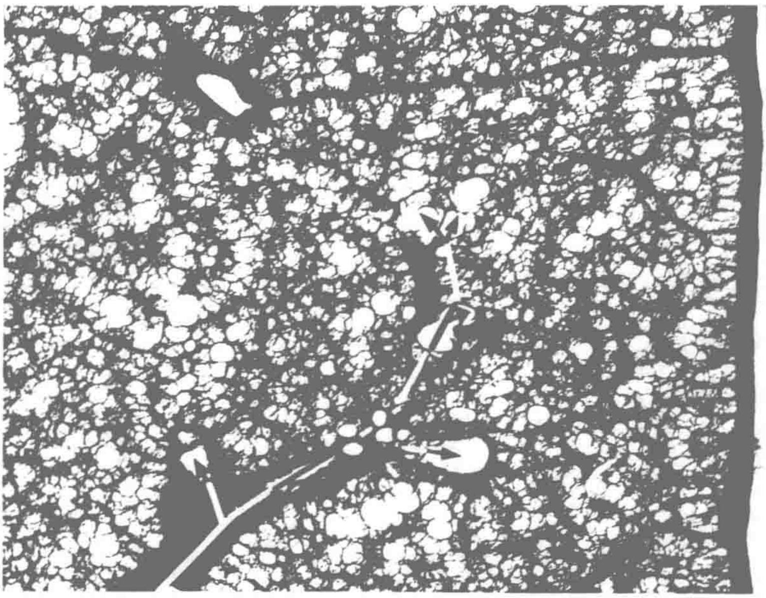

Fig. 3. Adult human lung prepared as a thick section. The bronchiole at lower left divides into respiratory bronchioles which, in turn, produce alveolar ducts. The dark structure near the center is the accompanying artery. More distal branches of theartery are seen in their characteristic forking pattern at upper right. Across the top is a thin interlobular septum containing a vein. 12× Zenker-formol fixation (from a slide prepared by Dr. *Robert R. Wright*, U. of Calif. Med. Center. San Francisco).

Fig. 3 shows one of these "3-D" preparations, given to me by Dr. *Robert R. Wright* of the University of California Medical Center in San Francisco. As seen before, subpleural connective tissue extends down into an interlobular septum which lodges a vein (upper left). The bronchiole, entering the field from below on the left, may be followed to a respiratory bronchiole and upward, in the photograph, through a short series of alveolar ducts. An accompanying branch of the pulmonary artery lies close by and enters the plane of section near the center of the field. More distal branches of the vessel fork repeatedly as they extend toward the periphery (see Y-shaped configuration at upper right). This angular type of branching is characteristic of the

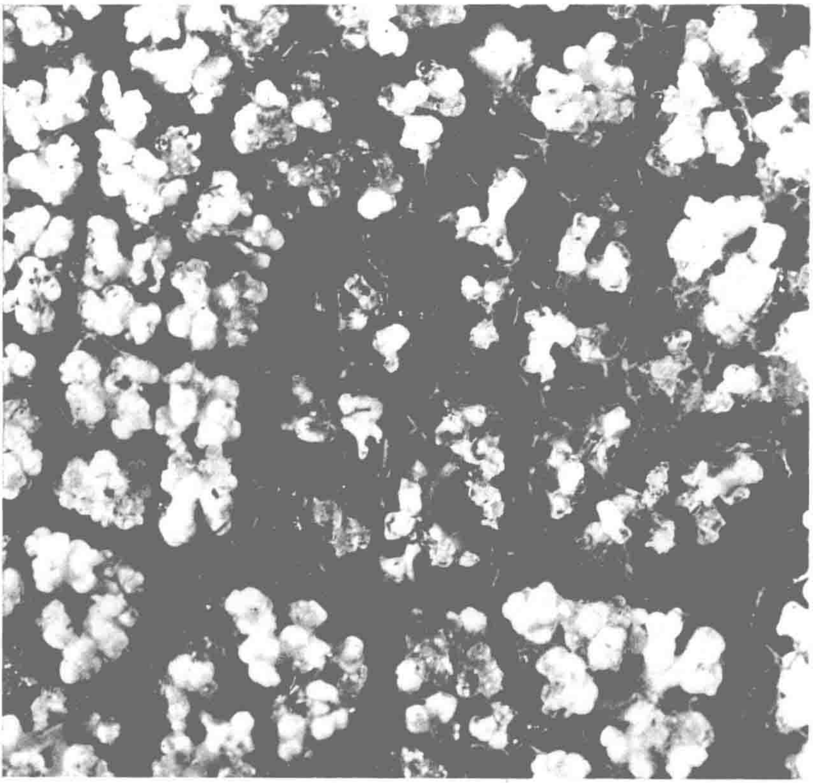

Fig. 4. Lung of human fetus near term in which airways (white) and pulmonary veins were injected with vinylite resin. This shows the characteristic relationship of the peripheral veins to groups of alveoli. The veins disappear from view in the narrow interlobular clefts (positions of septa) 18 × (from a specimen in the Dept. of Anatomy, U. of Md. School of Medicine, Baltimore. Md.).

proximal parts of the pulmonary circulation. Peripherally, however, there is a marked change in the mode of branching; this will be demonstrated somewhat later.

Three-dimensional studies are made possible, also, by corrosion preparations of lung. Fig. 4 shows a close-up view of the corroded lung of a human fetus near term. The airways have been injected with a white resinous material and show families of alveoli and alveolar sacs, separated by small clefts which originally contained connective tissue. One group of air spaces did not take the injection mass as well as the rest so that pulmonary veins which have been injected with a contrasting medium are seen in their spatial relationships to the terminal airways. Instead of having an angular branching pattern like the airways and their accompanying arteries, the veins, so to speak, droop down over the groups of alveoli and alveolar sacs, collecting blood from their capillary networks, and then extend over to the nearest cleft, nearest interlobular septum or interlobular space, and descend within it as shown in the previous illustrations.

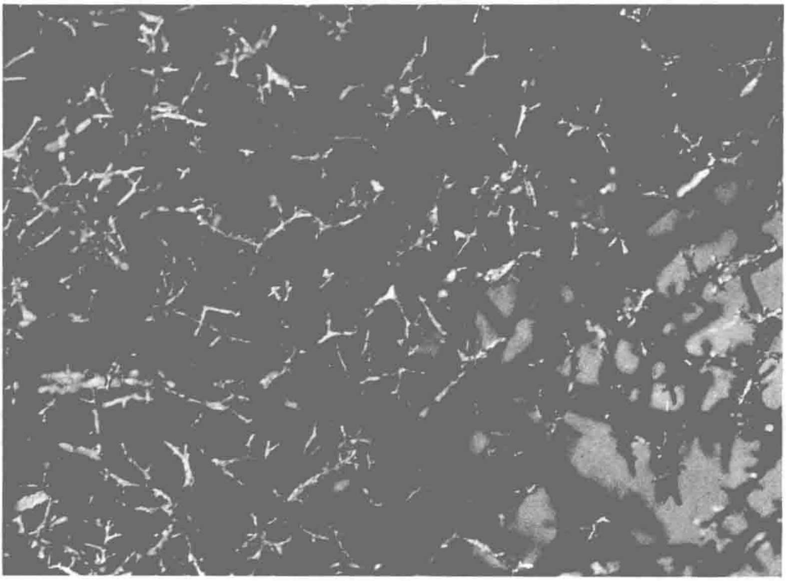

Fig. 5. Corrosion preparation of human infant's lung in which pulmonary arteries were injected with vinylite resin. Note characteristic angular branching pattern. c. 12 × (Specimen in Department of Anatomy, U. of Md. School of Medicine, Baltimore, Md.).

The next illustration (fig. 5) shows a corrosion preparation of the lung of a human infant in which the pulmonary arteries were injected with vinylite resin. The arteries and arterioles form distinct angulations at their origins, sometimes bifurcating, trifurcating, sometimes giving off monopodial branches, but always at a distinct, sharp angle. This branching pattern differs distinctly from that of the veins that were shown previously. Corrosion preparations are useful because they afford an opportunity to study the airways and their vessels in all three dimensions of space.

The next preparation (fig. 6) was supplied through the kindness of Dr. *Daniel Jenkins* of the Baylor School of Medicine in Houston, Texas. Here, following pulmonary arterial injection with a radio-opaque substance, thin slabs of the lung were placed on x-ray film and the films were exposed. Fig. 6 is a photographic print of a portion of one of these films. The way in which the ramifications of the pulmonary

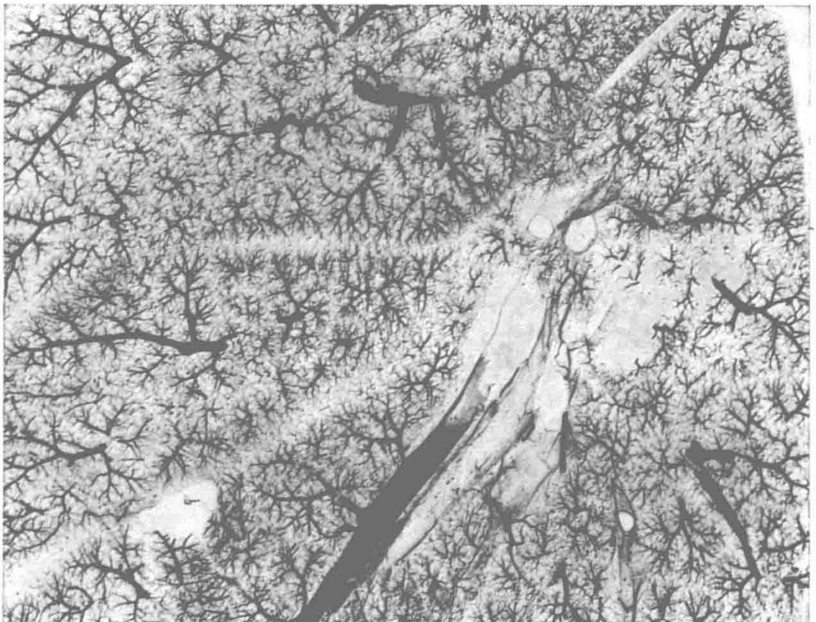

Fig. 6. Photographic print from radiograph of a thin slab of adult human lung in which pulmonary arteries were injected with a radio-opaque substance. This demonstrates clearly the characteristic branching pattern of pulmonary arteries and arterioles within pulmonary lobules (from a radiograph provided by Dr. *Daniel Jenkins*, Baylor School of Medicine, Houston, Texas).

artery imitate the lobular arrangement of the peripheral airways is clearly demonstrated. This is a convenient and informative method of studying normal vascular patterns in lungs. Striking differences in this pattern are detected when the same method is applied in diseased (ex.: emphysematous) lungs.

In the peripheral portions of the pulmonary vasculature there occurs an abrupt change in the mode of branching. In fig. 7, the vessel at the top of the photograph arose at one of the fork-like branchings, just described. The space above it is the lumen of a terminal bronchiole. This peripheral vessel is quite small and it is intimately related to the pulmonary parenchyma. It now begins to give off small right-angled branches which break up almost immediately into the dense capillary networks of the pulmonary alveoli. This lung was prepared by injecting a small quantity of dilute India ink into the heart of an anesthetized mouse. As the heart continued to beat it pumped some of the ink into the capillary bed. The preparation demonstrates the short, right-angled type of branching that is so characteristic of the peripheral pulmonary circulation.

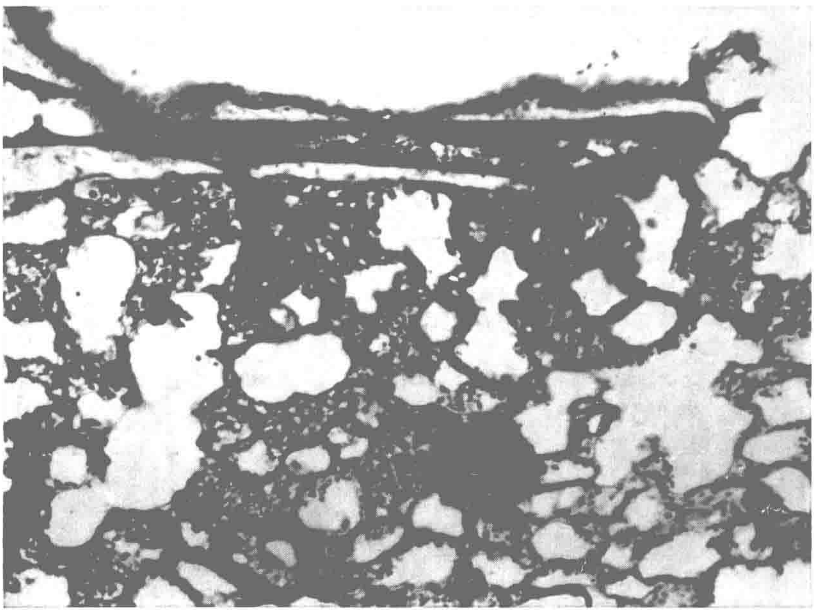

Fig. 7. Mouse lung with alveolar capillaries delineated by India ink. Note the supply of capillary networks by short arterioles originating at right angles from their parent vessel (fixation by tracheal instillation of Zenker-formol solution. H and E).

The next illustration (fig. 8) shows the relationship of a small peripheral artery to a respiratory bronchiole. Elastic fibers in the thin connective tissue sleeve of the artery intermingle with those in the wall of the airway. This intimate relationship evidently precludes the presence of alveoli on the side of a respiratory bronchiole to which the vessel is applied. One of the short, right-angled arterioles is seen in the lower right part of the photomicrograph.

Fig. 9 illustrates how somewhat larger, distributing vessels are related to the pulmonary parenchyma. This is in the lung of a guinea pig, in which there is an unusual type of musculature along parts of these arteries. It is arranged as a series of muscular cuffs so that the artery takes on the appearance of a string of link sausages. The short, right-angled branches arise in the intervals between the muscular cuffs. Although the activity of such vessels has not been studied *in vivo*, it is at least conceivable that the musculature might contract in a segmental fashion and thereby regulate the flow of blood to relatively small groups of alveoli. If such an artery were as intimately re-

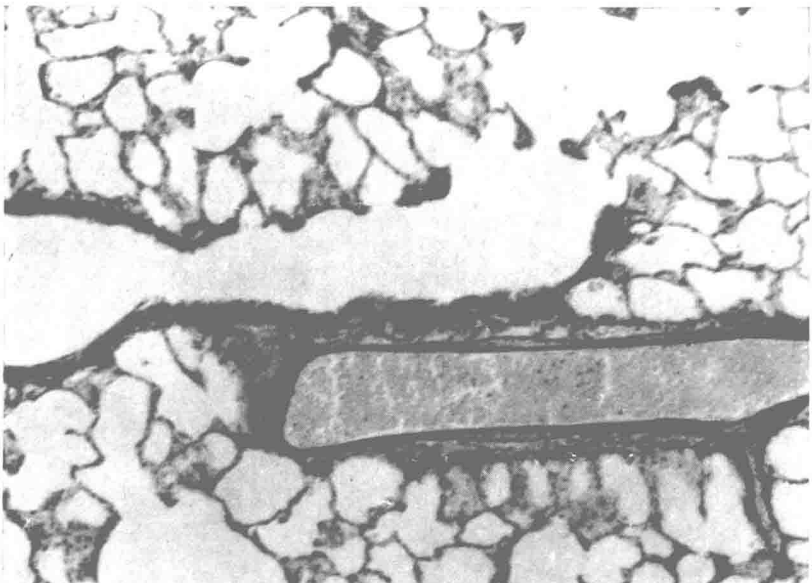

Fig. 8. Rat lung showing respiratory bronchiole and accompanying artery. Note thin connective tissue sleeve of artery and the short branch arising at nearly a right angle at lower right (Fixation by tracheal instillation of Zenker-formol solution. Orcein).

lated to the parenchyma as some of the more peripheral ones are, its contractions would undoubtedly produce tension and perhaps deformation of the delicate pulmonary parenchyma. But along the medium-sized vessels, as along the larger airways, there is an investment of loose connective tissue which can give and take as the vessels constrict and relax. The investing sleeve of connective tissue is quite obvious in fig. 9 because the vessel was maximally contracted at the moment of fixation.

Obviously, two-dimensional specimens (thin sections) and three-dimensional preparations of lungs (corrosions, air dried, fume-fixed specimens, etc.) have been and will continue to be useful in the study and teaching of pulmonary histology. However, we must never lose sight of the fact that animals and their tissues live in *four* dimensions —the three dimensions of space and the very important one of time. Only if we study organs in four dimensions can we hope to learn the detailed microanatomy and physiology of their tissues and to discover what the structures that we can see in three dimensions are doing with respect to time. For the past year or two I have been engaged in devising ways and means of studying living lungs; not in the

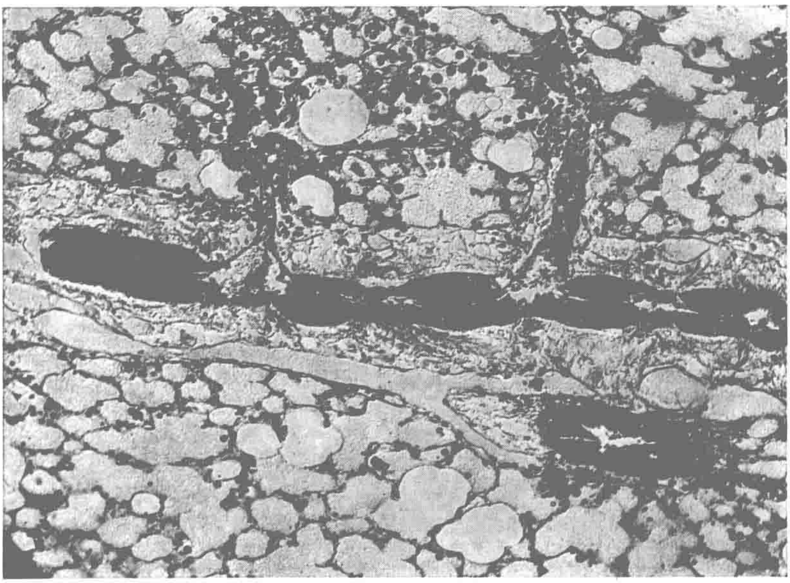

Fig. 9. Guinea pig lung showing segmented arrangement of arterial smooth muscle, and right-angled branches arising in intervals between muscular cuffs. Note loose connective tissue investment of the artery. 100 ×.