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STUDIES ON THE LUNG AFTER LIGATION OF THE PULMONARY ARTERY

II. ANATOMICAL CHANGES*

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The study of the collateral circulation of the lung is assuming new significance as methods are being developed for its clinical evaluation, and as its implications concerning the work of the heart are becoming understood. A great and rapid rise in the amount of blood circulating through the bronchial arteries in the dog after ligation of the pulmonary artery was demonstrated in bronchospirometric studies reported elsewhere.[1] The anatomical changes in the lungs of such animals are the subject of the present report.

Schlaepfer,[2,3] in similar experiments, observed that the bronchial arteries were greatly enlarged, but he did not follow them far into their intrapulmonary ramifications. Observations dealing with the effect of ligation of the pulmonary artery to a single lobe were made by Mathes, Holman, and Reichert.[4] By means of a roentgenographic technic involving the injection of bismuth oxychloride in acacia (Hill's mass), and in a specimen cleared by the Spalteholz method, they demonstrated the great increase of the collateral circulation and the retrograde filling of the pulmonary artery with this material. The early work has been reviewed by Berry, Brailsford, and de Burgh Daly.[5]

For an accurate study of the relations of the vessels it is advantageous to see them in the round and to be able to manipulate them. The preparation of durable casts of the bronchovascular structures serves this purpose and was employed in the present observations.

METHODS

The details of the method of producing bronchovascular casts in vinylite plastic have been presented elsewhere.[6] Briefly, the procedure

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consists of the injection of black vinylite into the aorta while the lungs remain *in situ*. The lungs are then inflated in a vacuum jar and the pulmonary arteries and veins are injected with red and green plastic respectively by means of cannulas brought out through the cover of the jar. The bronchi are finally filled with white plastic and the specimen is allowed to harden. Blocks can be removed at this stage for histologic study. The tissue is then corroded away in concentrated hydrochloric acid, leaving a multicolored cast that exhibits the bronchi and vascular structures of the lung in three dimensions. By varying the procedure, injections of vessels of any desired size can be achieved. With experimental material, the entire thorax and its contents can be suspended in the vacuum jar, after injection of the aorta *in situ* through an intercostal space. This has the advantage of confining the lungs within their natural cavities during inflation, and maintaining intact the internal mammary vessels and their branches. After digestion, a cast of the main vasculature of the entire thoracic cage remains in its proper relations with the bronchovascular structures.

Gross Observations

Origin and Course of the Bronchial Arteries in the Dog

Bruner and Schmidt,[7] in their dissections of 75 dogs, found that the right bronchial artery came from the 5th or 6th intercostal artery (1st or 2nd aortic intercostal) in 60 per cent of the cases. In the remainder, the blood supply was stated to come from the internal mammary artery or other vessels.

In our own less extensive observations, of 11 bronchovascular casts, the main supply of the bronchial trees of both sides was invariably found to be derived from the right intercostal vessels (Table I). In no case

TABLE I

Source of Principal Bronchial Arteries in Eleven Dogs

Source		Number
Right	Left	
A2	A2	3
A3	A3	3
A2	A3	2
A1	A2	1
A1	A1 and A2	1
A2	A1 and A2	1
Total		11

"A" refers to aortic intercostal.

did a left intercostal artery, or the aorta itself, give rise to a major bronchial branch, although small supplementary branches were observed in three instances. Major branches to the left side from these sources were observed in the dog by Berry, Brailsford, and de Burgh Daly.[5] The most common source was the 2nd or 3rd aortic intercostal artery supplying the 6th or 7th intercostal space. The same intercostal vessels usually supplied the esophagus, sometimes by a trunk in common with the bronchial artery. The existence of an accessory supply from many other arteries is implied by the huge collaterals that develop from them after ligation of the pulmonary artery.

The bronchial arteries in the normal dog branch and anastomose profusely within the walls of the bronchi, where their major trunks tend to pursue a spiral course. In contrast with the pulmonary arteries, these vessels are anything but end arteries. Since some of the branches of the bronchial arteries soon pass into the superficial layers of the mucosa where they anastomose with other arterioles, nothing short of complete transection of the bronchus will interrupt the flow of blood. Thus it is most unlikely that the arterial supply to the nerves of the lung can be easily interrupted in the intact animal, as it can, with damage to reflex function, in the heart-lung preparation.[5,8]

According to Miller,[9,10] a common capillary bed with the pulmonary artery is normally found only in the walls of the respiratory bronchioles. His experiments, and those of Ghoreyeb and Karsner,[11] suggest that the capillaries of the alveoli are perfused from the bronchial arteries if the pressure in the pulmonary arteries falls sufficiently low.

The Bronchial Circulation after Ligation of the Pulmonary Artery

A well developed collateral circulation was already apparent in the earliest available successful bronchovascular cast, from an animal that died 9 weeks after ligation of the left pulmonary artery. Mathes, Holman, and Reichert[4] found by their roentgenographic technic that the bronchial vessels were already moderately enlarged 7 days, and markedly enlarged 16 days, after ligation of a lobar pulmonary artery. Schlaepfer,[2] however, remarked that the dilatation was first noticeable in gross dissections after 66 days.

In the casts derived from animals dying 2¼ to 23½ months after ligation, a rough correlation could be made between the extent of the collateral circulation and the length of survival after operation. Dog 33, however, which survived 12½ months, had the most extensive collateral circulation, surpassing that of dog 9, the longest survivor.

Some conception of the appearance of the expanded bronchial circulation can be drawn from a study of the cast of dog 15, which died at the end of the third month. In contrast with the normal (Fig. 1), in which the vinylite injection mass penetrated only to branches of the bronchial artery of the 4th to the 6th order, the black plastic here extended much farther out in the bronchial tree, especially on the left side (Figs. 2 and 3). In this instance, the bronchial arteries to both sides arose from a common trunk derived from the second right aortic intercostal artery. This parent trunk, after giving origin to the left superior bronchial artery, divided into a left inferior bronchial artery and the single right bronchial artery. The common derivation of both left and right bronchial arteries may account for the dilatation of the latter. Each of the two left bronchial arteries measured 2 mm.* at the source. The superior artery looped over the left stem bronchus, and the inferior passed along the lower, medial aspect of the lower lobe bronchus. These two vessels were joined by an almost angiomatous rete of large arterial channels which embraced each of the major bronchi of the left side. Added to this plexus were a large communicating branch from the right bronchial artery and many fine recurrent branches from an esophageal artery that was itself derived mainly from the left inferior bronchial artery, and indirectly from another esophageal artery stemming from the third right aortic vessel.

As the lungs lay *in situ,* additional sizeable collaterals from the phrenic, pericardiophrenic, and distal branches of the esophageal arteries were seen to enter the lung through the pulmonary ligament (Fig. 4). Here some of them ramified in stellate fashion within the superficial layers of the pleura where they are said not to exist normally in the dog.[10] In the dissection of the lung from the thorax, although in general the pleural cavity was free, dense fibrous adhesions were noted between portions of the upper lobe and the parietal pleura in the bed of the operative incision. Within these, numerous small vessels derived from the enlarged distal portions of the 4th and 5th intercostal arteries were seen to enter the lung. These were constantly found in all of the animals and are illustrated from another instance (Fig. 5).

As the vessels were traced distally about the bronchi of the left lung, their enormously increased size accentuated their spiral course and the plexiform anastomosing arrangement of their branches. There was little diminution in the caliber of the branches in comparison with the parent stem, and sometimes these vessels were so varicose that there might actually be an increase in the size of a distal segment. The arrangement of these vessels was identical with that of the bronchial collaterals seen in cases of bronchiectasis[12] and congenital heart disease[13] in man.

* These dimensions refer to the casts and therefore to internal diameters.

In dog 15, 3 months after operation, there was only suggestive evidence in a few places of retrograde injection of some of the pulmonary arterioles. Retrograde injection of the pulmonary arteries from the bronchials was observed 10½ months after ligation of the left stem pulmonary artery in dog 11. The most striking example of this process was in another animal, dog 33, sacrificed at 12½ months. Inspection of the upper lobe bronchus of this dog revealed a pulmonary artery regularly distributing one branch to each branch of the bronchus (Fig. 6). The tortuous bronchial arteries, of which there were several intercommunicating branches to each bronchus, were more intimately related to the lumen than the pulmonary vessels. The main bronchial arterial trunk accompanying the 3rd order branches of the lobar bronchus was only slightly smaller than the pulmonary artery at the same level. The points of communication between the bronchial and pulmonary vessels were beyond the 6th order branches of the latter. These communicating vessels were usually multiple and formed a basketwork about the bronchioles. Retrograde injection with the vinylite indicated that the vessels had reached a diameter in excess of 50 μ. Some of these vessels had a diameter as large as 200 μ. Their appearance in another animal (dog 11) was identical with that described here for dog 33 (Fig. 7).

It is surprising to find anastomoses even at the 6th order branches of the lobar bronchus, when one considers that normally the common capillary beds of the pulmonary and bronchial arteries are found only in the walls of the respiratory bronchioles. Apparently, certain of the capillaries in this bed become so widely dilated as to reach a macroscopic size. Thus the tissues at their origin are pushed aside and the bridge between the vessels appears to occupy a more central position. Mathes, Holman, and Reichert[4] stated, on the basis of a preparation cleared by the Spalteholz method, that such anastomoses were single and along the 3rd order bronchi. The vinylite casts, which have the advantage of manipulability, and which show the bronchovascular tree as a whole, have in no instance revealed them that close to the hilum. No precapillary communications between the bronchial arteries and the pulmonary veins were demonstrated.

As the vessels were traced from the periphery toward the hilum, there could be seen in the interlobar fissure and posteriorly, the well filled main pulmonary artery which terminated in a rounded protuberance at the confluence of the upper and lower lobe arteries. Here the retrogradely injected pulmonary artery was enshrouded in a close-meshed rete of collateral vessels which coursed subpleurally in the depths of the fissure and through the posterior mediastinum (Fig. 8). These bronchial arteries merely lay adjacent to, but did not communicate with, the main pulmonary arteries near the heart, but only far at the periphery where the anastomoses have been described. The plexus of collateral arteries was derived from a left bronchial trunk 3.5 mm. in internal diameter which sprang, in common with a right bronchial artery, from the 3rd right aortic intercostal (Fig. 9).

Even where no retrograde injection with the vinylite from the bronchial arteries had occurred, complete patency of the main pulmonary artery distal to the point of ligature was demonstrated by injection in all four instances where it was attempted (Fig. 10). Schlaepfer[2,3] has previously observed that the pulmonary artery distal to the ligature does not become thrombosed, although he described it as "contracted." In the present experiments, the distal pulmonary arteries of the left side appeared only slightly, if at all, smaller than those of the same order on the right side, when injected with the same material at the same pressure. Obviously, the failure of retrograde injection of the pulmonary arteries from the bronchial arteries in these specimens does not indicate that the systems do not communicate by means of channels of lesser diameter than 50 μ.

Histologic Observations

Microscopic study of the bronchi and lungs confirms what is seen grossly in the casts. The bronchial arteries not only become enormously increased in size, but new, or previously minor, channels become greatly thickened (compare Figs. 11 and 12). They are prominent not only about the bronchi but also in the septa and in some portions of the pleura.

It is difficult to compare the cross-sectional areas of the pulmonary arteries with those of the bronchial arteries about the largest bronchi, since the latter vessels here are so tortuous that many are met obliquely, or met more than once, in section. About the terminal bronchi, however, the bronchial arteries are arranged in less tightly coiled spirals and a more significant comparison is possible. Here the bronchial arteries are usually multiple. Their total area in cross section generally exceeds that of the pulmonary artery that accompanies the terminal bronchus (Fig. 13). The latter vessel at this point, however, is usually larger in cross-sectional area than the largest of the comitant bronchial arteries.

The walls of the enlarged collateral vessels consist chiefly of a thick layer of large smooth-muscle fibers. There is muscular hypertrophy as well as hyperplasia (compare Figs. 14 and 15). Foci of subendothelial fibrosis do not significantly encroach upon the lumen. The internal elastic lamella is irregularly thickened and fragmented, and even in the largest vessels only small segments of elastica remain. In the relatively normal bronchial arteries which accompany the main bronchi of the right side there is a complete internal elastic membrane (Fig. 14). The main pulmonary arteries appear to have well preserved fibro-elastic walls (Fig. 16).

An increase of elastic tissue in the walls of the alveoli and of the collagenous tissue about the bronchovascular rays was noted by Schlaepfer[2,3] and was thought by him to account for the shrinkage of the lung to two-thirds of its original size. In the present material the pleura and adventitial tissues of the bronchi likewise appear slightly thickened. The alveoli, however, are slightly thickened, if at all, and are indistinguishable in size from those of the relatively normal right lung in the same animal. Their capillaries do not appear to be especially engorged. No anatomical impediment to their function appears to exist.

Discussion

After a study of such specimens as are demonstrated in Figures 8 and 9, the large collateral flows (often in excess of 1 liter/M^2/min.) observed in the quantitative physiologic studies[1] become less surprising. In comparison with the normal pulmonary arteries at their source, the calibers of the vessels that give rise to the collateral supply are small, but the extremely profuse branching and the large size of the derivatives of the bronchial arteries suggest that the resistance to the flow of blood within them is not high. The sum of their cross-sectional areas about any terminal bronchus exceeds that of the pulmonary artery at the same level.

When the precapillary anastomoses have formed, the pulmonary arterial system becomes a huge diverticulum of the circulation now supplied by the bronchial arterial vessels. It may in part absorb the impact of the systemic arterial pressure before the capillaries of the alveoli are reached. Through these large anastomoses, the blood from the bronchial arteries also gains more direct access to the capillaries of the alveoli.

In the present experiments in which the pulmonary artery has been ligated proximally, most of the blood derived from the left side of the heart via the aorta must be returned directly to the left auricle through the pulmonary veins. The burden of the collateral flow therefore falls on the left ventricle. The same is probably true in congenital pulmonic stenosis in which collateral flow may also be extensive,[13] but here the right ventricle has excessive burdens of its own. In bronchiectasis, however, with much of the alveolar capillary bed obliterated, and with enormous collateral channels that anastomose with the pulmonary arteries,[12] it is possible that blood, entering at the points of anastomosis under systemic pressure, may pass retrogradely toward the hilum in the pulmonary arteries.

Summary and Conclusions

Following ligation of the pulmonary artery, there occurs an enormous expansion of bronchial collateral circulation that is well advanced within 12 weeks. The pulmonary artery does not become thrombosed distally. By 42 weeks, in some animals, precapillary anastomoses with a diameter greater than 50 μ develop between the bronchial and pulmonary circulations. These are associated with bronchioles beyond those of the 6th order in relation to the lobar bronchus. The bronchial arteries associated with the terminal bronchi have a relatively larger total cross-sectional area than the pulmonary artery at the same level. This, together with the absence of microscopic changes in the alveoli, suggests that the peripheral resistance to blood flow in the lungs remains low. The extent of the collateral circulation demonstrated anatomically appears to be compatible with the great magnitude of the flow as determined in physiologic experiments. The collateral flow as observed in these experiments, and as deduced for congenital pulmonic stenosis and bronchiectasis in man, has significant clinical implications in respect to the work of the heart.

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[*Illustrations follow*]

DESCRIPTION OF PLATES

PLATE 27

FIG. 1. Normal dog. Cast of lung viewed from posterior aspect. With the vinylite as employed here, the normal bronchial arteries soon become attenuated below a caliber that will be injected (approximately 50 μ). The right bronchial artery is derived from the 1st right aortic intercostal. The left bronchials, two in number, are derived from the 1st and 2nd right aortic intercostals respectively. The aorta and its branches were injected with black plastic, the pulmonary arteries with red, the pulmonary veins with green, and the bronchial tree with white. The left pulmonary artery is labelled "L" and the interlobar trunk of the right, "R." Approximately two-thirds actual size.

FIG. 2. Dog 15. Sacrificed 3 months after the ligation of the left pulmonary artery. Anterior view of cast. There is a much more extensive plexus of bronchial arteries on the left side. Those on the right are enlarged also, probably on account of their origin in a common trunk with the left. Huge plexuses of vessels are seen astride the left upper lobe bronchus and medially to the left lower lobe stem. The pulmonary veins were injected on both sides, but the pulmonary artery only on the right. Approximately two-thirds actual size.

FIG. 3. Rear view of cast shown in Figure 2. The common origin of the bronchial vessels to both sides is apparent. Very extensive plexuses embrace the bronchi posteriorly on the left, where they can be seen extending to the tips of some of the bronchioles in the lower lobe from which the pulmonary veins have been dissected away. The aorta has been removed. For comparison with Figure 1. Approximately 1½ times actual size.

FIG. 4. Anterior view of injected specimen shown in Figures 2 and 3 before digestion of tissue. The cut distal end of the esophagus has been displaced to the left. Collaterals from the pericardio-phrenic, phrenic, and esophageal vessels are visible. Some of these ramify within the pleura of the left side.

FIG. 5. Dog 33. Sacrificed 10½ months after ligation of the left pulmonary artery. An enlarged intercostal artery is shown extending branches into the left lower lobe. These traversed adhesions before digestion of the tissue. In this instance the entire thorax was dissolved in concentrated hydrochloric acid, thus preserving the relations of the injected vessels. Approximately 1½ times actual size.

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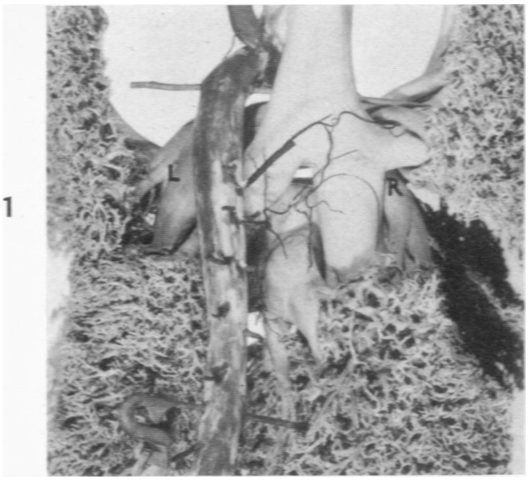

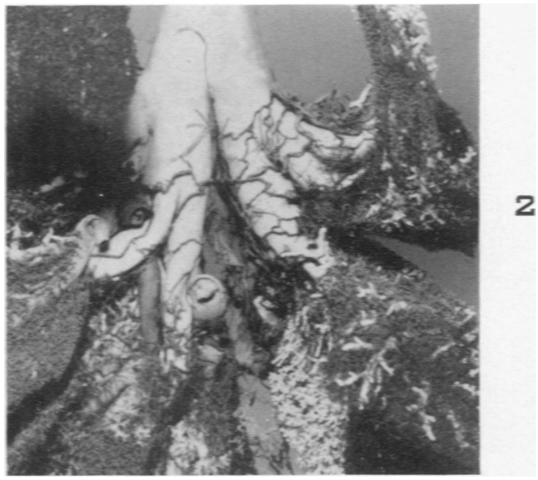
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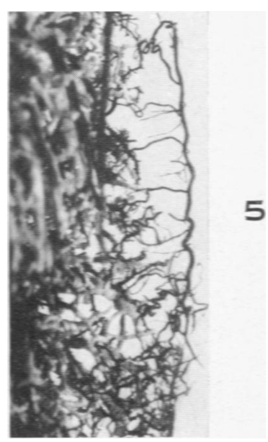
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PLATE 28

FIG. 6. Dog 33. A portion of the left upper lobe bronchus and associated vessels is shown. There has been retrograde injection of the pulmonary artery from the enormously enlarged bronchial vessels. The spiraling, many-branched trunks of the latter are more intimately applied to the main bronchus than the pulmonary artery, which faithfully pursues the frond-like distribution of the bronchus. Beyond the 3rd order branches of the lobar bronchus, the comitant main bronchial is only slightly smaller than the pulmonary artery at the same level (see Fig. 13). The exact points of communication of the two systems are not clearly shown in the figure, but are demonstrated in Figure 7. $\times$ 2½.

FIG. 7. Dog 33. A peripheral sub-segment of the left upper lobe. The bronchus can be distinguished in faint outline. Its branches are followed by those of a pulmonary arterial trunk (gray, originally in red) which is mottled with the jet black plastic that has entered from the bronchial arteries. The latter are tightly wound about the branches of the bronchus. Their calibers diminish less rapidly than that of the pulmonary artery as they proceed peripherally. In the uppermost branch of the bronchus, the bronchial artery (the tortuous vessel at the right) has nearly the same diameter as the pulmonary artery before it joins it (arrow) via several minute branches located about a bronchus of the 6th order. $\times$ 3½.

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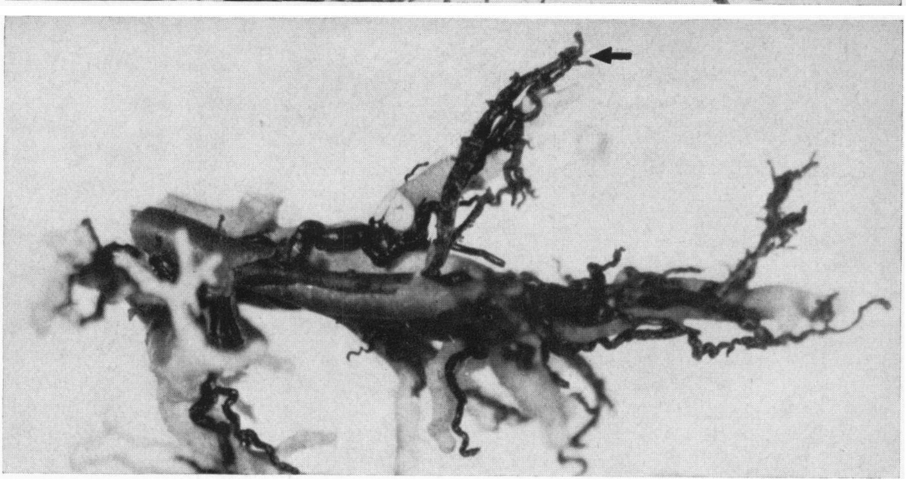

PLATE 29

FIG. 8. Dog 33. An immense plexus of bronchial arteries covers the retrogradely injected pulmonary artery in the interlobar fissure of the left lung. This pulmonary artery had been ligated 10½ months previously. The trunk of the left bronchial artery (arrows) sweeps anteriorly of the aorta from its source in the 3rd right aortic intercostal to supply this plexus. $\times$ 2.

FIG. 9. Dog 33 (as in Figs. 5 to 8). Posterior view of cast shown in Figure 8. The greatly enlarged right 3rd intercostal with the 2.5 mm. bronchial trunk (arrow) sweeps downwards from it and then anteriorly of the aorta. The cast has been made by digesting the entire thorax in concentrated HCl after injection. Actual size.

FIG. 10. Dog 11, sacrificed 12½ months after ligation of the left pulmonary artery. Posterior view of cast. The bulbous, ligated end of the cast of the left pulmonary arterial trunk (LP) can be seen just above the upper lobe bronchus. Below it can be seen the distal portion of the left pulmonary artery (LD) which was injected in the same fashion as the trunk. It may be noted that it has the same diameter as the right interlobar branch (**R**) that is glimpsed between the right upper and lower lobe bronchi. The 1st and 2nd right aortic intercostal vessels are the source of the huge plexus of bronchial arteries that is distributed to the left bronchial tree. (See also Fig. 7.) This plexus contributes only a few small branches to the right lung but sweeps beneath the carina to the left. Actual size.

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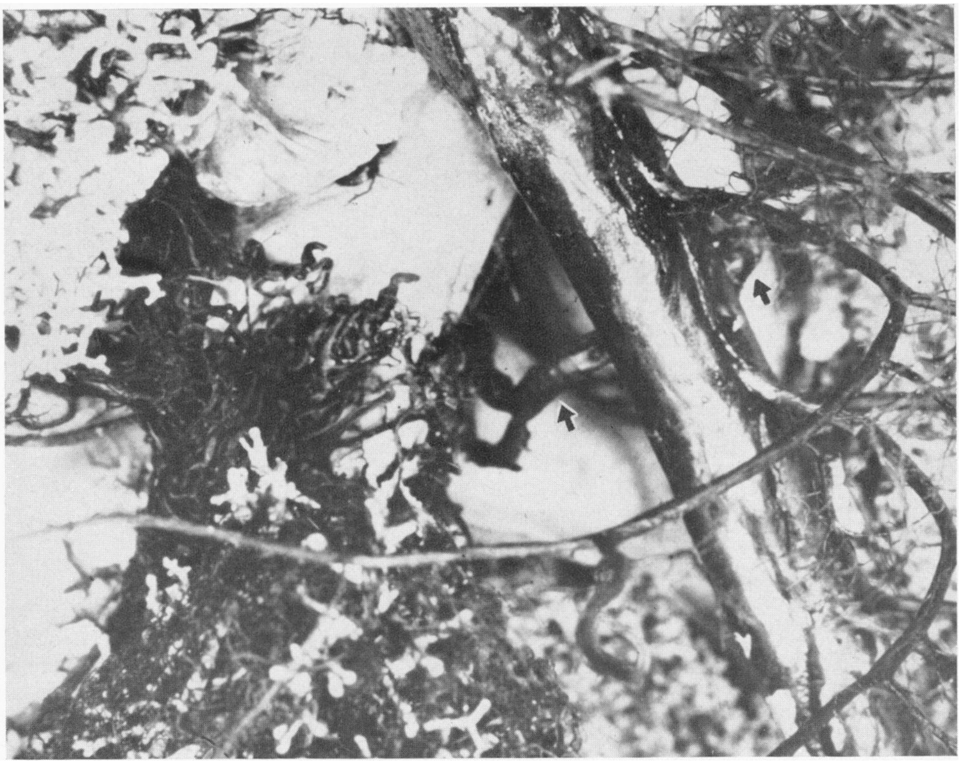

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Plate 30

Fig. 11. Dog 56. Right lung. Control. A bronchial arterial branch of the usual size is seen (arrow). Verhoeff's elastic stain. × 18.

Fig. 12. Dog 56. Left lung. Pulmonary artery ligated 7 months previously. Plexus of enormously enlarged bronchial arteries in the walls of the lower lobe bronchus. Vessel marked X is shown under high magnification in Figure 15. Verhoeff's elastic stain. × 18.

Fig. 13. Dog 36. Left lung, 13½ months after ligation of its pulmonary artery. A terminal bronchus approximately 1 by 0.5 mm. in major diameter is shown. The pulmonary artery (P.A.), largely of elastic structure, is seen at the right. More intimately related to the wall of the bronchus are the four lumina of greatly enlarged bronchial arteries, with thick muscular walls. The area of the cross section of the largest bronchial artery in this instance exceeds that of the pulmonary artery. Normally, the bronchial vessels at this level would be represented by arterioles, much smaller than the least of the bronchial arteries seen here. The effective flow of blood through the bronchial collateral vessels in dog 36 was estimated at 1239 cc./M^2/min.[1] × 55.

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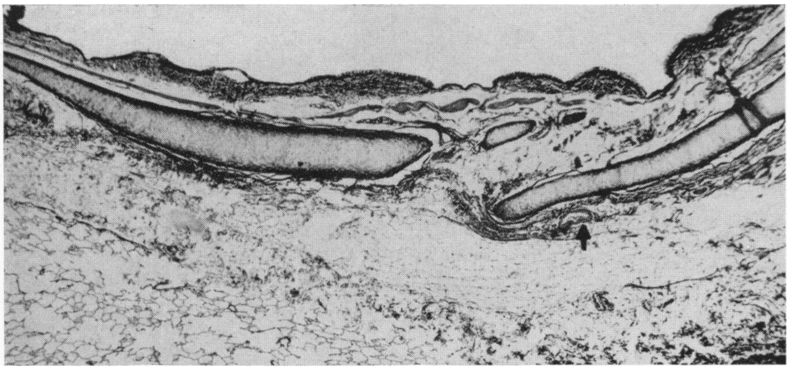

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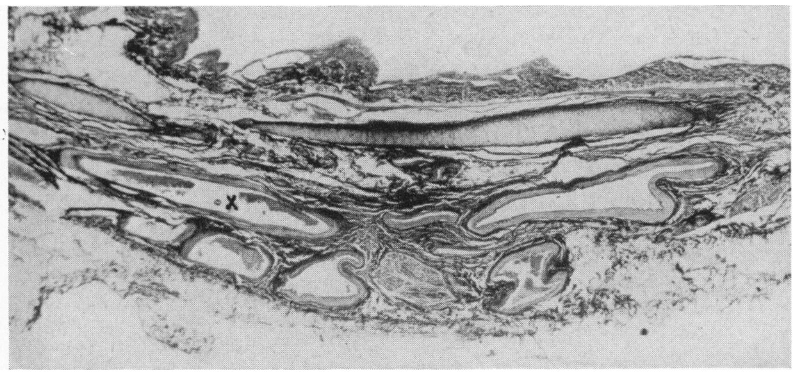

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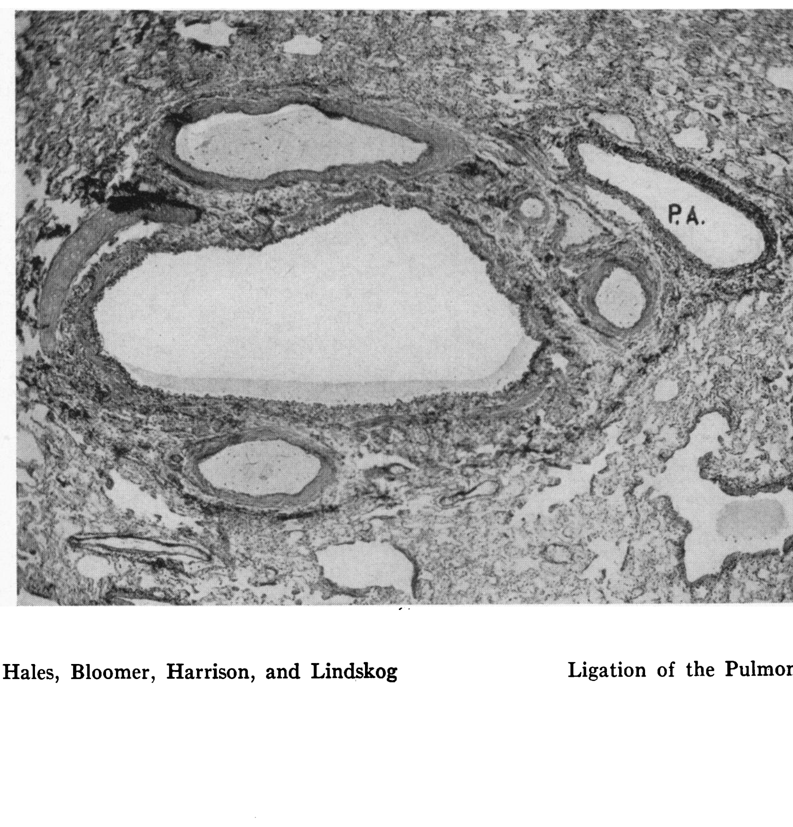

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Plate 31

Fig. 14. Dog 56. The largest bronchial artery from the wall of the main right upper lobe bronchus of the control lung, enlarged from Figure 11. The internal elastic lamella is a sharply defined continuous band. Most of the wall of the vessel consists of smooth muscle. There are no intimal changes. × 270.

Fig. 15. Dog 56. Left lung. Enlarged bronchial artery shown in Figure 12. Subendothelial pillows of connective tissue. Fragmentation of thickened elastic tissue. Hypertrophy of muscle. × 270.

Fig. 16. Dog 56. Trunk of left pulmonary artery beyond point of ligation showing unaltered, largely elastic, structure. × 270.

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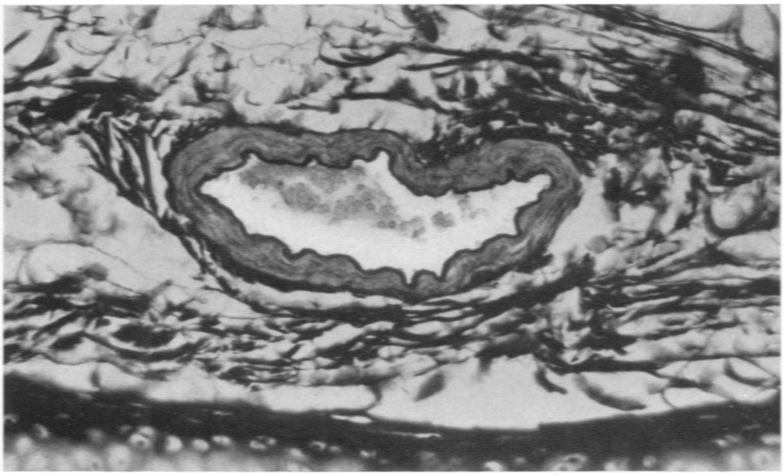

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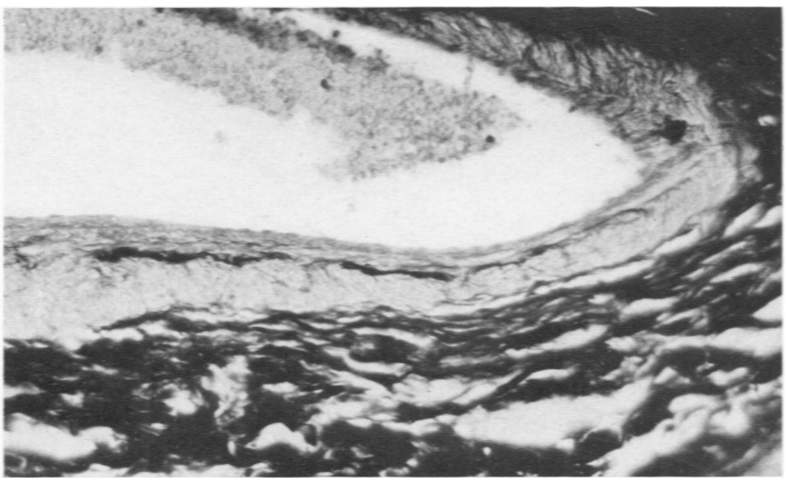

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