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Arteriovenous shunts in the peripheral pulmonary circulation in the human lung[1]

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The presence of arteriovenous shunts in the human lung has been suggested by many studies. Among these are blood gas analyses by Riley and Cournand (1949), the passage of embolic clots, parasites, and foreign bodies—many times the accepted diameter of capillaries—through the pulmonary circulation to other parts of the body (Brink, 1950), together with the formation of pulmonary telangiectasis, aneurysms, and fistulae (Yater, Finnegan, and Giffin, 1949; Carswell, 1950; Lindskog, Liebow, Kausel, and Janzen, 1950; Standefer, Tabakin, and Hanson, 1964; and others). Morphological studies of the pulmonary vessels by De Busscher (1947), Kucsko (1953), Weibel (1959), and von Hayek (1960) also indicate that shunts between pulmonary arteries and veins do exist in normal lungs, yet the presence of such shunts has been denied by Miller (1947), Liebow, Hales, Harrison, Bloomer, and Lindskog (1950), and other investigators. However, the utilization of glass spheres by Prinzmetal, Ornitz, Simkin, and Bergman (1948), and Rahn, Stroud, and Tobin (1952), and plastic spheres by Parker, Andresen, and Smith (1958), together with the cine-fluorographic study of radiopaque media passing through the pulmonary circulation by Rahn *et al.* (1952) have further verified the presence of these shunts in living animals. Isolated, post-mortem human lungs have also been used to demonstrate the presence of these shunts by means of injected glass spheres (Tobin and Zariquiey, 1950b) or radiopaque liquid latex or plastics to form casts of the pulmonary vessels (Tobin and Zariquiey, 1950a and 1953).

The morphology of these shunts in normal lungs is not well understood, since they do not have distinctive morphological features in sections from normal lungs, whereas in pathological lungs the vessels have been observed to vary in form from enlarged 'capillary-like vessels' to a complex of glomus-like bodies as described by Harris and Heath (1962).

The present study was undertaken in an attempt to locate the arteriovenous shunts in the peripheral part of the secondary lobule[3] of the lungs, since this is the site where the shunts would most likely be of functional significance in bypassing the alveolar capillary circulation, although shunts have been described as being present in the pleura and near the hilus of the lung by von Hayek (1960) and Tobin and Zariquiey (1950b).

MATERIAL AND METHODS

Pulmonary tissues from two different sources were studied.[4]

PLASTIC CASTS Casts of the secondary lobules from 10 human lungs, in which the pulmonary vessels and the respiratory passageways had been injected by the method of Tompsett (1959), were studied by means of a dissecting microscope. At least 50 secondary lobules were obtained from each lung. The lobules were mounted with a transparent adhesive[5] on coloured cardboard and orientated to show certain structures to maximum advantage. Photographs were then made of representative casts. The casts were dissected only where the pulmonary vessels could be visualized to better advantage by the removal of overlying respiratory tissue.

FRESH LUNGS Ten lungs (five pairs) were obtained from cases of accidental death.[4] The heart, lungs,

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[3]The secondary pulmonary lobule is that portion of the lung consisting of a group of terminal bronchioli, respiratory bronchioles, alveolar ducts, atria, and alveoli together with their associated blood vessels and connective tissue, as defined by Reid (1958) and Krahl (1959)

[4]The pulmonary casts were from four normal adults (ages unknown) and six cases (aged 3, 8, 8, 10, 12, and 23 years) in which death was due to cardiac malformations. In none of the latter cases were the bronchial arteries enlarged. The fresh lungs were from necropsies of four patients (10, 20, 23, and 24 years) who had died as a result of injuries from traffic accidents and from one (19 years) who had died from coal-gas poisoning

[5]Copydex Ltd.

pericardium, oesophagus and thoracic aorta were removed as a unit, put in a plastic bag, and frozen until ready for experimental use. After two to three days' storage the specimens were thawed completely under running warm tap-water. The pericardium, heart, oesophagus, and thoracic aorta were then removed from the specimen. The pulmonary vessels were cannulated with plastic or glass cannulae. A rubber stopper (bung), perforated to transmit either a large injection needle or a glass tube, was inserted into the trachea, and a ligature was applied to the trachea to retain the stopper in place.

The lungs were expanded several times with compressed air from an enema syringe and then allowed to deflate. Normal saline was perfused into and through the pulmonary artery until a relatively clear perfusate flowed from the pulmonary veins. A solution of Micropaque,[6] made up of eight parts powder and seven parts normal saline solution, was then diluted with equal amounts of 10% neutral formalin for injection into the pulmonary vessels by means of a hand syringe. The solution injected into the pulmonary artery was coloured with powdered vermilion pigment and the solution injected into the veins was coloured with powdered ultramarine pigment. The pigments were approximately 5% of the injection solution.

The initial 200 ml. injection made into the pulmonary artery contained 2,000 to 5,000 glass spheres,[7] 200 ± 25 μ in diameter. Injection was continued until the pigmented solution appeared at the pleura, but complete filling of all branches of the pulmonary vessels was not attempted.

For one lung, approximately 20,000 glass spheres were suspended in the stock solution of Micropaque for 24 hours. The excess solution was decanted and the spheres were washed in saline. They were then suspended in a 10% formalin solution and injected into the pulmonary artery. The Micropaque solution adhered to the surface of the spheres and made them radiopaque.

After injection of the pulmonary vessels a solution of 10% neutral formalin was perfused by gravity pressure into the trachea via the needle or tube through the bung. The perfusion was continued until the lungs were expanded, but the lobes were not separated from one another. The vascular cannulae were then ligated, the trachea occluded, and the lungs immersed in a container of 10% neutral formalin for 48 to 72 hours.

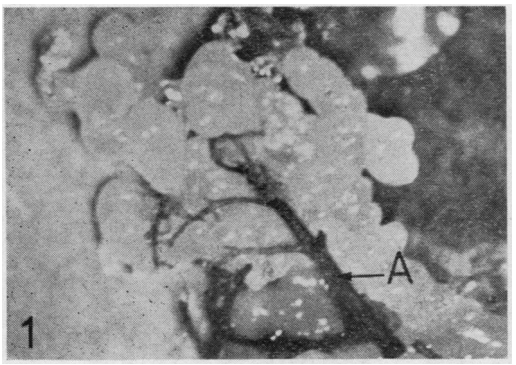
Sample slices, approximately 1 by 2 by 4 in. (25·4 by 50·8 by 101·6 mm.) in size, were taken from each lobe. These sections were placed between sheets of plexiglass, and ligatures were placed around the plexiglass to hold the slices flat while they were stored in a freezer. After being frozen for 24 hours, the slices were cut by means of a band saw into sections approximately 2 mm. thick. The surfaces of each section were washed gently under running tap-water to remove any lung tissue, injection media, or glass spheres which might have been carried by the teeth of the saw blade to another part of the section. The sections were then marked for later orientation and identification by coding them with staples (clips) placed along the periphery of the section. Each section was radiographed with a Newton Victor Machine (40 kV, 3 mA, 30 seconds, 14 in. tube to plate distance) with the sections placed horizontally on plastic overlaying sheets of Kodak Commercial Orthochromatic film. After radiography the sections were stored in 10% formalin. The radiograph for each section was studied under a dissecting microscope while the radiograph was transilluminated over a viewing box. The location of the glass spheres was determined from the radiographs, and either pieces of the tissue containing the beads or the whole section was used to prepare microscopic or macroscopic sections. The microscopic sections were cut at either 10 or 300–400 μ in paraffin, and the sections were prepared by the customary histological methods and stained lightly with haematoxylin and eosin. The macroscopic sections were made by dehydrating and clearing the larger sections and mounting them in a petri dish containing Gurr's DePoX in sufficient amount to immerse the section. Small glass cubes, thicker than the macroscopic sections, were used to support the circular cover glass over each section.

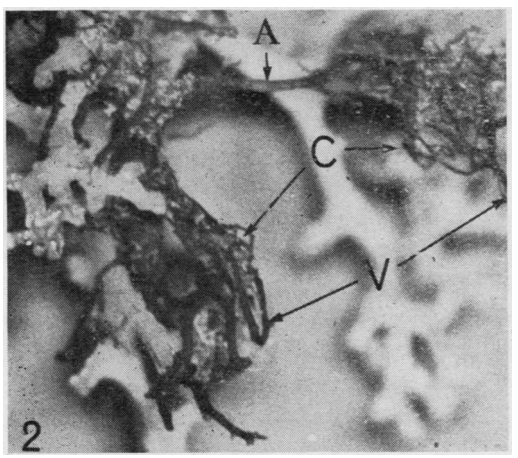
[6]Damancy and Co., Ltd.
[7]The glass spheres were obtained from B. F. Drakenfeld, 45-47 Park Place, New York, N.Y.

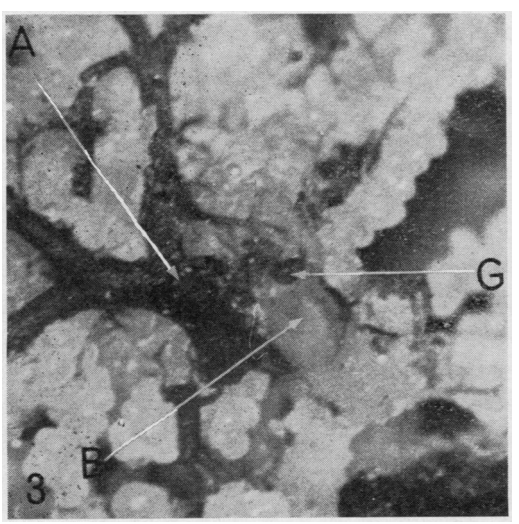
OBSERVATIONS

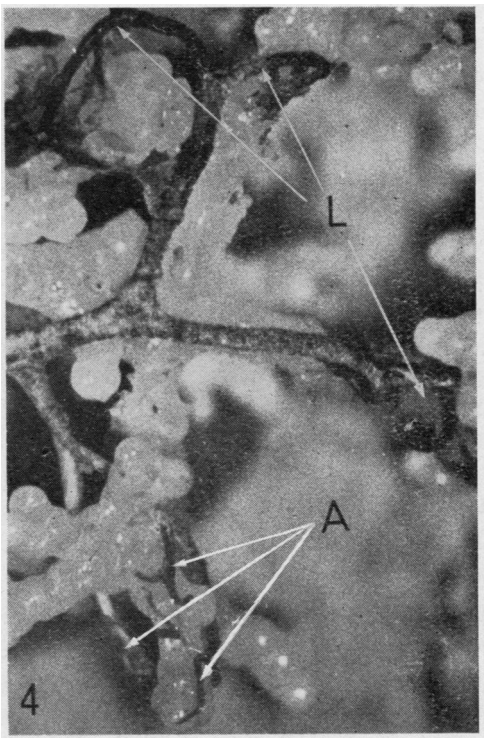
The alveoli within a primary lobule are usually described as being supplied by only one branch of the arteriole accompanying the bronchiole into that lobule (Fig. 1). This arteriole supplies the capillary network on the surface of several alveoli, and these capillaries then empty into a venule and finally into a branch of the pulmonary vein (Fig. 2). However, at the apex of the secondary lobule a glomus-like swelling may be found attached to the wall of the arteriole (Fig. 3). Further study of casts in which the alveoli were not completely filled demonstrated that the arteriole may be in the form of a loop at the beginning of the primary lobule (Figs 4 and 5). This loop terminated in a pulmonary venule or small pulmonary vein.

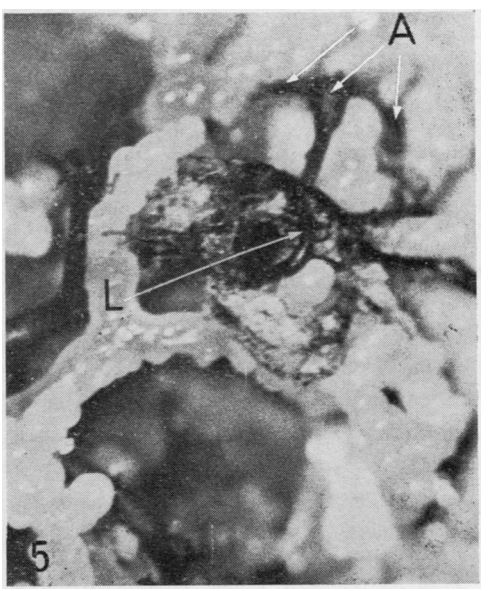
In addition to the arteriole from the loop which supplies the capillary plexus, other arterioles are also found on the walls of the alveoli. These additional arterioles may be derived from the arterial loop, the arteries within the connective tissue septa or within the pleura, or even the branches of the bronchial artery accompanying the main bronchi (Figs 4 and 5). The attachment of the glomus-like swellings to the wall of the arterial loop is shown in Figures 6 and 7. Although these glomus-like bodies varied in size, they were



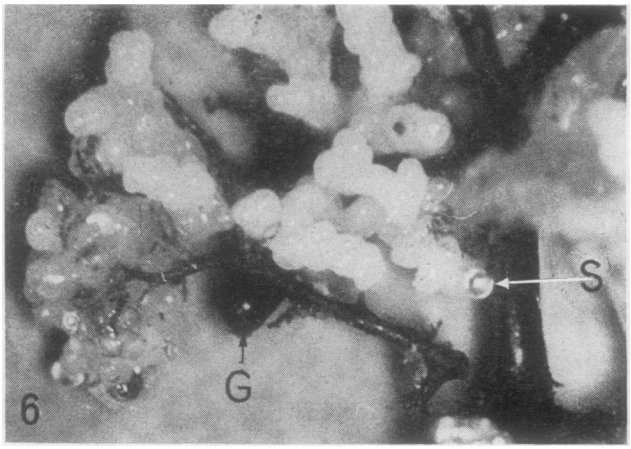


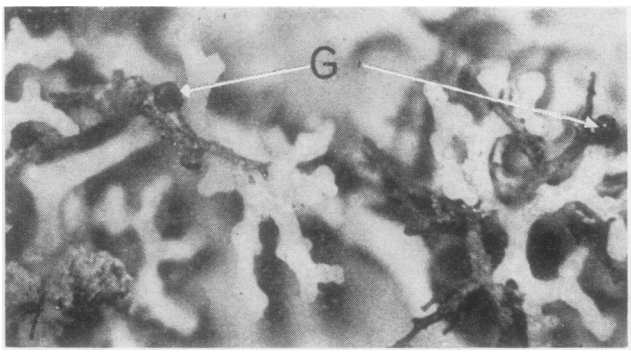


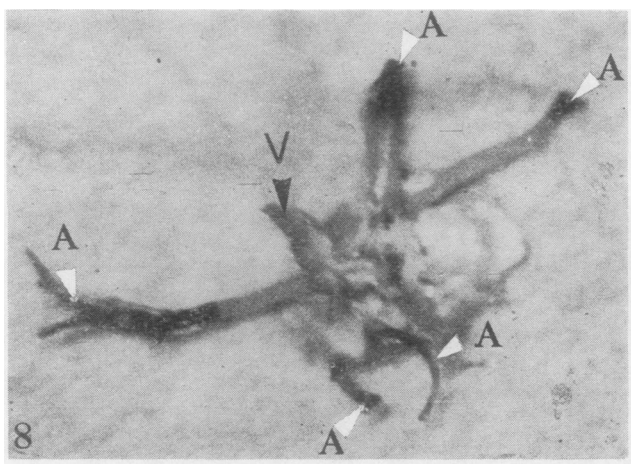


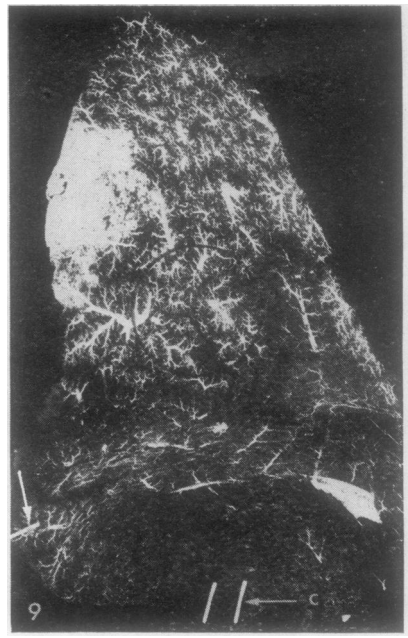


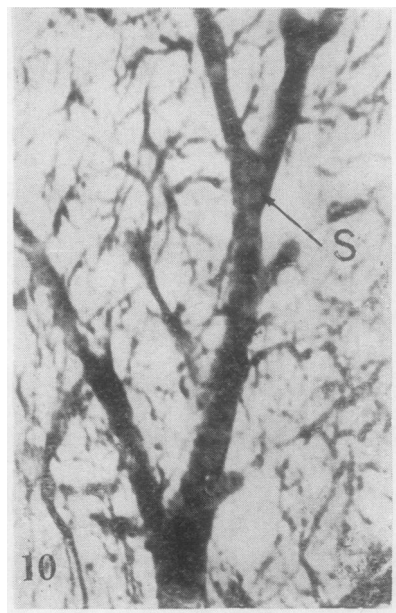
For legends to Figs 1 *to* 5 *see p.* 202.



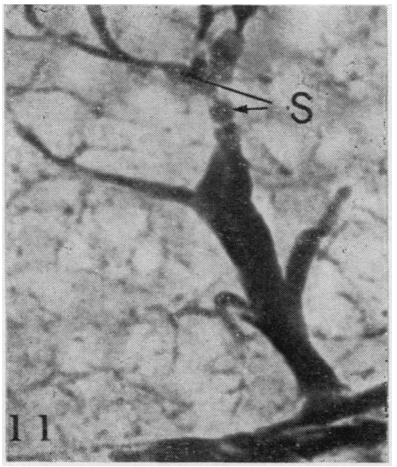


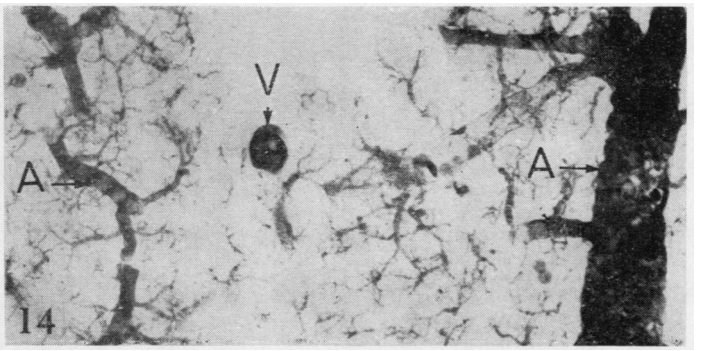


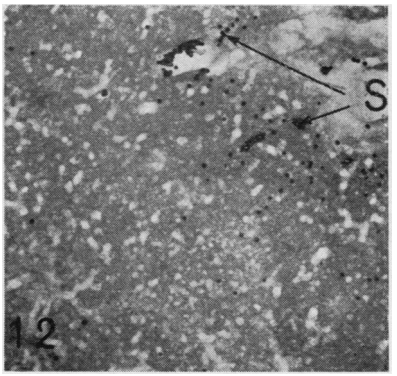


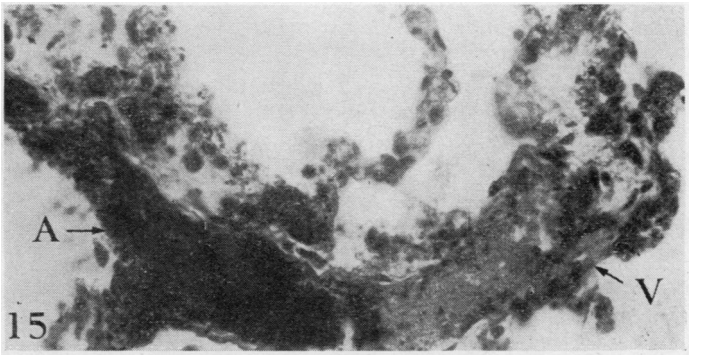


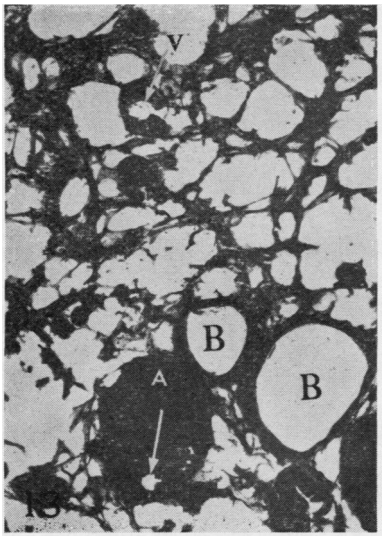
For legends to Figs 6 *to* 10 *see p.* 202.

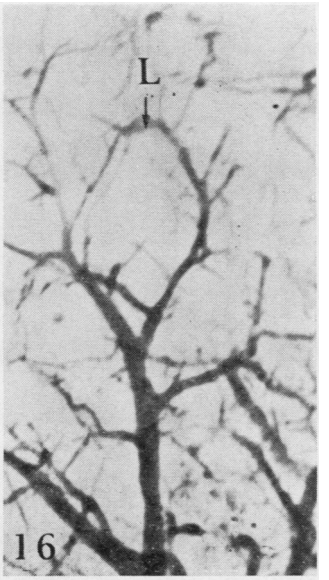


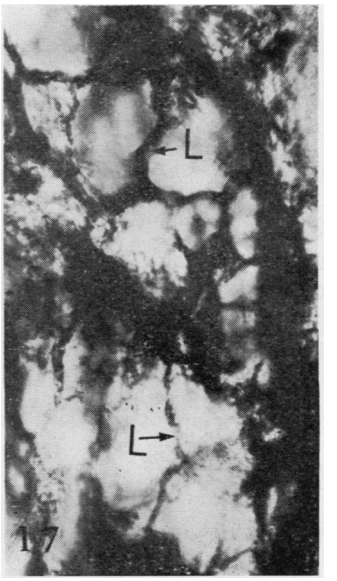












For legends to Figs 11 *to* 17 *see p.* 202.

LEGENDS TO FIGS 1 TO 17

FIGS 1 *to* 8 *are photomicrographs of plastic casts from pulmonary lobules.* × 18.

FIG. 1. *The course of a pulmonary arteriole (A) in its relationship to several alveoli is shown.*

FIG. 2. *Capillary (C) networks originating from pulmonary arterioles (A) and terminating in pulmonary venules (V) are on the surface of alveoli. The alveoli were not completely filled with the injected plastic.*

FIG. 3. *View from the apical (proximal) part of a secondary lobule, showing the course of the pulmonary artery (A) and the accompanying bronchiole (B). A glomus-like (G) enlargement is present on the wall of the artery.*

FIG. 4. *Area in which the capillary bed was not injected, demonstrating the loop-like (L) form of the arterioles which supplied the alveoli. Note the course of three small arterioles (A) near the walls of the alveoli.*

FIG. 5. *Another view of an arteriole loop (L) and three arterioles (A) coursing along the walls of the alveoli.*

FIGS 6 and 7. *Glomus-like (G) swellings are present on branches of the pulmonary arterioles. A glass sphere (S), 200 μ in diameter, was pasted on the wall of the arterial cast in the same optical plane as the glomus-like swelling in Fig. 6 to indicate the size of these structures.*

FIG. 8. *Cast of a pulmonary vein (V, black arrow point) dissected from a secondary lobule showing the connexions of the pulmonary arterioles (A, white arrow points) to the pulmonary vein. The latter were the sites of arteriovenous anastomoses, since the plastic used for injection did not traverse the capillary bed.*

FIG. 9. *Photograph from a radiograph of a lung section in which the pulmonary artery was injected with a solution of Micropaque containing glass spheres, 200 μ in diameter. Each section, approximately 2 mm. thick, was code marked with metal clips (c) for identification. Note the different degrees of arterial injection: from complete capillary filling (solid white area, on upper left); arterial and arteriole filling (branching, white slender vessels); to very little vascular filling (lower part of figure).* × 1.

FIGS 10 and 11. *Enlargements from area outlined in black on the radiograph shown in Figure 9. In Fig. 10, note glass spheres (S) displacing the Micropaque within the lumen of the arteriole. In Fig. 11, glass spheres (S) are located in the pulmonary arteriole just proximal to its terminal loop.* × 13.

FIG. 12. *Photographic print from a radiograph of a lung in which the glass spheres were coated with Micropaque solution and suspended in 10% formalin for injection into the pulmonary artery. The coated spheres appear as black dots (S). The branches of the terminal bronchi and the bronchioles contain air and appear as clear channels.* × 6.

FIG. 13. *Section of lung cut at 400 μ, stained with haematoxylin, mounted, and photographed to show part of a glass sphere displacing the Micropaque in a branch of the pulmonary artery (A) adjacent to a division of the bronchus (B), and part of another sphere displacing the Micropaque within a small vein (V).* × 70

FIG. 14. *Photograph from a radiograph showing spheres within a large branch of the pulmonary artery (A) on the right side of this figure, a smaller branch of the pulmonary artery (A) on the left side of this figure, and also in a centrally located branch of the pulmonary vein (V).* × 10.

FIG. 15. *Photograph from a histological section showing Micropaque containing red pigment (dark colour) in the arterial end (A) in contact with the injection mass containing the blue pigment (lighter colour) in the venous end (V) of the vascular loop. Note the thin wall of this vessel.* × 340.

FIG. 16. *Photograph from a radiograph of a lung in which the pulmonary artery was injected with Micropaque. Note the size, shape, and position of the arteriole loop (L).* × 18.

FIG. 17. *Photograph of a thick (2 mm.) cleared section from an injected lung showing vascular loops (L) near the base of alveoli. Focus was at a depth to show the loops; however, a few capillaries can be seen originating from the loops.* × 85.

present in 47% of the 512 lobules examined and they were attached to that part of the arteriole which is known to have very little muscle or elastic tissue in its walls. Since the injected plastic does not traverse the capillary bed, in specimens in which the branches of the pulmonary artery were filled a direct connexion between the pulmonary arteriole and the vein could be ascertained by the juxtaposition of the different coloured plastics used to inject the vessels. As shown in Fig. 8, these sites of meeting of the colours are also the points at which the glomus-like bodies are found.

The size, course, and relationships of the pulmonary arterioles could be determined readily from the radiographs (Figs 9, 10, 11, 14, and 16) and from sections of the tissues injected with different colours added to the radiopaque injection media (Fig. 15).

In addition, the location of the glass spheres in branches of the pulmonary artery (Figs 10, 11, 12, 13, and 14) and in the arteriole loop (Fig. 11), as well as their final location within the pulmonary veins (Figs 13 and 14), further substantiates the presence of these shunts. The position of the pulmonary veins was determined by their location

in the periphery of the lobules (Figs 13 and 14), whereas the bronchi and branches of the pulmonary artery are usually located in the central part of the lobules.

DISCUSSION

Evidence for the presence of arteriovenous shunts within the secondary pulmonary lobules is based on the observations that (*a*) there is an arterial loop at the apex of the primary lobule; (*b*) this loop (in normal lungs) has very little muscle or elastic tissue in its walls, in support of the observations by von Hayek (1960) and others; and (*c*) this segment can be dilated to form glomus-like protrusions or to allow the passage of glass spheres, many times the accepted diameter of capillaries, into the pulmonary veins. Why then are these shunts not seen as definite structures in microscopic sections from apparently normal lungs? The contraction of the pulmonary tissue due to the inherent elasticity of the whole lung when it is removed from the thorax, plus the additional chemical fixation shrinkage of this tissue when it is prepared for preservation, both influence the contraction of the pulmonary artery and its branches.

These arteries can be kept expanded if, as in the techniques used in the current studies, the pulmonary arterial system is injected with either plastic, radiopaque, or other media before the respiratory tissue is injected. Filling the latter tissue will impinge on the walls of, or occlude, the pulmonary arterioles. Besides, the viscosity of the media used has to be low enough to allow its passage into most of the vessels but not to make a complete transit of the capillary bed. In the present experiments gelatin was not used in conjunction with the injection media, although this admixture has been used by some investigators (Reid, 1955; Reid and Heard, 1963; Turner-Warwick, 1963), since both the viscosity of the gelatin and the necessity of warming the tissues thoroughly may interfere with adequate filling of the arteriole loop and the passage of material into the veins and hence lead to an inability to identify the arteriovenous shunt.

The question may also be asked whether the glomus-like formations and the passage of the glass spheres may have been due to excessive pressure being used to distend artificially the vascular channels described as being the arteriovenous shunts. That this was not a factor was ascertained by the fact that in the case of the injection of the plastics there was no rupture of the capillary beds (which have much thinner walled vessels than the arterial loop) and secondly, as shown in Fig. 9, there was incomplete filling of the pulmonary vessels in all sections of the lung radiographed or sectioned.

That the arterial loop was not an artifact of the injection technique is confirmed by the fact that Clara (1936) has observed similar structures. Irwin, Burrage, Aimar, and Chesnut (1954), Knisely (1960), and Reeves, Leathers, and Quigley (1965) have shown that branches of the pulmonary artery arise at right-angles to the parent trunk and may have a loop-like configuration.

The studies also confirm the observations of others that the alveolar capillary bed is supplied by more than one arteriole. These additional vessels may arise from the septal, pleural, or bronchial arteries, and whether to call these latter arteries branches of the pulmonary or bronchial supply to the lungs is debatable, since Verloop (1948), Tobin (1952), Turner-Warwick (1963), and others have shown that there may be connexions between the bronchial and pulmonary arteries in many parts of the normal lung.

Glomus-like bodies were found by other investigators and can be seen in Figs 2 and 4 in the paper by Pump (1962), where similar glomus-like bodies are depicted on the walls of the pulmonary arterioles, although they are not described in the text.

SUMMARY

Studies of plastic casts from human lungs, and injection of radiopaque material and glass spheres, 200 μ in diameter, into the pulmonary artery of intact post-mortem lungs demonstrated that an arterial loop is present at the apex (proximal part) of the acinus. This loop has relatively little muscle or elastic tissue in its walls and hence is capable of dilatation to form glomus-like protrusions or to allow the passage of glass spheres, 200 μ in diameter, into the pulmonary veins, thus functioning as an arteriovenous shunt.

These peripheral arteriovenous shunts are usually not obvious in normal lungs, since the elastic contraction of the lung and the additional chemical-fixation shrinkage contracts all the pulmonary tissue, including the arterial loop. Besides, in injected specimens filling of the respiratory tissue with the injection mass before injecting the pulmonary artery will compress the wall of the arterial loop.

The observation that the alveolar capillary bed may be supplied by more than one artery confirms the findings of other investigators.

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