# PULMONARY HYPERTENSION IN RATS LIVING UNDER COMPRESSED AIR CONDITIONS

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PLATES 16 TO 18

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In a previous publication (1) we described vascular lesions in the pulmonary arteries of rats following prolonged exposure to an environment of compressed air, having an oxygen tension of approximately 635 mm. Hg. The changes from normal in the pulmonary arterioles consisted of thickening and hyalinization of the walls with narrowing of the lumina. We commented upon the similarity of these lesions to those seen in the arterioles of the human kidney of patients with progressive vascular nephritis and hypertension.

The present study was undertaken in order to determine whether or not such vascular changes are accompanied by an increase in the pulmonary arterial pressure and to see if blood vessels other than the pulmonary arteries are affected.

## *Methods*

*1. Animals.*—58 albino rats between the ages of 120 and 175 days were studied. Male and female rats were used in equal numbers. They were maintained on a standard diet which had proved satisfactory in other experiments (2).

*2. Apparatus.*—An environment of compressed air, containing a high oxygen tension, was obtained by using the compressed air equipment described by Thompson, Yaglou, and Van Woert (3). The humidity, temperature, and barometric pressure were kept constant by automatic regulators.

*3. Conditions.*—The barometric pressure was maintained at approximately 3040 mm. Hg (45 pounds gauge pressure) except for a drop to 2280 mm. Hg (30 pounds gauge pressure) for 10–15 minutes twice a week when the animals were being fed. Once a week the pressure was lowered to 2280 mm. Hg for 2–2½ hours while the pulmonary arterial pressure of a series of rats was being determined inside the pressure chamber. The oxygen tension, except for these insignificant periods, was approximately 635 mm. Hg, corresponding to an 83.6 per cent mixture

of oxygen at normal barometric pressure. The dry bulb temperature remained at 28°C. plus or minus 1°C., while the relative humidity ranged from 49–50 per cent. The total period of time during which the rats were kept in an environment of high oxygen tension identical with that of the previous experiments (1, 2) was 38 days.

*4. Determination of the Pulmonary Arterial Pressure.*—The pulmonary arterial pressure was determined on a series of rats after 3, 10, 17, 24, 31, and 38 days of exposure. It was measured directly on a water manometer connected with a cannula which was inserted into the arch of the pulmonary artery. A description of the method employed has been given in a previous paper (4).

*5. Pathological Technique.*—Each rat upon which the pulmonary arterial pressure had been satisfactorily determined was autopsied as soon as decompression was completed, usually within a period of 2–4 hours after death. The esophagus, trachea, heart, lungs, and thoracic aorta were removed in one piece, examined, and placed in fixative. After hardening, blocks of tissue were selected for microscopic study from similar areas in each organ. The brain, spleen, and liver were removed separately while the kidneys with the abdominal aorta and inferior vena cava were removed in one piece so as to enable us to obtain sections of the large abdominal vessels. Cross-sections of the femoral vessels and surrounding muscles were taken. Tissues were routinely fixed in Zenker's fluid. However, in a small series of rats, representative of varying periods of exposure to compressed air, the tissues were fixed in 10 per cent formaldehyde solution in order that fat stains on frozen sections might be made and thus the presence or absence of fat in sclerosed arteries be determined. Microscopic sections were stained routinely with methylene blue and eosin and phosphotungstic acid hematoxylin. In representative groups of rats, frozen sections from all organs were stained with Scharlach R.

## *The Pulmonary Hypertension*

In a preliminary study of normal rats (4) the average pulmonary arterial pressure in a series of 34 animals was found to be 256 mm. $H_2O$. The results of all determinations in the present investigation are presented in Table I.

The pulmonary arterial pressures were within normal limits during the first 17 days of exposure except for one unusually low reading after 3 days exposure, when many of the animals showed the effects of acute oxygen poisoning, and one high reading on the 10th day. Definite pulmonary hypertension was present in one rat after 24 days of exposure while all of the other readings made on that day corresponded to the upper limits of the normal series.

All animals subjected to the environment of compressed air for 31 and 38 days respectively were found to have definite pulmonary hypertension.

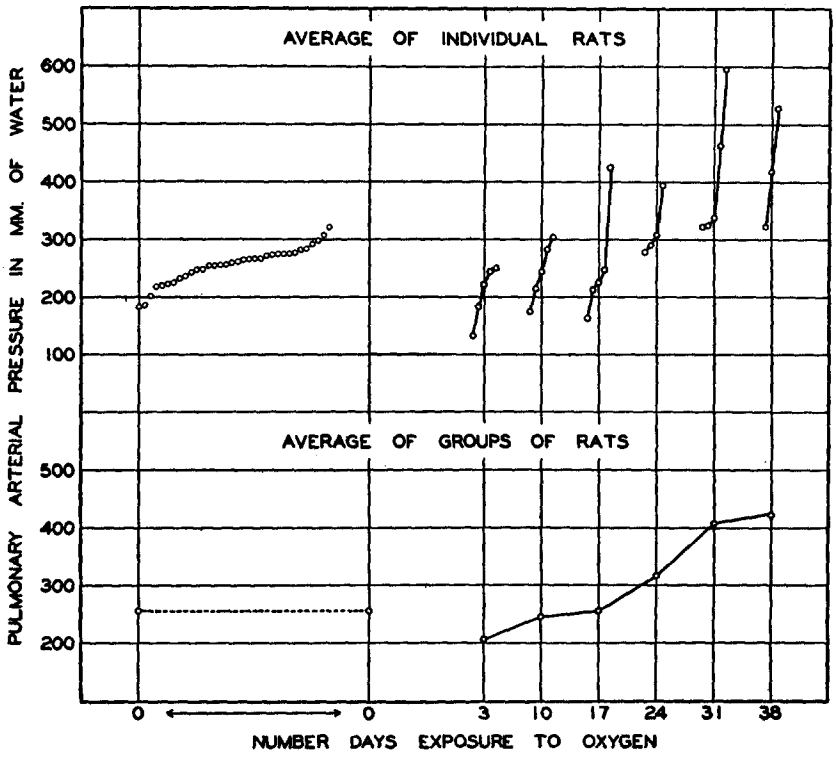
TABLE I

*Pulmonary Arterial Pressure in a Series of Rats Exposed to Compressed Air for Varying Periods of Time*

| Animal No. | Age | Sex | Duration of experiment | Duration of exposure to 83 per cent oxygen tension | Pulmonary arterial pressure |
|---|---|---|---|---|---|
| | *days* | | *min.* | *days* | *mm. $H_2O$* |
| 11-1 | 139–140 | M | 3½ | 3 | 245 |
| 11-4 | 139–140 | M | 3 | 3 | 133 |
| 11-5 | 122–140 | F | 5 | 3 | 250 |
| 11-7 | 122–140 | F | 7 | 3 | 184 |
| 11-8 | 122–140 | F | 5 | 3 | 222 |
| | | | | Average.... | 207 |
| 11-9 | 146–147 | M | 5 | 10 | 176 |
| 11-10 | 146–147 | M | 4 | 10 | 214 |
| 11-11 | 129–147 | F | 5 | 10 | 304 |
| 11-12 | 146–147 | M | 5 | 10 | 244 |
| 11-13 | 129–147 | F | 5 | 10 | 283 |
| | | | | Average.... | 244 |
| 11-14 | 136–154 | F | 5 | 17 | 212 |
| 11-16 | 153–154 | M | 5 | 17 | 249 |
| 11-17 | 136–154 | F | 6 | 17 | 227 |
| 11-18 | 136–154 | F | 5 | 17 | 425 |
| 11-19 | 153–154 | M | 5 | 17 | 163 |
| | | | | Average.... | 255 |
| 11-21 | 160–161 | M | 5 | 24 | 309 |
| 11-22 | 160–161 | M | 5 | 24 | 394 |
| 11-25 | 143–161 | F | 2 | 24 | 279 |
| 11-26 | 143–161 | F | 1½ | 24 | 290 |
| | | | | Average.... | 318 |
| 11-28 | 167–168 | M | 4 | 31 | 463 |
| 11-29 | 167–168 | M | 10 | 31 | 339 |
| 11-30 | 150–168 | F | 5 | 31 | 322 |
| 11-31 | 150–168 | F | 5 | 31 | 597 |
| 11-33 | 167–168 | M | 3 | 31 | 324 |
| | | | | Average.... | 409 |
| 11-42 | 174–175 | M | 1¼ | 38 | 419 |
| 11-44 | 157–175 | F | 5 | 38 | 322 |
| 11-45 | 174–175 | M | 5 | 38 | 529 |
| | | | | Average.... | 423 |

The average pulmonary arterial pressure of the normal and experimental series of rats are plotted in Text-fig. 1, both as individual rats and as groups, showing the rapid elevation of pressure that occurs in weekly intervals after the 24th day of exposure.

No attempt was made to determine the systemic arterial blood pressure of rats during their stay in an environment of compressed air.




TEXT-FIG. 1. The pulmonary arterial pressure in normal and experimental animals plotted individually and as groups, illustrating the gradual development of pulmonary hypertension during exposure to compressed air.

However, such determinations were made on a series of five rats which had been exposed for 38 days, decompressed, and kept at normal barometric pressure for 7–10 days. In these animals the carotid artery was cannulated and the arterial blood pressure measured directly on a mercury manometer. After the initial carotid arterial pressure had

been recorded, the pulmonary artery was cannulated as in previous rats, in an effort to simultaneously measure the pulmonary arterial pressure.

The average carotid arterial blood pressure in these five rats was 55 mm. Hg, the lowest individual average pressure being 48 mm. Hg, and the highest 59 mm. Hg. Thus in each instance the systemic blood pressure of the exposed rats was slightly less than one-half of the average normal (113 mm. Hg) in four rats which we examined and the average normal systemic pressure of 119 mm. Hg as reported by Durant (5). Although the number of rats upon which these determinations were made was small, the consistently low pressure readings in each instance provide additional evidence of an important degree of arterial obstruction in the lesser circulation. Gibbon, Hopkinson, and Churchill (6) demonstrated that when the pulmonary artery in cats was obstructed to from 60 per cent to 85 per cent of its cross-sectional area, there was a reduction in cardiac output, attended by a fall in the systemic blood pressure and a rise in venous pressure.

An attempt to make simultaneous determinations of the systemic and pulmonary arterial pressures failed in two of the five rats. In the remaining three rats the average pulmonary arterial pressure was 296 mm. $H_2O$ which was considerably higher than the average pressure of 179 mm. $H_2O$ in three control rats in which simultaneous pressure readings were made. The fact that the average pulmonary pressure in both the exposed and normal rats is lower than in corresponding groups of animals in which only the pulmonary artery was cannulated, suggests that the added manipulation and blood loss entailed in measuring the systemic pressure may have resulted in readings that were not as high as the actual pulmonary pressure in these animals.

### *Pathological Findings*

Gross and microscopic examination of the brain, liver, and kidneys did not show any constant abnormality. Microscopic examination of the blood vessels of these organs as well as of the aorta in both the thoracic and abdominal portions and the femoral arteries, revealed no pathological change. The spleen in all animals appeared normal on gross examination but in practically all instances there was a recognizable increase in the amount of hemosiderin in the exposed rats. Scharlach R stains made on frozen sections failed to demonstrate the presence of pathological fat in the blood vessels or parenchyma of any of the above organs.

The heart and lungs alone showed constant or important changes from normal.

Macroscopic examination of the heart after death did not reveal as striking changes as did direct observation of the exposed and functioning heart while the pulmonary pressure determinations were being made. At that time, in rats exposed to compressed air for 24 days or more, the heart action usually appeared more forceful than normal and the right ventricle was constantly dilated so that its prominent borders partially obscured the adjacent margins of the left ventricle. The conus arteriosus instead of tapering gradually into the pulmonary artery as it did in normal rats was markedly ballooned out and obscured the ventriculoarterial junction.

In one instance (Rat 11-28) very interesting correlations between the markedly increased pulmonary pressure and the pathological changes in the right ventricle were possible. In this rat the right ventricle was tremendously dilated when first exposed. When the cannula was inserted into the pulmonary artery, the pressure rapidly mounted to 500 mm. $H_2O$, where it remained in equilibrium for a few seconds and then rapidly fell as the right ventricle became even more dilated, slowed down, and almost ceased beating. By lowering the pressure in the manometer to a subnormal level, enough blood was expelled from the right ventricle to allow it to recover temporarily and the elevated initial pressure was almost totally regained and sustained for $2\frac{1}{4}$ minutes. At this time the right ventricle again became decompensated and failed to revive. Examination of the heart after death showed an area 4 x 3 mm. in diameter in the wall of the right ventricle which had the gross characteristics of a cardiac aneurysm. This portion of the myocardium bulged out from the surrounding musculature and when sectioned across was found to consist of a very thin fibrous membrane. Microscopic examination of this lesion showed that the muscle fibers had almost entirely degenerated, leaving only thin dense scar tissue which presumably had become markedly stretched out. Two other hearts showed similar but smaller defects in the right ventricular musculature which were recognizable on macroscopic examination. These hearts were the most damaged of any in the series, although microscopic examination revealed slight to moderate scarring in the right ventricle of most of the animals which had been exposed to compressed air for 31 days or longer. Such areas of scar formation were usually small and consisted only of connective tissue increase between muscle fibers. In a few instances, however, there was a slight infiltration with mononuclear leucocytes and, in one example, on the sixth day of exposure, a widespread and active myocarditis of the right ventricle was present. In this instance the muscle fibers were degenerating, as shown by large amounts of finely divided particles of fat and there was a heavy inflammatory cell infiltration. In a number of sections the auricular musculature showed similar areas of inflammatory cell infiltration or connective tissue increase between muscle fibers.

Macroscopic and microscopic examination of the lungs confirmed in most respects our previous observations (1). On the 3rd day of exposure the lungs showed an acute inflammatory reaction characterized chiefly by marked perivascular edema, alveolar edema, and pleural effusion. In numerous areas the alveoli

contained fibrin and a scattering of mononuclear and polynuclear inflammatory cells. The alveolar walls showed an increase in polymorphonuclear leucocytes. As in the previous series of rats, the trachea, bronchi, and bronchioles showed no evidence of injury except in occasional instances in which a small amount of mucopurulent exudate was present within the larger bronchi. In the present study it was noted that the pulmonary arterioles stood out more prominently than normal. This fact was due chiefly to the surrounding zone of edema and dilatation of the accompanying lymphatics. However, because of a slight alteration in the staining quality of the media and because of a tendency to separation of fibers in the arterial walls in occasional vessels, we believe that even at this early period there was injury to the pulmonary arteries (Fig. 1). One of the most striking histological abnormalities was the apparent increase in the thickness of the walls of occasional arterioles with a corresponding narrowing of the lumina (Fig. 2) which in occasional vessels gave the appearance of complete closure. The large pulmonary arteries were not appreciably thickened after an exposure of 3 days. There was, however, marked perivascular edema about them, and slight to moderate fraying of the fibers in the adventitia. The fibrils of the connective tissue about many of the large pulmonary veins were spread apart by edema. This abnormality was not as extensive or as constant as in the case of the pulmonary arteries. In several sections the walls of the large veins showed scattered areas of degeneration characterized by edema, disappearance of muscle fibers, and a moderate to heavy infiltration of inflammatory cells which consisted chiefly of mononuclear leucocytes. Scattered polymorphonuclear leucocytes were also present. Such lesions were not accompanied by thrombus formation.

After more prolonged exposure the alterations noted in the alveolar units of the lungs were essentially the same as those previously observed and described (1), the most striking change being hyperplasia and hypertrophy of the alveolar lining cells. There were also progressive changes in the large pulmonary arteries which became prominent after 10 days of exposure.

A tabulation of the measured thickness of the walls of the large pulmonary arteries and aorta of the individual rats throughout the experiment is given in Table II. Such measurements were made on microscopic sections with an ocular micrometer which had been calibrated on a stage micrometer. While it is true that some variations in the diameters are no doubt due to variations in the locations at which the measurements were made and to the difference in the age of the various rats, nevertheless we are satisfied that the averages by periods of exposure are approximately correct. Sections from approximately the same anatomical levels were selected and only those arteries which were squarely cut across were measured. One sees from these measurements of the large vessels that the thickness of the wall of the

aorta remained practically constant, whereas the wall of the pulmonary artery doubled in thickness within a period of 10 days and became three times its normal thickness after 1 month. Increased resistance met in attempting to insert the cannula through the wall of the main pulmonary artery in all animals exposed to compressed air for 24 days or longer provided additional evidence of this sclerosing process. No variations from normal were noted on microscopic examination in any arteries of the systemic circulation.

TABLE II

*A Comparison of the Average Thickness of the Large Pulmonary Artery and Aorta in Normal Rats and Rats Exposed to Compressed Air for Varying Periods of Time**

| Animal series | Duration of exposure to compressed air | No. of animals in each group | Average thickness of aortic wall | Average thickness of wall of pulmonary artery |
|---|---|---|---|---|
| | *days* | | *mm.* | *mm.* |
| Control | 0 | 13 | 0.0982 | 0.0477 |
| Experimental | 3 | 5 | 0.1029 | 0.0531 |
| " | 10 | 5 | 0.0929 | 0.1029 |
| " | 17 | 5 | 0.1095 | 0.1162 |
| " | 24 | 3 | 0.0941 | 0.0941 |
| " | 31 | 5 | 0.1062 | 0.1382 |
| " | 38 | 3 | 0.1328 | 0.1992 |
| " | 38† | 5 | 0.1162 | 0.1714 |

* The thickness of the blood vessel walls was measured with an ocular micrometer, calibrated on a stage micrometer.

† Animals decompressed after 38 days exposure and kept at normal atmospheric pressure for 7 to 10 days.

The microscopic changes noted in the large pulmonary arteries after 3 days of exposure consisted of a slight increase in prominence of the alternate layers of elastic tissue and smooth muscle with some fraying of the adventitia, presumably due to perivascular edema (Figs. 3 and 4). After 10 days of exposure the layers of muscle cells and elastic tissue appeared even more prominent and slightly thickened. At that time a progressive increase in connective tissue external to the media became evident. In the beginning this tissue was loose textured and slight in amount. With each succeeding week of exposure this fibrous tissue increased and became condensed so that in the late stages of the experiment (24 days or more) a thick layer of dense hyalinized fibrous tissue had formed (Fig. 5). As in the previous experiment, this occasionally resembled fibrocartilage. The

marked increase in the thickness of the arterial walls was due largely to this fibroblastic proliferation outside of the media and not to as extensive an alteration in the media as we had formerly thought. It is also worthy of emphasis that the thickening process in the large pulmonary arteries began to make its appearance at an earlier date than we previously stated (1). No comparable changes were detected in the walls of the large pulmonary veins in the late stages of the experiment.

Although a moderate increase in thickness of the walls of the small pulmonary arterioles, together with a visible increase in their number, was seen in this series of rats (Figs. 6–8) the marked degree of hyalinization described in the former series had not uniformly developed by the end of this experiment. In the previous study (1) we commented that: "After 1 month of exposure, the small arterioles of the lungs became prominent and apparently more numerous. . . . Their walls were thickened and the lumina narrowed. Later, hyalinization of the walls occurred and occasionally thrombosis. . . . These changes in the walls made the small vessels stand out prominently, which probably accounted for the apparent increase in number." Owing to the fact that in this experiment exposure to compressed air was not carried beyond the 38th day, it seems reasonable to believe that the small arterial lesions were not uniformly as marked only because insufficient time had elapsed.

## DISCUSSION

The anatomical and physiological alterations demonstrated in this investigation can be partially explained by a correlation with observations already established in clinical and experimental studies by other workers.

Of the mechanical factors stated by Wiggers (7) to conceivably alter the pressure and volumes of blood in the pulmonary vessels when operating separately or together, namely (1) the minute output of the right ventricle, (2) the resistance and capacity changes in the pulmonary circuit, (3) back pressure resistance produced in the left heart by changes in the systemic circuit, the second factor would seem to apply more directly in the present interpretation.

In these studies, pathological changes have been found in the lungs which are of such a nature that one might expect them to offer increased resistance to the pulmonary circulation. During the stage of acute oxygen poisoning there is injury to the arterioles as evidenced by a thickening of the walls and narrowing of the lumina together with alterations in staining properties, as well as capillary injury which results in pulmonary edema and marked pleural effusion. The latter

must necessarily cause considerable lung compression, and lung compression by pleural exudates has been cited as a probable cause of elevation of pulmonary arterial pressure (8). With continued exposure the pulmonary edema disappears but the arteriolar changes persist and become more marked and are accompanied by simultaneous hyperplasia and hypertrophy of the alveolar lining cells with resultant thickening of the alveolar walls and a decrease in the number of visible blood-filled capillaries. Patchy areas of atelectasis are constantly associated with these changes.

Other factors being equal, it would be expected that all of these changes, whatever the exciting cause, would increase the resistance to blood flow in the lesser circulation and consequently give rise to an elevation of blood pressure in the pulmonary artery and right ventricle beginning with the onset of acute oxygen poisoning. The fact that pulmonary hypertension was not demonstrable by the method employed (4) until after 24 days of exposure, does not necessarily mean that an elevation of pressure was not present in the intact rat prior to that time. During the period in which there was pleural effusion, the fluid escaped on opening the thorax to expose the pulmonary artery, thereby eliminating the effect of lung compression on the pulmonary resistance. Subsequent to this the increased resistance caused by atelectasis and early changes in the alveolar walls and arterioles is probably removed when the thorax is opened and the lungs subjected to forced artificial respiration, so that the existence of pulmonary hypertension cannot be demonstrated until after the 3rd week of exposure when the alterations in the arterioles become sufficiently advanced to cause permanent obstruction to the pulmonary circulation in spite of the minimizing influence of the experimental methods.

The increase in thickness of the walls of the large pulmonary arteries which was constantly present after the 10th day and progressive throughout the duration of the experiment was present before pulmonary hypertension was demonstrable. It would seem reasonable to believe that this change was due to prolonged stretching from overdistension secondary to pulmonary hypertension which we believe to be present from the beginning, although not detectable by this experimental method until later. This sclerosing process consisted chiefly of the formation of new connective tissue around the media of

the wall, thereby differing markedly from any common type of arteriosclerosis. While it is true that this fibrosis occurred in the regions where marked edema was present during the acute stages of oxygen poisoning, the fact that comparable fibrosis did not occur around veins where edema had also been demonstrated would seem to rule out tissue edema as the cause for this prominent anatomical abnormality. It appears improbable that such changes could have been a factor in the production of the pulmonary hypertension.

Dilatation and hypertrophy of the right side of the heart and dilatation of the conus arteriosus are common signs of pulmonary hypertension in man (9). These changes were observed in rats dying of acute oxygen poisoning and were likewise prominent in surviving rats on prolonged exposure. Increased venous pressure is given as one of the important physical signs of pulmonary hypertension in man (9) and decreased systemic blood pressure with an increase in venous pressure has been demonstrated in animals to result from constriction of the pulmonary artery (6). In the present series of animals a low systemic blood pressure was found to be present in each of a small series of rats after 38 days of exposure to compressed air. Thus the anatomical and physiological alterations observed in rats in this study resemble in many respects the outstanding features of pulmonary hypertension in the human subject.

## SUMMARY

1. Pulmonary arterial hypertension was demonstrated in a series of rats that had been kept for 24–31 days in an environment of compressed air, having a barometric pressure of 3040 mm. Hg. The partial pressure of oxygen was 635 mm. Hg, which is equivalent to an 83.6 per cent oxygen mixture at normal barometric pressure.

2. Sclerosing changes in the pulmonary arterioles have been observed which precede the development of demonstrable hypertension in the pulmonary circulation. These vessels showed histological changes that were indicative of injury after 3 days of exposure. There was a thickening of the walls which stained more intensely with eosin, as well as marked perivascular edema and often a narrowing of the lumina. Progressive thickening, narrowing, and hyalinization of the pulmonary arterioles occurred later, after the disappearance of

perivascular edema. These changes appeared very similar to the renal arterial lesions seen at autopsy in patients dying from malignant hypertension.

3. Pathological examination did not reveal significant or constant changes from normal in any organs except the lungs and heart. The blood vessels of the systemic circulation showed no pathological change.

4. The walls of the large pulmonary arteries increased in thickness rapidly after the 3rd day of exposure. This change was due to the progressive formation and condensation of fibrous tissue outside of the media and to a lesser extent to thickening of the alternate layers of elastic tissue and smooth muscle in the arterial wall.

5. Marked dilatation of the right ventricle and conus arteriosus as well as small areas of scar tissue formation in the right ventricle were present on prolonged exposure. A few hearts showed larger areas of fibrosis that were visible on macroscopic examination.

6. The systemic arterial blood pressure of a small series of rats exposed to compressed air for 38 days and examined 7 to 10 days after decompression was in each instance less than one-half the average normal pressure.

7. The findings in this study are consistent with the clinical and pathological signs of pulmonary hypertension in man.

8. The anatomical alterations observed in the alveolar units of the lungs were essentially the same as those previously described (1).

9. A method has been devised whereby pulmonary arterial hypertension, accompanied by important sclerotic changes in the arteries of the pulmonary circulation can be induced for investigation.

It is a pleasure to express our gratitude to Dr. C. K. Drinker for helpful suggestions throughout this study and for technical assistance in the determination of the systemic blood pressure. We are also indebted to Mr. R. M. Thompson for assistance in operating the pressure chamber.

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## EXPLANATION OF PLATES

### PLATE 16

FIG. 1. Lung of a rat exposed to compressed air for 3 days showing marked perivascular edema and leucocytic infiltration about large and small pulmonary arteries. One should also note the intensity with which the small arterioles have stained and the marked thickening of the wall and narrowing of the lumen of one arteriole. Section stained with eosin and methylene blue. × 82.

FIG. 2. A thickened and narrowed pulmonary arteriole, such as were occasionally seen after 3 days of exposure to compressed air. Eosin and methylene blue. × 215.

FIG. 3. Large pulmonary artery in a normal rat. Eosin and methylene blue. × 86.

### PLATE 17

FIG. 4. A large pulmonary artery of a rat exposed to compressed air for 3 days. Note the marked perivascular edema, cellular infiltration, and fraying of the adventitia. Eosin and methylene blue. × 82.

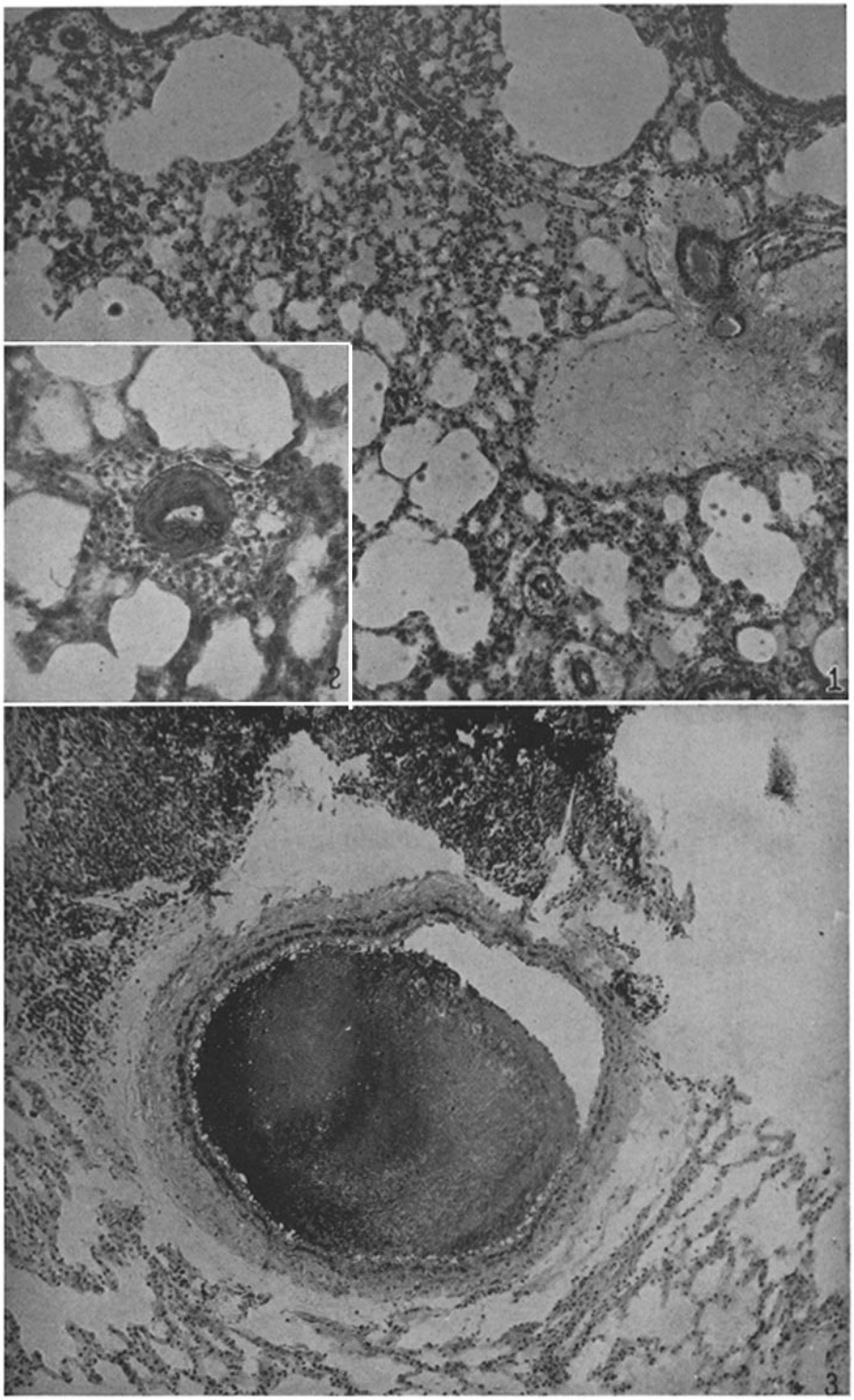
FIG. 5. A large pulmonary artery comparable in size to Figs. 3 and 4, showing marked increase in fibrous tissue external to the media. Rat exposed to compressed air for 38 days. Hematoxylin and eosin. × 82.

### PLATE 18

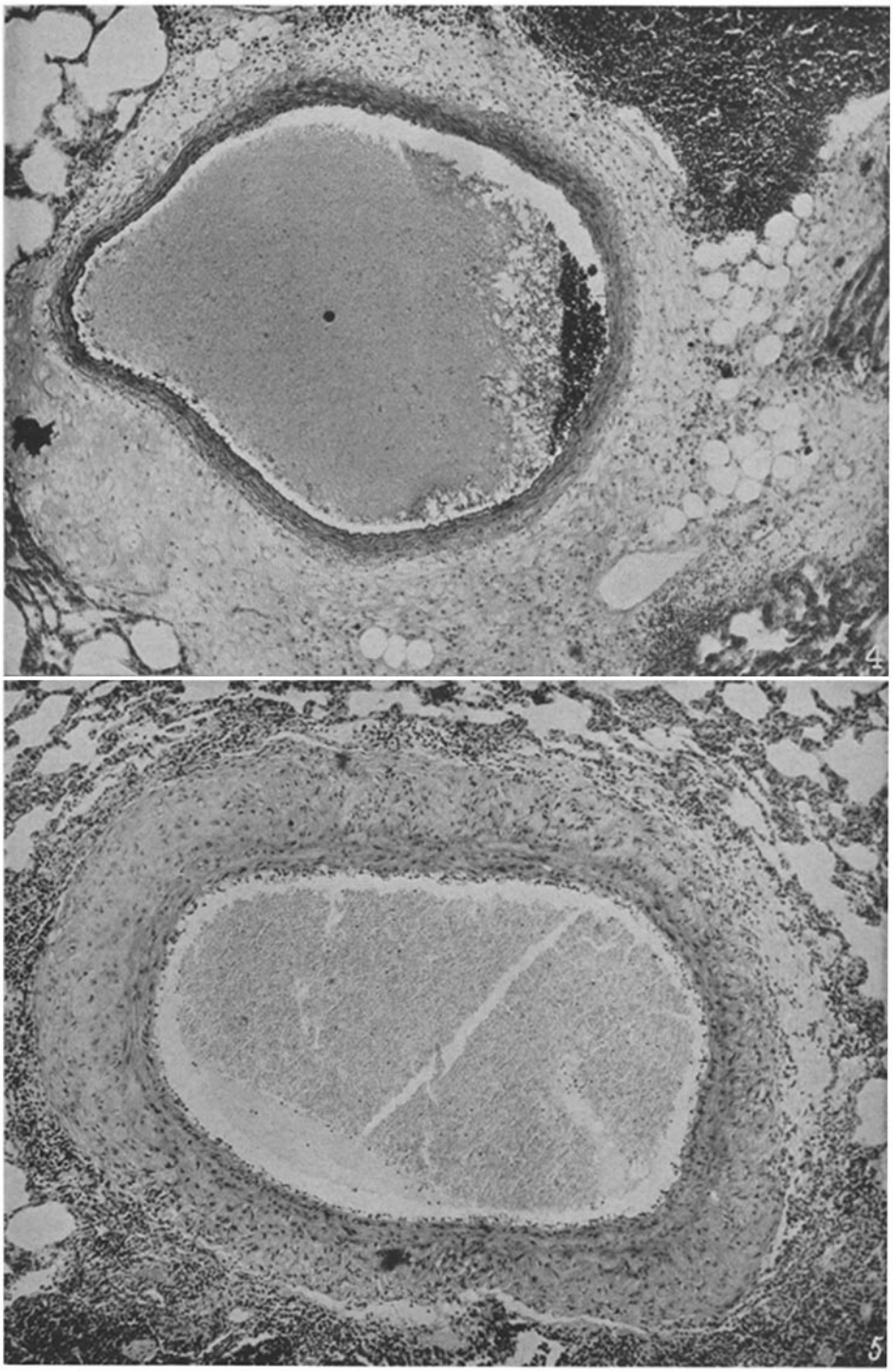
FIG. 6. Lung tissue of a rat which had been exposed to compressed air for a period of 38 days. Note the increased cellularity of the alveolar walls and the numerous and prominent thick walled pulmonary arterioles. Hematoxylin and eosin. × 82.

FIG. 7. Three thick walled hyalinized arterioles. Rat exposed to compressed air for 38 days. Hematoxylin and eosin. × 180.

FIG. 8. A greatly thickened, narrowed, and hyalinized pulmonary arteriole. Duration of exposure 38 days. Hematoxylin and eosin. × 500.




(Bennett and Smith: Pulmonary hypertension)

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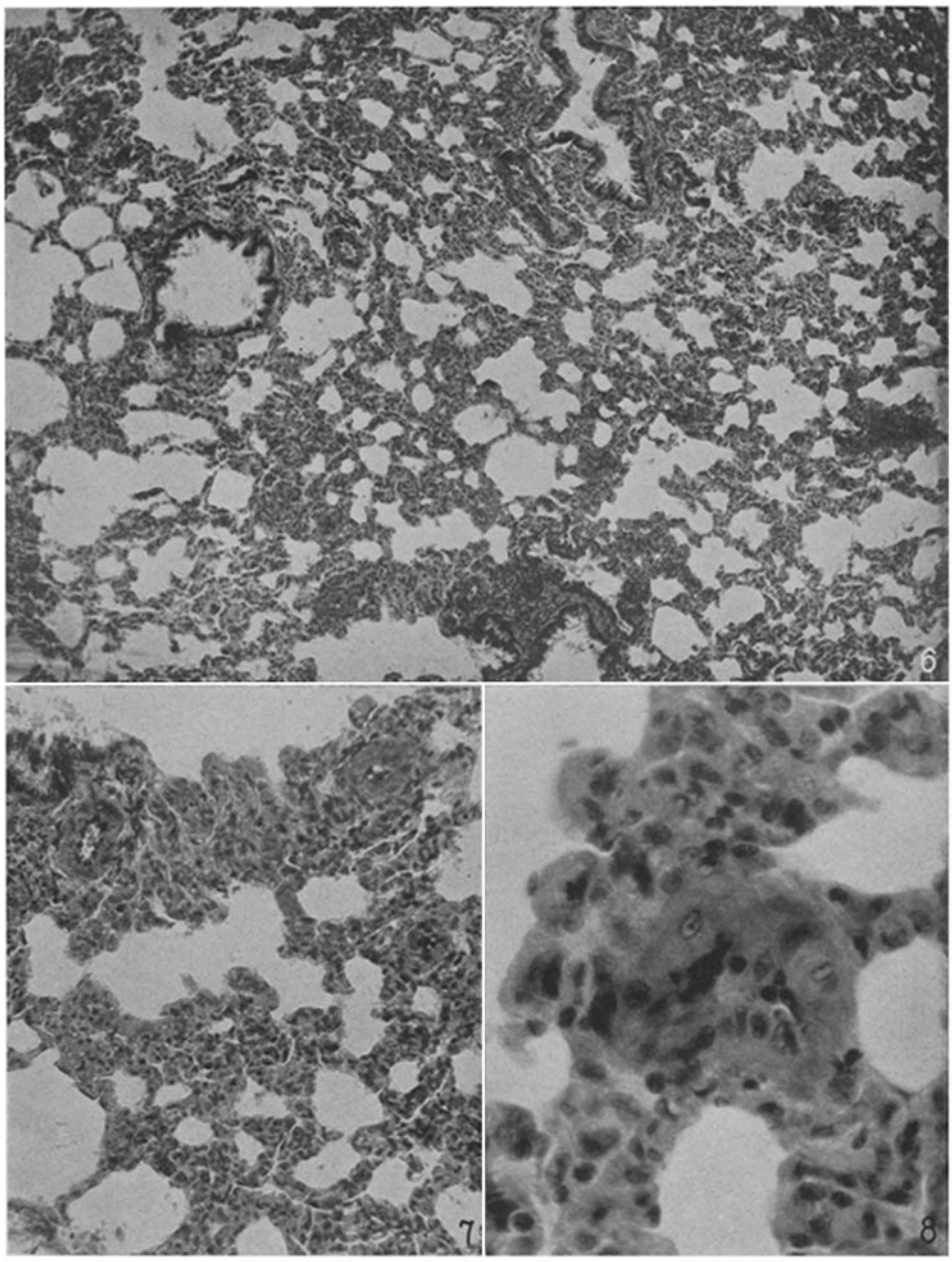


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