THE POSSIBLE relationship between pulmonary vascular pathological changes and an increased pulmonary blood flow and pulmonary-arterial blood pressure has been the subject of investigation for many years. Muller et al.1 and Ferguson et al.2 have demonstrated the development of vascular changes in the lungs following the surgical production of aortopulmonary shunts. The physiological changes associated with this procedure are complicated, involving changes of pulmonary blood flow, pulmonary-arterial pressure, and pulmonary-venous pressure. In an attempt to study the effects of increased pulmonary blood flow, long-term observations have been made in a group of animals in which the total pulmonary vascular bed was restricted by means of pneumonectomy or ligation of one pulmonary artery, thereby diverting the total cardiac output through the remaining lung tissue. Since the histological features of the small pulmonary vessels are different in young animals as compared with the adult,3 possible differences in the effects of these procedures in puppies as compared with adult dogs were also examined.

Methods

The studies were conducted in five adult female mongrel dogs weighing 12 to 15 Kg., and in eight puppies aged one to two months. The animals were anesthetized with intravenous sodium pentobarbital (30 mg./Kg.). The trachea was intubated with a polyvinyl tube with an inflatable cuff, and positive-pressure ventilation maintained with a Palmer respiratory pump. In four of the adult dogs, and in four puppies, a complete left pneumonectomy was performed. In one adult dog and one puppy, the left pulmonary artery was completely occluded by ligation with two polyvinyl ligatures. In two puppies, only partial occlusion of the left pulmonary artery to about half the original diameter was produced by means of a polyvinyl ligature. One littermate was used as a control with no surgical procedure. The main pulmonary-arterial and aortic pressures were measured by means of needle puncture at the time of thoracotomy before and after occlusion of the left pulmonary artery in eight instances. In some animals, polyvinyl catheters were inserted into the pulmonary artery and left atrium and brought out through the skin at the back of the neck. These were maintained for repeated measurement of pulmonary-arterial pressure in the unanesthetized animal, as previously described.4 Serial observations of pulmonary-arterial pressure were made at rest in all animals. In two animals, cardiac output was determined repeatedly by the dye-dilution technique. In several other animals, arteriovenous oxygen differences were observed before and after the surgical procedure, but oxygen consumption was not measured. Pressures were measured with Statham P 23 D pressure transducers and recorded on a Sanborn four-channel direct-writing oscillograph. Dye-dilution cardiac output was measured using indocyanine green indicator, injected into the pulmonary artery, with sampling from the femoral artery or from a catheter maintained chronically in the aorta, and recorded through a Colson densitometer. Oxygen saturation and oxygen capacity were determined spectrophotometrically, as previously described.5

In 11 of the animals studied, pulmonary arteriograms were performed at various stages after pneumonectomy. A large polyvinyl catheter was inserted into the pulmonary artery through a peripheral vein and 1.0 to 1.5 ml./Kg. of 90 per
PNEUMONECTOMY AND PULMONARY CIRCULATION

Figure 1

Effects of left pneumonectomy or left-pulmonary-artery occlusion on pulmonary-arterial (PA) pressure in five adult dogs.

Cent Hypaque was rapidly injected and serial x-ray films obtained with a rapid cassette changer. In four animals, serial arteriograms were obtained 1 to 19 months after operation.

Histological examination of the lung was undertaken in biopsy specimens obtained from the left lung at the surgical procedure, and from the right lung when the animals were sacrificed. The specimens were fixed in formalin and stained with hematoxylin-eosin and elastic van Gieson.

Results

The five adult dogs all survived the surgical procedure and were followed for periods of 6 to 17 months, after which time they were sacrificed. All the puppies survived the procedure itself, but one succumbed to hemorrhage on the first postoperative day. One of the puppies with partial occlusion of the left pulmonary artery died after one month due to infection and anemia, and one (C) was sacrificed after one month when pulmonary-arterial pressure had fallen to below control levels.

In eight dogs (two adults and six puppies), the pulmonary-arterial pressure was measured during the operative procedure, before and after occlusion of the left pulmonary artery. No significant differences were observed in the adults and puppies, and pulmonary-arterial mean pressures rose 1 to 2 mm. Hg in five, fell 1 to 2 mm. Hg in two, and remained the same in one.

The pulmonary-arterial pressure changes following left pneumonectomy (D, H, X, Y) and left-pulmonary-artery occlusion (L) in the adult dogs are demonstrated in figure 1. The pulmonary-arterial mean pressures within two to three days after surgery were 12 mm. Hg, and these pressures then rose rapidly to levels of 16 to 28 mm. Hg within the next 10 days. Following this, there was a still further rise over the next few months. The pattern of rise varied in different animals, and in one dog (D), after a rise to 30 mm. Hg in the first two months after surgery, there was a gradual decline of pulmonary-arterial mean pressure. In the remaining four animals, the pulmonary-arterial pressure continued to rise for periods of 6 to 17 months to levels of 21 to 36 mm. Hg. Figure 2 demonstrates the changes in pulmonary-arterial mean pressure in the seven puppies which survived the first day. Partial ligation of the left pulmonary...
artery was effected in puppies (C) and (D). Puppy (C) showed a small initial rise of pressure from 14 to 17 mm. Hg within one month; the pressure then fell rapidly to 9 mm. Hg. The puppy was sacrificed at this stage. Puppy (D) showed a rise of pulmonary-arterial mean pressure from 8 to 24 mm. Hg in the first month, but at the time of measurement of the last pressure, the animal was pyrexial and anemic and died the next day with severe infection.

Control puppy (G) was a littermate of puppies (B, C, D, F) and was not subjected to any surgical procedure. Nine months after the initial pulmonary-arterial mean-pressure measurement of 14 mm. Hg, obtained by venous catheterization, the pressure was 12 mm. Hg.

The remaining puppies (B, F, Me, Mo) will be discussed as a group and used as a basis for comparison with the adult animals. The pulmonary-arterial mean pressures rose rapidly from levels of 8 to 14 mm. Hg two to three days after surgery to levels of 23 to 28 mm. Hg within a six-week period. Following this, there was a drop in pressure in one animal (B) in which complete pulmonary-artery occlusion had been performed. The remaining three puppies showed a continued increase in pressure over the next 12 to 14 months to levels of 25 to 36 mm. Hg. In one puppy (Mo), a decrease of pressure was then observed at 17 months after pneumonectomy.

Figure 3 shows the serial observation on pulmonary-arterial systolic and diastolic and mean pressures in puppy (F).

Cardiac-output determinations were made at rest in one adult animal and one puppy before and after pneumonectomy and under similar experimental circumstances. In puppy (B), the cardiac output before operation was 0.9 L./min., and 10 weeks later it was 1.1 L./min. In the adult dog (H), the cardiac outputs before and four weeks after operation were 1.5 L./min. and 1.6 L./min., respectively. In several animals, arteriovenous oxygen differences after surgery showed no significant changes from preoperative measurements.

Pulmonary arteriograms revealed a progressive dilatation of the main and right pulmonary arteries and the branches, with development of tortuosity first observed in the tertiary branches. Figure 4 demonstrates the appearance of the pulmonary-arterial system in the control puppy (G) at age 10 months, and represents the appearance in the normal dog. The dilatation of the pulmonary arteries was more prominent in the adult animals as compared with the puppies and varied in degree in different animals. The most striking changes occurred in the adult animal (L), and figure 5 (left upper, right upper, and right lower) depicts the serial changes observed in this animal. These studies were performed at periods of 6, 9, and 17 months after left-pulmonary-artery ligation. The less striking dilatation of the pulmonary artery in puppies is shown in figure 6, which represents the pulmonary arteriogram in puppy (F) 13 months after pneumonectomy.

Histological examinations of the lungs were performed by Drs. J. Craig and G. Vawter. These studies indicated that, in the animals subjected to pneumonectomy or pulmonary-artery occlusion, there were definite changes in the medium and small pulmonary arteries.
in the right lung as compared with the control left lung. There was dilatation and tortuosity of the intermediate vessels. There was also some intimal and medial thickening of the medium and smaller vessels, with occasional fibrous plaques. The smallest arterioles usually showed dilatation, and decrease in lumen size was rare. However, the wall-to-lumen ratio was definitely increased from 1:12 to 1:24 in the control lung to 1:2 to 1:10 in the remaining right lung. There were no apparent differences in the histological features in the puppies as compared with the adult animals.

Discussion

A number of observations have been made on the effects of pneumonectomy or occlusion of one pulmonary artery on the pulmonary circulation. Acute occlusion of one pulmonary artery produced only small changes in the pulmonary-arterial pressure in the studies here reported. Pneumonectomy or left-pulmonary-artery occlusion resulted in a rapid rise of pulmonary-arterial mean pressure commencing one to two days after surgery and reaching levels of 130 to 350 per cent of control levels in the first two months. In the puppies, the pulmonary-arterial mean pressure reached levels of 155 to 350 per cent of control with an average of 240 per cent, whereas in the adult dogs, the pulmonary-arterial mean pressures were 130 to 230 per cent of control levels, with an average of 165 per cent. Following this, there was a contin-
ued slow rise in pulmonary-arterial pressure in all but two animals over the subsequent months.

On the basis of these and other studies, the pulmonary-arterial hypertension is apparently not related to a change of cardiac output. There were also no changes in resting left-atrial pressure. The possible role of pulmonary-venous hypertension cannot, however, be completely eliminated, since it is possible that with the increased pulmonary flow through one lung, a gradient between pulmonary vein and left atrium was established.

The pathological changes in the small pulmonary blood vessels were mild and could not be clearly related to the degree of pulmonary-arterial hypertension. There were also no significant differences in the histological appearances of the small vessels in the puppy as compared with the adult dogs. There was, however, a considerably greater degree of dilatation of the main and right pulmonary arteries and of the major branches in the adult animals as compared with the puppies, demonstrated in the angiographic studies.

This difference in the response of the major pulmonary arteries in the adult dogs as compared with the puppies could well be related to the difference in the histological features of the walls of these vessels. The wall of the pulmonary artery is thicker and probably less compliant in the immature animal as compared with the adult animals, and it is postulated that the increased flow and increased pressure associated with pneumonectomy or pulmonary-artery occlusion results in a greater distention of the pulmonary artery in the adult animal. This difference in the nature of the walls of the pulmonary vessels may also be the cause of the somewhat greater hypertensive response in the puppies.

The decrease in pulmonary-artery pressure noted in two puppies and one adult dog, which occurred some months after the initial rise in pressure, has also been observed by others and is difficult to explain. This phenomenon could be related to either hyperplasia with an increase in the total number of vessels, to a distention of small pulmonary blood vessels, or to an improvement in the histological features.

Summary

Serial observations were made on the changes in pulmonary-artery pressure, radiological, and histological features of the pulmonary vasculature after pneumonectomy or ligation of a single pulmonary artery in adult dogs and in puppies. Acute occlusion produced only insignificant changes in the pulmonary-artery pressure. After one to two days, a rapid rise in pulmonary-arterial pressure was observed. The pressure then gradually rose and in the subsequent months reached somewhat higher levels in the puppies as compared with the adult dogs. A decrease in pulmonary-arterial pressure which occurred after the initial rise in pressure was noted in one adult dog and two puppies. Comparison of the histology of the remaining lung with the control lung showed the development of medial hypertrophy of the smaller and medium-sized vessels, with an increase in the wall to lumen ratio. No significant difference
was noted between the histological features of the adult and young animals. Pulmonary arteriograms revealed progressive dilatation and tortuosity of the main pulmonary artery and its major branches, less striking in the puppies as compared with the adult dogs.

References
Effects of Pneumonectomy on Pulmonary Circulation in Adult and Young Animals
ABRAHAM M. RUDOLPH, EDWARD B. D. NEUHAUSER, RICHARD J. GOLINKO and PETER A. M. AULD

Circ Res. 1961;9:856-861
doi: 10.1161/01.RES.9.4.856

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1961 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/9/4/856

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/