Pressure Changes in the Dog Lung Secondary to Hemorrhagic Shock:

Protective Effect of Pulmonary Reimplantation

W. L. Sugg, M.D., W. D. Craver, M.D., W. R. Webb, M.D., R. R. Ecker, M.D.

From the Division of Thoracic and Cardiovascular Surgery, Department of Surgery, University of Texas, Southwestern Medical School, Dallas, Texas

Congestive atelectasis of the lung has been observed following hypoxemia, rapid decompression, blast injuries, burns, excessive and rapid transfusion of blood and fluids, and several different methods of shock.[8]

Sealy[12, 16] and Henry[5] observed this lesion in experimental animals after hemorrhagic shock and attempted to explain the pathogenesis as due to low blood flow.

Guyton[4] presented evidence implicating left ventricular failure in the genesis of the pulmonary lesion accompanying prolonged shock. Others[2, 7] deny the importance of heart failure in shock, but the differences appear to be due to studies of different stages of shock.

Previous work in our laboratory[13] showed that in the dog two hours of hypovolemic shock at 40 mm. Hg followed by rapid reinfusion of the shed blood produced typical gross and microscopic findings of congestive atelectasis. These lesions are intense capillary congestion, interstitial edema, polymorphonuclear infiltration and intra-alveolar hemorrhage with atelectasis. The effects were not influenced by assisted ventilation, heparinization, vasodilator drugs, sympathectomy, vagotomy, body position or sodium depletion of the animal prior to hemorrhage. When one lung was totally denervated by removal and reimplantation prior to induction of shock, it was protected from developing congestive atelectasis, while the other lung of the same animal developed this lesion in unmodified form.[14]

The following experiments were performed to determine the pulmonary vascular pressure changes associated with hemorrhagic shock and to evaluate the influence of various drugs and surgical procedures on these pressures.

Methods

Dogs weighing from 12 to 15 Kg. were anesthetized with 25 mg./Kg. of pentobarbital sodium and given 3 mg./Kg. of heparin. Endotracheal tubes were inserted and the animals were ventilated with Harvard volume respirators using room air. In each experiment femoral artery cannula was attached to an E and M physiograph for monitoring arterial pressure, and another cannula inserted in a femoral vein for infusions and collection of blood samples. The left chest was opened through the fourth intercostal space and catheters were inserted into the pulmonary artery and left atrium (Kifa—2.8 mm. external diameter, 1.3 mm. internal diameter). Another catheter measuring 2.2 mm. external diameter, and 1.2 mm. internal diameter, was passed

Submitted for publication June 6, 1968.
Aided by grant HE08946-NIH-USPH.

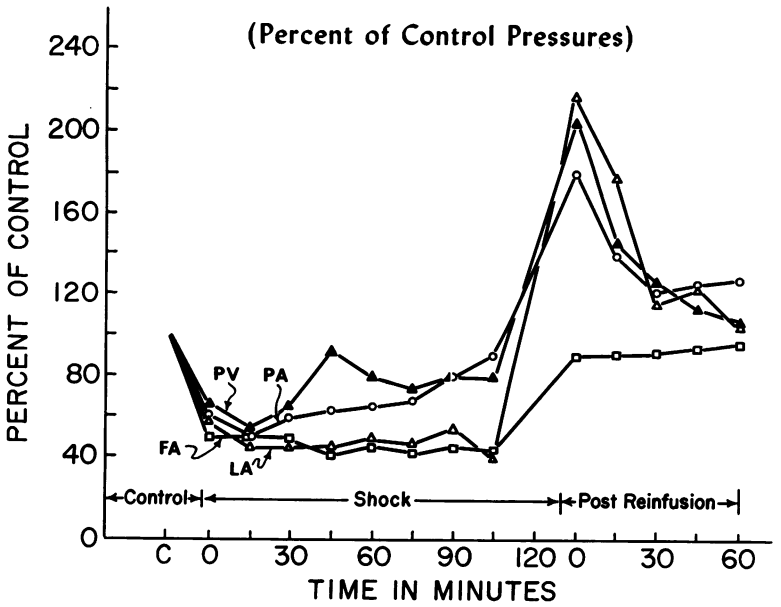

FIG. 1. Effects of hemorrhagic shock for 2 hours and reinfusion on femoral artery (FA), left atrium (LA), pulmonary artery (PA), and small pulmonary vein (PV) pressures in control group (Group 1) animals. Expressed as per cent of control.

through the left atrium into the pulmonary vein into the wedge position and withdrawn slightly as judged by the pressure tracings to measure small pulmonary vein pressure. In some animals catheters were placed in both right and left pulmonary veins. The chest was closed with water seal drainage and the dogs were bled slowly into an airless plastic reservoir to maintain mean arterial pressure of 40 mm. Hg for 2 hours. The blood was then rapidly reinfused, usually within 10 minutes. The animals either died shortly thereafter, or were sacrificed one hour post reinfusion. Pressures were recorded at 15-minute intervals throughout the experiment.

The animals were divided into the following groups:

Group 1. Seven animals were bled, maintained for 2 hours at mean arterial pressures of 40 mm. Hg and then reinfused while pressures were recorded. The animals were sacrificed and the lungs removed for gross and microscopic examination.

Group 2. Four animals were given 0.4 mg. of atropine, intravenously just prior to hemorrhage and again one hour later.

Group 3. Four animals underwent a similar procedure except that 250 mg. of aminophylline was given intravenously prior to shock and again one hour later.

Group 4. Four animals underwent a similar procedure, except that 1 mg./Kg. of phenoxybenzamine hydrochloride (Dibenzyline) was administered slowly intravenously during the hour prior to hemorrhage.

Group 5. Four animals had left cervical vagotomies prior to the above.

Group 6. Four animals had bilateral cervical vagotomies prior to hemorrhagic shock and reinfusion.

Group 7. In eight animals the left lungs were completely removed and reimplanted by serial transection and suturing of the pulmonary artery, pulmonary veins and bronchus. This allowed removal and reimplantation with less than 30 minutes of pulmonary ischemia. Four animals were studied immediately and four were studied a month later. Pressure cannulas were inserted to measure small pulmonary vein pressures in both lungs of these animals.

Results

All groups except the animals subjected to reimplantation of left lungs showed vary-

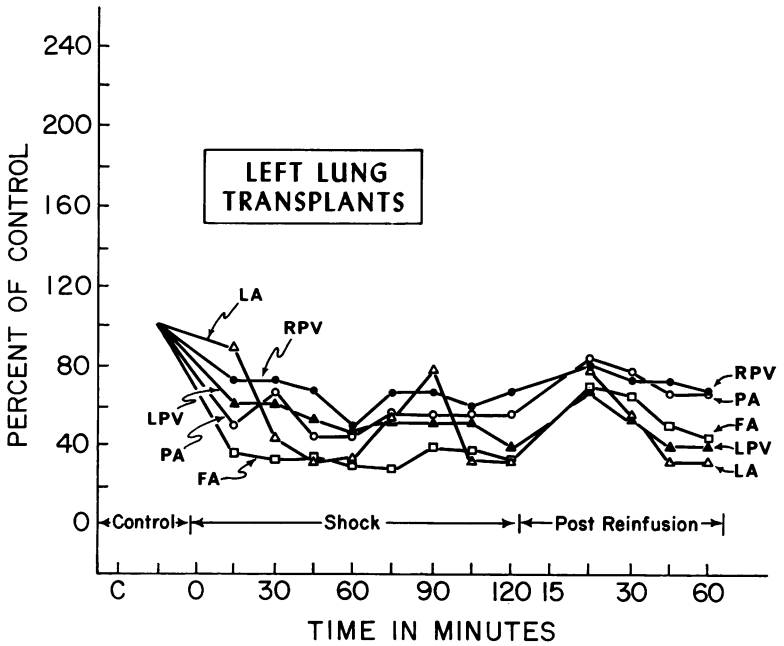

FIG. 2. Effects of shock in animals undergoing left lung reimplantation. Expressed as per cent of control (RPV), right small pulmonary vein; LPV—left small pulmonary vein. (Group 7.)

ing degrees of gross and microscopic congestive atelectasis. The reimplanted left lungs appeared normal grossly, while contralateral right lung had patchy areas of consolidation. Microscopically, in each instance, the reimplanted lung was normal, while the contralateral lung showed typical areas of congestive atelectasis.

Pressure Studies

Group 1. All pressures fell with hemorrhage, though pulmonary artery, femoral artery, and small pulmonary vein pressures fell less than left atrial pressures (Fig. 1). Immediately postreinfusion, pressures in the pulmonary artery, small pulmonary vein, and left atrium were significantly higher than control pressures but approached control values during the subsequent hour. Small pulmonary vein and pulmonary artery pressures were almost identical with small pulmonary vein pressure being only slightly lower than pulmonary artery pressure throughout the experiment.

Group 2. Animals receiving atropine maintained higher left atrial pressures during reinfusion, but otherwise responded as the control animals.

Group 3. Animals receiving aminophylline had transient increases in left atrial pressure with the second injection of the drug but these rapidly declined to control levels during the reinfusion period. Femoral artery pressures remained low throughout the period.

Group 4. Animals receiving Dibenzyline had lower central pressures during shock and less elevation of all pressures with reinfusion. It did not, however, increase the gradient between the pulmonary artery and small pulmonary vein.

Group 5. Dogs undergoing left cervical vagotomies had higher small pulmonary vein pressures in the left lung than in the right lung and after reinfusion left atrial pressures were significantly higher than those of other groups.

Group 6. Animals with bilateral cervical vagotomies had higher pressures in the small pulmonary veins in both lungs, but only modest postreinfusion elevations of pressures.

Group 7. Animals undergoing left lung

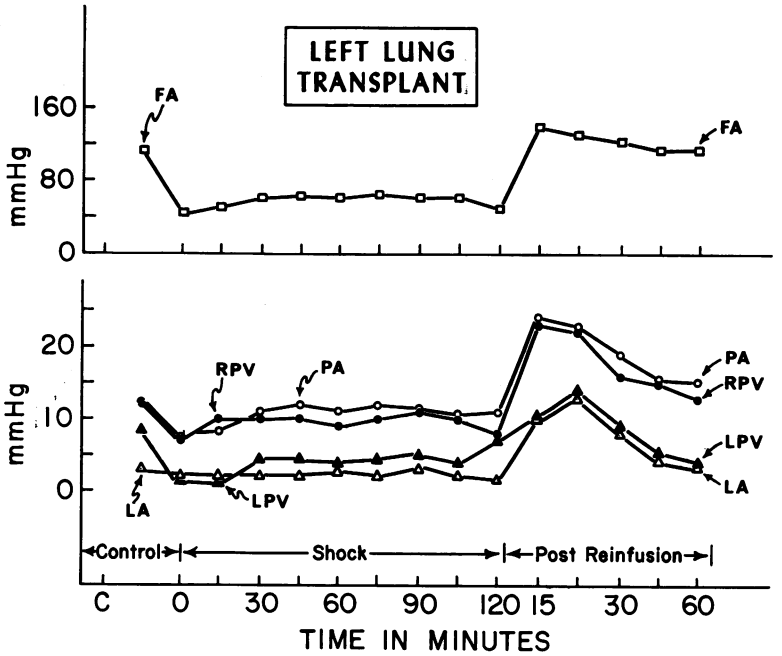

FIG. 3. Changes in Group 7—left lung reimplantation expressed in absolute values.

reimplantations had decreases in pressures in the left small pulmonary veins which were consistently lower than right small pulmonary vein pressures (Fig. 2). Right small pulmonary vein pressures were almost identical with pulmonary artery pressures, whereas the left small pulmonary vein pressures closely followed left atrial pressures during both shock and the reinfusion period (Fig. 3). Grossly and microscopically each of the reimplanted lungs appeared normal; whereas contralateral right lungs in each instance showed congestive atelectasis (Fig. 4).

Discussion

For total denervation of the lung complete excision and reimplantation or at least total hilar stripping and bronchial transection are required.[11] Lower small vein pressures and lack of pathologic changes in reimplanted denervated lung suggest that the neural supply plays an important role in the formation of congestive atelectasis, probably by mediating constriction of the postcapillary bed at the small pulmonary vein level.

Keller and associates [9] also attribute congestive lesions of the lung to pressure changes in the pulmonary venous circulation. In dogs subjected to hypovolemic shock and retransfusion, they found a rise in small pulmonary venous pressure and resistance after transfusion in contrast to pulmonary arterial and left atrial pressures which did not differ significantly from controls. These animals had typical lesions of acute congestive atelectasis, which they believed were secondary to constriction of the small pulmonary veins. This caused engorgement of capillaries, interstitial edema and hemorrhage with encroachment upon surrounding alveoli to cause subsequent collapse. Our observations confirm the increase in small pulmonary vein pressures. Neither Keller's nor our experiments support the suggestion that left ventricular failure is a significant factor since left atrial pressures remained much lower than the pulmonary venous pressures in all experiments.

Kuida and associates [10] studied the effects of gram-negative endotoxin on pulmonary circulation in intact animals, open

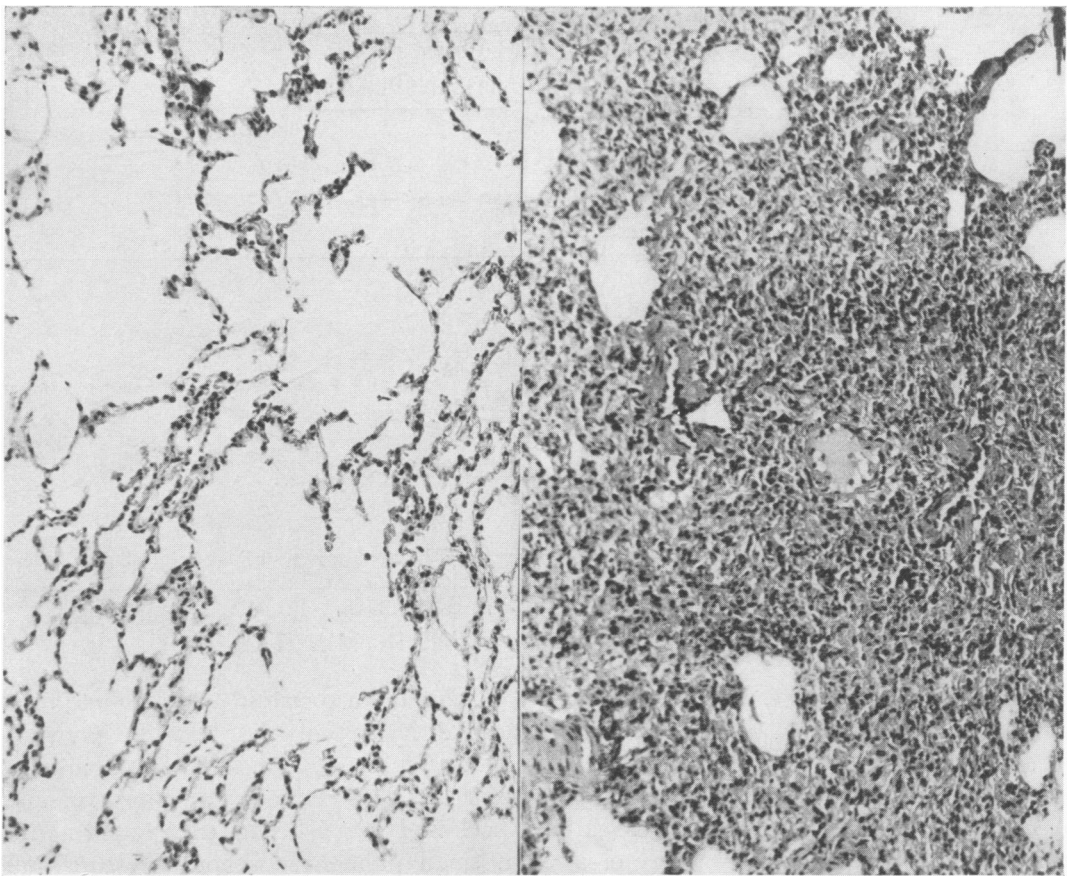

FIG. 4. Photomicrograph ×130 of the left (reimplanted) lung and the right lung of the same animal undergoing shock and reinfusion of the blood. The left lung (left) was protected and appears normal whereas the right lung (right) shows the lesion of congestion.

chest animals and in isolated perfused lungs. They found that pulmonary artery pressures increased in all preparations following the injection of endotoxin without rise in left atrial pressures. Pulmonary artery wedge and small pulmonary vein pressures uniformly increased. Further experiments evaluated [8] the effects of histamine and 5-hydroxytryptamine on arterial and venous segmental resistances in isolated perfused dog lungs. Histamine usually increased venous resistance more than arterial resistance while in contrast 5-hydroxytryptamine usually increased arterial resistance more than venous resistance. Small pulmonary vein pressures rose after the administration of epinephrine, nor-epinephrine, histamine and 5-hydroxytryptamine, thus, further demonstrating constriction of pulmonary veins. Sukhnandan and Thal [15] studied the effects of histamine, serotonin, epinephrine, bradykinin, endotoxin shock and blood transfusion on isolated perfused dog lungs. All except bradykinin proved to be vasoconstrictor, both at the arteriolar and small pulmonary vein levels. Dibenzyline pre-treatment diminished pulmonary arteriolar and small vein constriction, having its most pronounced effect on the postcapillary bed. The isolated perfused lung appeared to become less edematous. In our experiments, however, although dibenzyline lowered all pressures it was not more effective on the postcapillary

bed nor was it sufficient to prevent the congestive atelectasis in intact animals.

Daicoff *et al.*[1] showed that serotonin injected intravenously in anesthetized dogs produces pulmonary arterial hypertension and intrapulmonary venous hypertension without significant changes in left atrial pressures or pulmonary vein pressures measured just outside the pericardium.

Our experiments attempted to determine the effect of severance of nerves on vascular pressures in the lung during hemorrhagic shock. The drugs were used in an attempt to alleviate small pulmonary vein constriction which is believed to cause the congestive lesions. It has been demonstrated that pressures in the large pulmonary veins fluctuate over a much narrower range than pressures in small pulmonary veins in intact anesthetized dogs.[6]

That small pulmonary veins can constrict and cause congestive atelectasis seems reasonable. That these changes were prevented by complete removal and reimplantation of the lung appears to incriminate a neurogenic factor in the atelectasis. Dibenzyline lowered pressures as compared to controls but did not increase the gradient between the pulmonary artery and small pulmonary vein and thus did not prevent capillary hypertension. Willwerth and his associates[16] using a similar technic of hemorrhagic hypotension found congestive lesions in the functional lung but none in the contralateral lung which had the pulmonary artery and veins clamped during the period of shock. They believed the lesion was secondary to functional demand on the lung in the face of low blood flow. Their study did not exclude the possibility that circulating vasoactive substances would be excluded from the occluded lung during shock. Also, the single functional lung was subjected to higher flows and pressures during the period of hypovolemia which might favor perivascular extravasation. In our studies, the reimplanted denervated lung was exposed to all the vascular factors and functional demand of the contralateral lung, but still did not develop congestive lesions.

Summary

1. Pulmonary vascular pressures were recorded in dogs subjected to hemorrhagic shock for periods of 2 hours at 40 mm. Hg, followed by rapid reinfusion of the blood which uniformly produced congestive atelectasis.

2. The influence of atropine, aminophylline, Dibenzyline, unilateral or bilateral cervical vagotomy, and reimplantation of the left lung were studied in this preparation. None of these procedures prevented congestive atelectasis or significantly influenced pressures except complete removal and reimplantation of the lung, both in acute and chronic preparations.

3. Small pulmonary vein pressures almost equalled pulmonary arterial pressures during the period of shock, and were considerably greater than large pulmonary vein or left atrial pressures.

4. Pressures in small pulmonary veins of reimplanted left lungs were considerably lower than pulmonary artery pressures or small pulmonary vein pressures in the contralateral right lungs.

5. The observations that reimplantation and thus denervation of the lung prevented the pathologic changes and that small pulmonary vein pressures in the reimplanted lung were lower than in the contralateral lung suggest that neural factors play an important part in the production of this lesion, probably by mediating constriction of the postcapillary bed at the small pulmonary vein level.

References

1. Daicoff, G. R., Chavez, F. R., Anton, A. H. and Swenson, E. W.: The Hemodynamic Effects of Serotonin in Pulmonary Embolism. Presented at the 48th annual meeting of the Amer. Ass. Thoracic Surg., Pittsburgh, April 24, 1968.
2. Gerst, P. H., Rattenberg, C. and Halady, D. A.: The Effect of Hemorrhage on Pulmonary

Circulation and Respiratory Gas Exchange. J. Clin. Invest., **38**:324, 1959.
3. Gilbert, R. P., Hinshaw, L. B., Kuida, H. and Visscher, M. B.: Effects of Histamine, 5 Hydroxytryptamine and Epinephrine on Pulmonary Hemodynamics with Particular Reference to Arterial and Venous Segment Resistances. Amer. J. Physiol., **194**:1, 1958.
4. Guyton, A. C. and Crowell, J. W.: Dynamics of the Heart in Shock. Fed. Proc., **20**:51, 1961.
5. Henry, J. N., McArdle, A. H., Scott, H. J. and Gurd, F. N.: A Study of the Acute and Chronic Respiratory Pathophysiology of Hemorrhagic Shock. J. Thorac. Cardiovasc. Surg., **54**:666, 1967.
6. Hyman, A. L., Burch, G. E., DePasquale, N. P. and Tyler, J. M.: Spontaneous Variations in Pulmonary Venous Pressure in Intact Dogs. Proc. Soc. Expen. Biol. Med., **112**: 1032, 1963.
7. Ibid.[1]
8. Ibid.[4]
9. Keller, C. A., Schramel, R. J., Hyman, A. L. and Creech, O., Jr.: The Cause of Acute Congestive Lesions of the Lung. J. Thorac. Cardiovasc. Surg., **53**:743, 1967.
10. Kuida, H., Hinshaw, L. B., Gilbert, R. P. and Visscher, M. B.: Effect of Gram-negative Endotoxin on Pulmonary Circulation. Amer. J. Physiol., **192**:335, 1958.
11. Nakae, S., Webb, W. R., Theodorides, T. and Sugg., W. L.: Respiratory Function Following Cardiopulmonary Denervation in Dog, Cat, and Monkey. Surg. Gynec. Obstet., **125**:1292, 1967.
12. Sealy, Will C., Ogino, S., Lesage, A. M. and Young, W. G., Jr.: Functional and Structural Changes in the Lung in Hemorrhagic Shock. Surg. Gynec. Obstet., **123**:754, 1966.
13. Sugg, W. L., Webb, W. R., Nakae, S., Theodorides, T., Gupta, D. N. and Cook, W. A.: Congestive Atelectasis—An Experimental Study. Ann. Surg., **168**:234, 1968.
14. Sugg, W. L., Webb, W. R. and Ecker, R. R.: The Prevention of the Lung Lesions Secondary to Hemorrhage Shock. Surg. Gynec. Obstet., **127**:1005, 1968.
15. Sukhnandan, R. and Thal, A. P.: The Effect of Endotoxin and Vasoactive Agents on Dibenzyline—Pretreated Lungs. Surgery, **58**: 185, 1965.
16. Willwerth, B. M., Crawford, F. A., Young, W. G., Jr. and Sealy, W. C.: The Role of Functional Demand on the Development of Pulmonary Lesions During Hemorrhagic Shock. J. Thorac. Cardiovasc. Surg., **54**:658, 1967.