3761

Experimental Production and Prevention of Acute Edema of the Lungs in Rabbits.

SCOTT JOHNSON. (Introduced by Leo Loeb.)

From the Department of Pathology, Washington University School of Medicine.

It is a common occurrence that the intravenous injection of large doses of adrenalin hydrochloride into rabbits causes the development of acute edema of the lungs and death shortly afterwards. It was found that injection of 1 cc. of 1/1000 solution of adrenalin hydrochloride (Parke, Davis & Co.) produces acute edema of the lungs in almost all medium sized rabbits.

While studying the effect of the action of adrenalin on the heart in the production of experimental myocarditis according to the method of Fleisher and Loeb,[1] we found that if the thorax of the animal is opened so that the heart and lungs are exposed to the air, and if then 1 cc. of adrenalin is administered intravenously, acute edema of the lungs does not occur. We also observed that acute edema of the lungs, which ordinarily would follow the injection of 1 cc. of adrenalin, could be prevented through the opening of the thorax by means of a cut made into the sternum in the midline and the subsequent opening of the pericardium, leaving at the same time the pleural sacs intact. This experiment was repeated several times with the same result. This observation was made independently by Dr. Leo Loeb[2] in 1909, but was never reported.

It occurred to us that the only factor that had been altered by opening the chest was the difference in pressure between the external air and the air in the lungs. We, therefore, attempted another experiment to confirm our previous observations. The rabbit was tracheotomized and a cannula was inserted tightly in the trachea. Air from an artificial respiration apparatus was allowed to pass into the lungs at a pressure greater than that of the atmosphere, the chest remaining intact. One cc. of a 1/1000 solution of adrenalin hydrochloride was then injected intravenously into the rabbit and acute edema of the lungs did not occur. The experiment has been repeated with the same result. In reviewing the literature we found that Haven Emerson[3] had made the latter observation in 1909.

We were able to observe directly the mechanism through which the pulmonary edema is produced, by watching the exposed heart after the administration of adrenalin in large doses. We thus

found that as a result of the peripheral vaso-constriction of the arterioles, and the subsequent rise in systemic blood pressure, the left ventricle attempts to compensate for this impediment to the flow of the blood by the increased force of its contractions. In several instances we have seen the left ventricle go into its systolic position and relax only very slightly in diastole while the right ventricle appears to contract more vigorously than normally. The result of these changes is an obstruction to the circulation of the blood on the left side of the heart, but not on the right. This eventually leads to an over-distention of the capillaries of the lungs with blood. If the capillaries distend widely enough the blood fluids escape through the capillary walls into the alveoli of the lung and edema is thus established. If the pressure on the capillary wall of the lungs and the subsequent distension becomes still greater, the red corpuscles may escape together with the fluids into the tissue spaces and alveoli.

It should be possible to prevent this type of edema by preventing the undue dilatation of the lung capillaries. Either through opening the chest or through inflating the lung under increased pressure with the chest closed, can this condition be fulfilled. A quantitative relation, undoubtedly, exists normally between the pressure of the air in the alveoli acting as a support of the capillaries from the outside, and the pressure of the blood inside the capillaries which depends directly upon the force of the contraction of the right ventricle. When pressure conditions are changed by obstruction in the left heart, or by increased strength of the beat of the right heart, or by both these factors combined, the capillaries of the lung become distended with blood, and if distended widely enough they leak. However, if the capillaries are prevented from over-dilating by increased air pressure acting on them from the interior of the lung, they do not leak and edema of the lungs is therefore prevented by these means.

Chillingsworth and Hopkins[4] were able to reduce the carotid pressure to zero by reducing the air pressure on the exterior of the body in dogs which had been placed in a plethysmograph, but the lungs of which were left in communication with the outside. It appears to us that acute edema of the lungs in rabbits due to the administration of large doses of adrenalin should also be preventable by the application of a similar method and we intend to test this suggestion in the near future experimentally.

[1] Fleisher, M. S., and Loeb, Leo, *Arch. of Int. Med.*, 1909.

[2] Loeb, Leo, personal communication.

[3] Emerson, Haven, *Arch. of Int. Med.*, 1909, iii, 68.

[4] Chillingsworth and Hopkins, *Am. J. Physiol.*, 1920, li, 289.