AN EXPERIMENTAL STUDY OF RESPIRATION MAINTAINED BY HOMOLOGOUS LUNGS

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AS CARDIAC surgery has developed, increasing interest has been stimulated in extrapulmonic introduction of oxygen into the system, and in mechanical methods of respiration. Our attempts, as well as those of others, to increase oxygenation by intravenous administration or by transperitoneal absorption have met with failure. The amounts of oxygen which can be given safely are too small to be of recognized value. Gibbon,[1, 2] Björk,[3] Jongbloed,[4] Dennis,[5] Clark,[6] and others have worked on the problem of constructing artificial lungs which will accomplish complete gaseous exchange for considerable periods of time.

The idea of maintaining respiration with homologous lungs presented itself during a discussion of means of oxygenation from this chance remark: "Why not attach a lung to a dog's leg?" Well, why not? Consequently, a technique has been evolved whereby anesthetized dogs have been kept alive two to three hours entirely on the lungs of another dog. This report is made only to record the fact that homologous lungs are effective respiratory organs. The possibility of practical application is dimly suggested, but it must not be assumed that respiratory failure can be supported by pinning a lung on the sufferer's shoulder. The experimental procedure, still rather crude and not even done under aseptic conditions, does however suggest a number of studies in the basic subject of respiration.

TECHNIQUE

Two dogs of about the same size, weighing approximately 20 pounds each, are chosen and matched for blood compatibility.

Dog A, the donor, is anesthetized with nembutal and is given 10,000 units of heparin* intravenously. The chest is widely opened by splitting the sternum longitudinally. The dog, of course, promptly dies as the chest is opened. The azygous vein, the superior and inferior vena cava, and the arch of the aorta are isolated, doubly ligated, and cut between the ligatures. The trachea is drawn down and cut leaving a long stump attached to the lungs. The heart and lungs are now carefully freed from their attachments in the chest and removed en masse. The main pulmonary artery is thoroughly isolated at the base of the heart and clamped. Another clamp is placed near the bifurcation. The pulmonary artery is then severed between the clamps, leaving as long a segment of the pulmonary artery as possible. The pulmonary veins are clamped, and the heart is cut away except for the left auricle. The end of a glass tube about 4 inches long and of proper size is tied into the pulmonary artery. A de Pezzer catheter with all but the flange removed is placed in the left auricle and fixed with a purse-string suture snugly tied around

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the catheter. It is important that the clamps on the pulmonary artery and the pulmonary veins be left closed while these tubes are being placed so that air may not enter the circulatory system.

The preparation, consisting of intact lungs, trachea, pulmonary artery, and pulmonary veins with properly placed tubes is now set aside and kept moist with saline solution.

The large blood vessels in the dead dog are opened, and the expressible blood is aspirated and placed in a basin for later use.

Dog B, the recipient dog, is now anesthetized with nembutal, 1 c.c. of a 1 per cent solution per 5 pounds of weight, and ⅛ grain morphine sulphate, and $1/100$ grain atropine sulphate given intravenously. A tracheotomy is done, and a well-fitting rubber tube is inserted into the trachea and snugly tied.

The abdomen is opened through a low right rectus incision. The aorta and inferior vena cava are isolated proximal to their level of bifurcation. At this point 10,000 units of heparin are injected into the inferior vena cava. Glass tubes of proper size are tied into the aorta and inferior vena cava. By means of long rubber tubing, connections are established with the lung preparation, the aorta being connected with the pulmonary artery, and the pulmonary veins with the inferior vena cava (Fig. 1). Again it is important while completing the connections to eliminate all air from the circulatory system.

Sufficient blood, previously collected, is pumped into the dog through the rubber tubing to replace what has been lost and to compensate for filling the tubes and the lung preparation.

We have inserted a glass T tube in the rubber tube going from the aorta to the lungs, and have connected it with a mercury manometer for continuous blood pressure recording.

An intratracheal tube is inserted into the trachea of the lung preparation, and to it is attached an anesthetist's soda lime cannister, oxygen tube, and breathing bag.

A small balloon filled with nitrogen is tied over the end of the tracheotomy tube of Dog B, the recipient. This balloon allows the dog to make respiratory movements, but does not allow any exchange of gases.

(Reference to the dog henceforth refers to the living animal, Dog B, or the recipient. The word "breathing" in quotation marks refers to manual respiration in the lungs removed from Dog A, the donor.)

"Breathing" in the lung preparation is immediately begun and maintained by rather rapid intermittent pressure on the anesthetic bag. The elasticity of the lungs is sufficient to collapse the lungs when pressure on the bag is released and thereby to provide to-and-fro movement in the soda lime cannister for absorption of carbon dioxide.

Within a couple of minutes after "breathing" has begun, dark, cyanotic blood can be seen coming from the aorta and pink, oxygenated blood going into the inferior vena cava. If there is any blood loss it is made up by injecting 50 c.c. of blood from time to time. After the technique was perfected this procedure has been repeated consecutively on six pairs of dogs without failure. The protocols of two experiments are briefly reviewed.

PROTOCOLS

EXPERIMENT 5.—March 6, 1951, at 10:50 A.M. the lungs of an anesthetized dog weighing 27 pounds were removed as outlined. Dog B, the recipient, was anesthetized and prepared. At 11:50 A.M. "breathing" was begun. In a very few minutes the dog's respiratory attempts became feeble, infrequent, and finally consisted of barely visible chest movements. At 12:50 P.M., one hour after "breathing" had been commenced, the dog ceased completely to make any respiratory motion. His chest remained completely inactive for the next hour and forty minutes. At 2:30 P.M., after the dog had been carried on the respiration of homologous lungs for two hours and forty minutes, "breathing" was stopped to see whether the dog would again make respiratory attempts. Perhaps we did not wait long enough to allow the carbon dioxide of the blood to build up sufficiently high to stimulate respiration, or it may be that the respiratory center becomes less responsive after a long period of disuse. Although the animal became visibly cyanotic, he made no attempt at respiration.

"Breathing" was again instituted and continued for another half hour. For some reason when "breathing" was stopped this time the dog began to breathe spontaneously. The nitrogen-filled bag was removed from his trachea and he was allowed to live until 4:45 P.M., when it seemed useless to prolong the experiment further.

EXPERIMENT 6.—March 9, 1951, at 10 A.M. the lungs were removed from an anesthetized dog weighing 18 pounds and prepared as above. Dog B, the recipient, was anesthetized and all connections made with the homologous lungs. At 11:07 A.M. "breathing" was begun (Fig. 2, *A*). Within *one* minute the dog stopped making any attempts at respira-

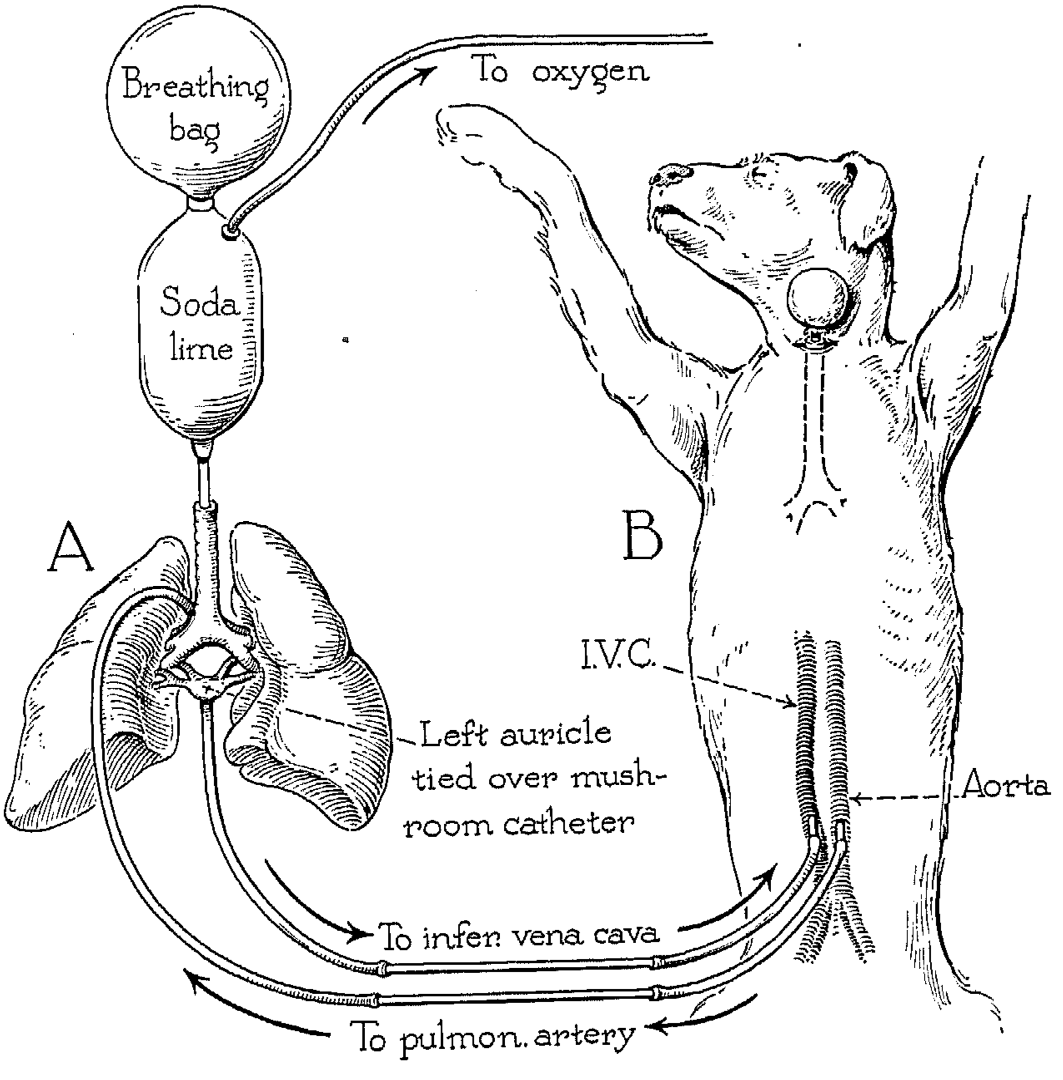

Fig. 1.

tion. His blood pressure and pulse remained normal. At 11:25 A.M. "breathing" was stopped (Fig. 2, *B*). After three minutes of complete apnea, respiratory attempts began and soon became very deep and labored. The blood pressure and pulse remained normal during this period of apnea. As soon as the animal showed signs of asphyxia "breathing" was again begun. Within twenty seconds the dog again ceased to make attempts at breathing. At 1:05 P.M., approximately two hours after respiration had been taken over by the homologous lungs, "breathing" was again stopped. This time the tubes leading to and from the lung preparation were clamped (Fig. 2, *C*). Immediately the dog began to try to breathe. After five minutes of no exchange of gases respiratory efforts ceased, but the pulse continued to beat, although slowly and irregularly. At the point it appeared that the dog was about to die, ''breathing'' was vigorously resumed. The blood promptly changed from black to pink, and in a few minutes the pulse and blood pressure had been restored to normal. The experiment was terminated.

DISCUSSION

In the finest microscopic unit of the lung there is a single cell separating air from blood. Whether this epithelium has a specific respiratory function or whether it acts merely as a mechanical structure which allows the interchange of gases has long been discussed and decided in favor of the latter premise. These experiments would appear to support that conclusion.

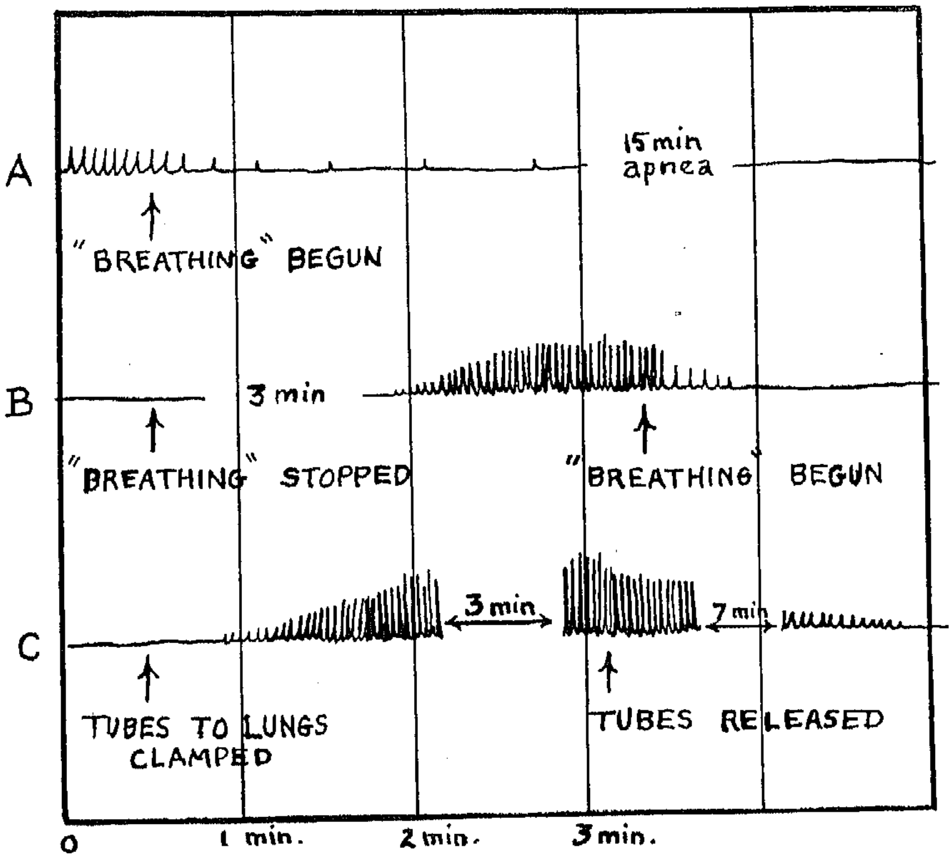

Fig. 2.—Spirogram, Experiment 6. *A*, Apnea occurred one minute after "breathing" with homologous lungs was begun and persisted for eighteen minutes. *B*, Three minutes after "breathing" was stopped the dog made respiratory attempts. When "breathing" was resumed the dog again promptly became apneic. *C*, When the blood flow to the homologous lungs was interrupted the dog began to make respiratory attempts. After five minutes when the animal seemed at the point of death, the tubes were released and vigorous "breathing" was resumed. The dog's condition quickly improved and after eight minutes he again ceased to make respiratory attempts.

In the early experiments ''breathing'' was carried on in the lung preparation continuously while the recipient dog was being prepared. In the last two experiments the lungs were simply laid aside for the hour necessary to prepare the second dog. No difference in the effectiveness of the lungs could be detected. In two experiments extensive pulmonary edema developed in the lung preparation after an hour and a half of ''breathing.'' Much frothy material was aspirated from the trachea. In the lung preparation which was used for breathing for over three hours no pulmonary edema developed.

We were more intent upon determining the feasibility of keeping a dog alive on the lungs of another and upon the technique involved in accomplishing this than upon the chemical changes in the blood. However, a few determinations showed that the oxygen content of the blood coming from the lung preparation was that of arterial blood, varying from 20 to 25 per cent, and that of the blood going to the lung preparation was low, varying from 14 to 20 per cent. The carbon dioxide content of both bloods showed the same variations, but both were below normal. This subject and the Ph of the blood require further study.

A series of experiments is planned in which all of the blood from the superior and inferior vena cava will be pumped through homologous lungs and back into the dog's aorta, completely by-passing the heart. Since the dogs in these experiments were able to live while only the blood from the distal aorta (approximately one-fifth of the total blood flow) was being pumped through the lung preparation, it appears likely that they can be maintained for long periods of time when all the blood is being pumped through the homologous lungs.

CONCLUSION

In six experiments it has been demonstrated that a dog not allowed to breathe with his own lungs can "breathe" for at least three hours by deflection of part of his blood through homologous lungs.

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