Improved Technic for Canine Lung Transplantation

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THE basic methods for transplanting canine lungs have been well defined for several years. Nevertheless, in most laboratories, technical problems result in a high mortality and impaired function in a large proportion of experimental lung transplants even when autografting eliminates the problem of allograft rejection. Thrombosis at the atrial suture line and necrosis of the transplant bronchus with leakage have been the most common complications.

Human lung transplant recipients will have impaired function in the remaining lung and thus will be dependent on function of the allograft. A method which permits allotransplantation of the lung with a high degree of technical success and which places total functional dependence on the transplant would facilitate experimental evaluation of immunosuppressive methods and tissue preservation technics.

The present report describes improvements in anastomotic technics involved in pulmonary transplantation. These improvements facilitate allografting in the dog with almost total elimination of left atrial thrombosis and bronchial leakage and permit total functional dependence to be placed on the graft.

Submitted for publication July 31, 1969.

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* Supported in part by grants from the U. S. Public Health Service (HE 11472 and HE 11567), the National Tuberculosis and Respiratory Disease Association, the Health Research Council of the City of New York, the Manning Foundation, and the Markle Foundation.

** Markle Scholar and Career Scientist of the Health Research Council of the City of New York.

Methods

Technic of Transplantation. Dogs weighing more than 15 Kg. were used although the procedure has been performed successfully in animals as small as 7 Kg. In the prospective recipient animal, a standard left thoracotomy is performed through the fifth intercostal space. The inferior pulmonary ligament is divided. The left pulmonary artery is dissected free of all adventitia from its first branch to its origin. The pericardium is opened over the main pulmonary artery and a clamp is placed on the visceral pericardial reflection overlying the main pulmonary artery. Traction on this clamp laterally and anteriorly facilitates dissection of the right main pulmonary artery (Fig. 1). Extensive posterior and superior exposure of this vessel permits circumferential dissection and encirclement with a ligature. The pericardial incision is then extended inferiorly exposing the anterior aspect of the left atrium and the right inferior pulmonary vein which drains the large diaphragmatic lobe of the right lung (Fig. 1). By traction exerted superiorly on the left lower lobe, it is possible to develop bluntly the avascular plane between the left mainstem bronchus and the left atrium. The posterior bronchial dissection is limited to division of the visceral pleura. With the exception of exposure of the right pulmonary artery, a similar dissection is carried out on the donor lung which should be of a comparable size or slightly larger than that of the recipient.

Paired straight or angled atraumatic clamps are placed across the left pulmo-

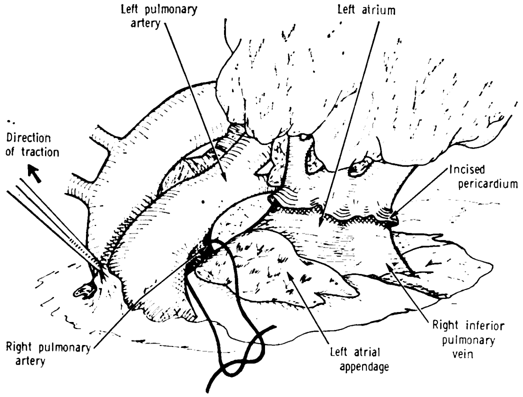

FIG. 1. Anterior view of completed dissection of the major hilar structures of the left lung. Note the ligature around the cleanly dissected right pulmonary artery and the short distance between the pulmonary veins of the left and right lungs. The arrow shows the direction of traction which facilitates dissection of the right pulmonary artery.

nary artery. Care is taken to place these clamps loosely to avoid intimal fractures. The recipient pulmonary artery is divided distally and the transplant artery proximally to provide adequate vessel wall for the subsequent anastomosis. These vessels should be divided obliquely as in Figure 3 although they may be cut transversely as in Figure 4. In either situation, a linear incision 3–5 mm. in length is made at the opposite angles of the recipient and transplant pulmonary arteries to facilitate creation of a distensible arterial anastomosis.

The recipient left mainstem bronchus is occluded with an angled atraumatic clamp and then divided just proximal to the origin of the upper lobe. Bronchial arteries transected with the bronchus are ligated with fine sutures. The bronchus of the transplant donor is divided 2 mm. proximal to the level of division in the recipient. This assures that the transplant bronchus will be slightly smaller than that of the recipient.

After division of the recipient pulmonary artery and bronchus, the pericardium overlying the posterior wall of the left atrium is incised. The left atrium is further mobilized by dividing the fat and visceral pericardium along the superior border of the left atrium. A thin bladed Satinsky-type atraumatic clamp is placed across the left atrium as far medially as possible without occluding the right inferior pulmonary vein. The left pulmonary veins are then transected at their junction with the left atrium, and the intervening tissue incised over a clamp (Fig. 2). This provides the maximal amount of tissue distal to the clamp and facilitates subsequent intima-to-intima anastomosis. The transplant atrium is divided as close as possible to a similarly placed Satinsky clamp. Two everting mattress sutures of 6-0 silk are placed superiorly and inferiorly in the atria and tied (Fig. 3). The anterior wall of the anastomosis is completed as a continuous everting mattress suture and then reinforced by a second over-and-over continuous suture. The posterior layer of the atrial anastomosis is performed with two similar continuous sutures (Fig. 4). This method prevents thrombosis by assuring intima-to-intima approximation and excluding intraluminal muscle.

The bronchial anastomosis is performed next. Two sutures of 4-0 dacron are placed as shown in Figure 5A. The inferior suture is tied and continued superiorly so as to draw or telescope the anterior wall of the transplant bronchus into the recipient bronchus. This suture is tied superiorly to

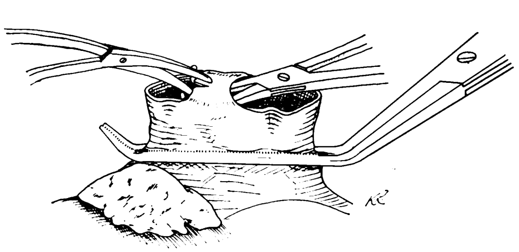

FIG. 2. Method for preparing the allograft recipient left atrial cuff with maximal preservation of atrial wall. The vascular clamp is placed so as to avoid occlusion of the right inferior pulmonary vein. The left pulmonary veins are divided just proximal to their junction with the atrium. Intervening tissue bridges are incised over a right angled clamp.

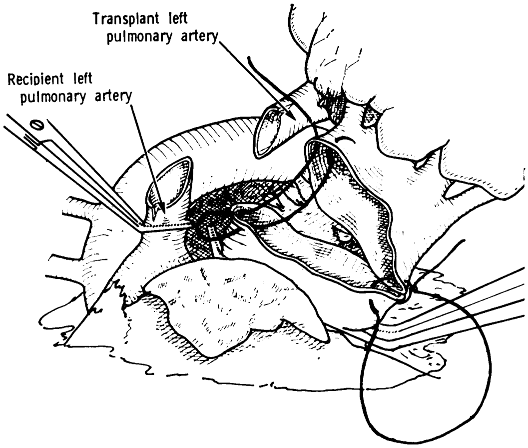

FIG. 3. Anterior view of allograft implantation which is begun by placing two horizontal mattress sutures at each end of the left atrial cuff. Note spatulation of donor and recipient pulmonary arteries which have been transected diagonally in this instance.

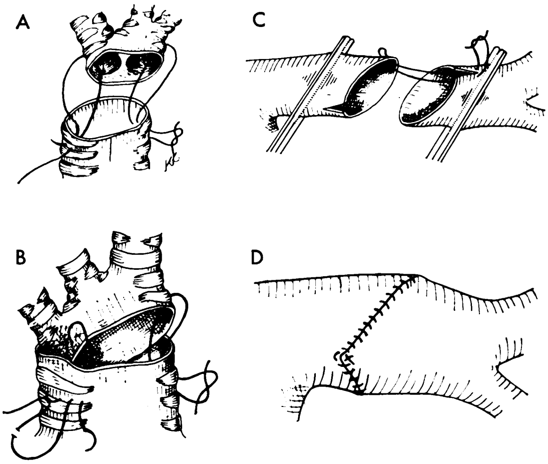

FIG. 5. A. Placement of corner sutures for telescoped bronchial anastomosis. B. Method for placing posterior continuous suture so that transplant bronchus is drawn within recipient bronchus. C & D. Details of distensible pulmonary artery anastomosis.

the corner suture which is continued, as shown in Figure 5B, so that the posterior wall of the transplant bronchus is drawn 1.0–1.5 cm. into the recipient bronchus. A second row of simple continuous sutures joins the end of the recipient bronchus to the peribronchial connective tissue of the transplant bronchus. This row can be placed superiorly, posteriorly and inferiorly. Anteriorly, however, this second layer

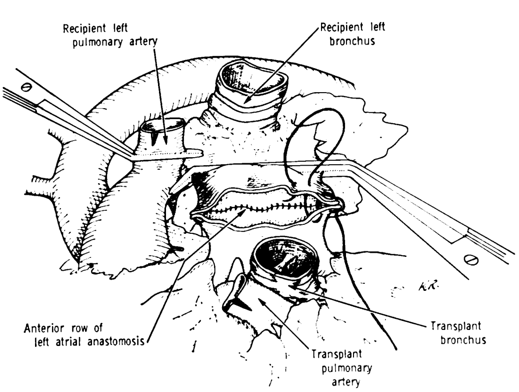

FIG. 4. Posterior view of allograft left atrial anastomosis. The posterior continuous horizontal mattress suture is being placed. Donor and recipient left pulmonary arteries have been spatulated but transected transversely in this instance. The atraumatic clamp occluding the recipient left mainstem bronchus has been omitted for clarity.

must be incomplete because the left atrium obscures exposure. As soon as the bronchial anastomosis is completed, the bronchial clamp is removed allowing expansion and ventilation of the transplant.

The spatulated donor and recipient pulmonary arteries are then approximated with 6-0 silk as shown in Figure 5C and 5D. Care is taken to place the sutures through all layers less than 1.0 mm. apart and less than 1.0 mm. from the vessel edge. Any distortion of the anastomosis by adventitial bands is avoided. The atrial and distal pulmonary artery clamps are removed, permitting the lung to be perfused in retrograde fashion. This prevents air embolization and distends the pulmonary artery at low pressure thus demonstrating any leaks or distortions which should be corrected at this point. The proximal pulmonary artery clamp is then removed. After ten minutes the ligature around the right pulmonary artery may be tied. To prevent subsequent recanalization of this vessel a second ligature is placed and tied 2–5 mm. distal to the first. After expanding the lungs, the chest is closed in layers without drainage.

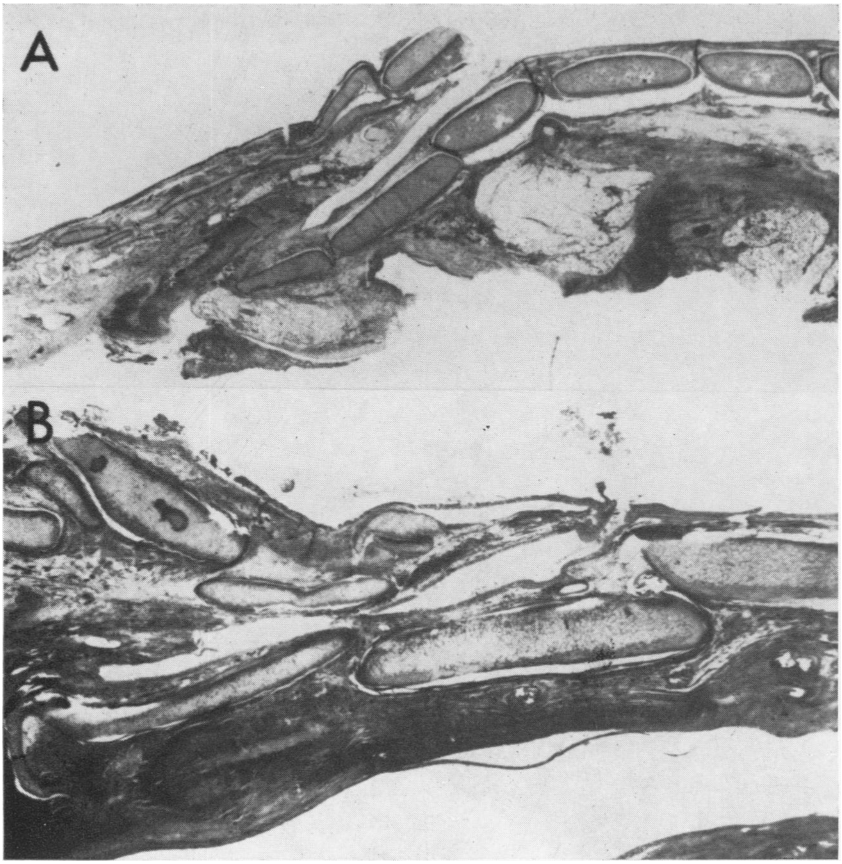

FIG. 6. Photomicrographs of well-healed telescoped bronchial anastomoses. In both instances the transplant bronchus is on the left and the epithelial surface is on the top. A. From a dog receiving a lung allograft 7 days earlier (×5, H&E). B. From a dog receiving a lung allograft 57 days earlier (×12, H&E).

Thirty-seven dogs received lung allografts and underwent simultaneous right pulmonary arterial ligation by this method. Another 32 animals had the identical operation with the exception that the bronchial continuity was restored by a simple end-to-end anastomosis of continuous dacron suture.

All animals received some form of immunosuppression. Several animals underwent pulmonary angiography after operation by a previously described technic.[5] All animals underwent postmortem examination. Care was taken to examine the vascular anastomoses for antimortem clot or fibrin deposition and the bronchial anastomoses for leakage. Longitudinal samples of tissue from the area of the bronchial anastomosis were fixed in 10% formalin and stained with hematoxylin and eosin.

Results

Three of the 69 animals succumbed from left atrial thromboses. In these animals, exposed muscle was present in the lumen. No animal died from a pulmonary arterial thrombosis.

Whereas 6 of 32 animals having standard bronchial anastomoses developed bronchial leaks or dehiscences, neither of these occurred in the 37 animals with telescoped anastomoses. There was no significant anastomotic narrowing in animals having telescoped bronchial anastomoses although some lived as long as 57 days. The histologic appearance of two typical telescoped

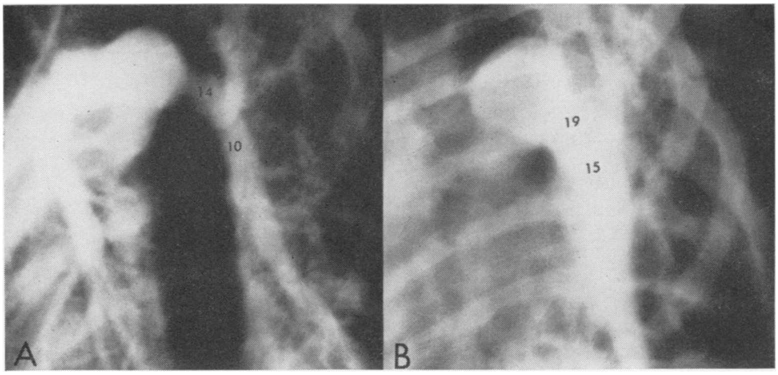

FIG. 7. Pulmonary angiograms from a single dog. A was taken prior to operation and B was taken 6 weeks after transplantation of the left lung and ligation of the right pulmonary artery. Note the postoperative dilatation of the left pulmonary artery. Numbers indicate in millimeters the actual measurements of vessel diameters on the original x-rays.

anastomoses is shown in Figure 6. Complete mucosal healing was commonly seen.

The importance of the distensible pulmonary artery anastomosis is shown in Figure 7. Pulmonary angiography before and after operation demonstrates the degree of widening of the anastomotic area of the left pulmonary artery which occurs with ligation of the right pulmonary artery.

Discussion

Technical complications resulting in high mortality and functional impairment are recognized features of lung transplantation in experimental animals.[1,4] Thrombosis originating at the left atrial suture line has been encountered by many investigators, and various measures surch as heparinization [2,8] and everting anastomoses [1,4] have been advocated to eliminate this complication. These simple measures have not been totally satisfactory. If muscular tissue is excluded from the atrial lumen as it can be by the present method, left atrial anastomotic thrombosis can be avoided. The second row of sutures prevents leakage which may otherwise be difficult to control.

Several workers have commented on the high incidence of ischemic bronchial necrosis in experimental lung transplants.[1,4] and a similar complication has occurred in man.[7] Numerous methods have been proposed to eliminate this complication. Transection of the transplant bronchus as close to the lung parenchyma as possible has been recommended, as has reinforcement of the bronchial suture line with peribronchial connective tissue.[1,4] Because of the marginal nature of the retrograde perfusion of the nutrient bronchial arteries of the transplant via collaterals from the pulmonary artery, neither method has been totally satisfactory in preventing necrosis and leakage. Some authors advocate suturing a button of donor aorta containing the bronchial artery orifice into the recipient aorta.[3] This, however, is unnecessarily complex and time consuming. Although the telescopic technique is not as applicable to thicker less flexible human bronchi, we have carried it out without difficulty in two cadavers.

The present work confirms previous observations that a distensible pulmonary artery anastomosis prevents fixed vascular resistance in pulmonary transplants and allows survival with transplantation of one lung and ligation of the opposite pulmonary artery.[5,6] Such a procedure places maximal stress on the transplanted lung since it must provide total respiratory and vascular function for the recipient animal. Thus, the distensible pulmonary artery anastomosis is the key to providing a method for evaluating the efficacy of immunosuppression since recipient survival depends entirely on allograft function. For similar reasons, this method of transplantation with occlusion of the contralateral pulmonary artery can be used to evaluate ischemic tolerances of the lung and methods of tissue preservation designed to prolong these tolerances.

The angiographic observation that transplantation of the left lung and ligation of the right pulmonary artery is associated with an increase in the diameter of the left pulmonary artery confirms previous direct measurements.[5] Both observations underscore the importance of large vessel distensibility in the vasodilatation that accompanies increased blood flow in the lung.

Technical refinements outlined in this report may not be necessary in transplantation of human lungs in which larger sized structures provide greater technical ease. However, that a single experimentally transplanted lung can provide adequate total pulmonary function from the moment it is inserted supports the feasibility of transplanting a single lung in patients with vascular and respiratory insufficiency in both lungs.

Summary

An improved method for allotransplantation of the canine left lung is reported. Key features include: 1) a two-layered everting atrial anastomosis which excludes atrial muscle from the lumen and prevents thrombosis, 2) a telescoped bronchial anastomosis which prevents leakage in the event of bronchial necrosis, and 3) a distensible pulmonary artery anastomosis which permits simultaneous ligation of the opposite pulmonary artery thereby placing total functional dependency on the transplant. All these features were employed in 37 dogs which received left lung allografts and underwent right pulmonary artery ligations. All recipient animals survived at least 5 days. None developed bronchial leak or stenosis. Complete healing of the bronchial mucosa was observed in many instances. The importance of pulmonary arterial distensibility and widening in the vasodilatation of increased flow is demonstrated by angiograms.

Acknowledgment

We thank Dr. Stanley Siegelman for performing the angiograms.

References

1. Blumenstock, D. A. and Kahn, D. R.: Replantation and Transplantation of the Canine Lung. J. Surg. Res., 1:40, 1961.
2. Garzon, A. A., Cheng, C., Pangan, J. and Karlson, K. E.: Hypothermic Hyperbaric Lung Preservation for Twenty-four Hours with Replantation. J. Thorac. Cardiovasc. Surg., 55:546, 1968.
3. Metras, H.: Preliminary Note on Lung Transplants in the Dog. Compte Rendue Acad. Sci., 231:1176, 1950.
4. Trummer, M. J. and Berg, P.: Lung Transplantation. Springfield, Illinois, Charles C Thomas, 1968, pp. 4–24.
5. Veith, F. J. and Richards, K.: Lung Transplantation with Simultaneous Contralateral Pulmonary Artery Ligation. Surg. Gynec. Obstet., 129:768, 1969.
6. Veith, F. J., Richards, K. and Lalezari, P.: Protracted Survival after Homotransplantation of the Lung and Simultaneous Contralateral Pulmonary Artery Ligation. J. Thorac. Cardiovasc. Surg., 58:829, 1969.
7. White, J. J., Tanser, P. H., Anthonisen, N. R., Wynands, J. E., Pare, J. A. P., Becklake, M. R., Munro, D. D. and MacLean, L. D.: Human Lung Homotransplantation. Canad. Med. Ass. J., 94:1199, 1966.
8. Yeh, T. J., Ellison, L. T. and Ellison, R. G.: Functional Evaluation of the Autotransplanted Lung in the Dog. Amer. Rev. Resp. Dis., 86:791, 1962.