

# Bilateral Simultaneous Canine Lung Allotransplantation

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MANY factors are probably responsible for the poor results obtained with human lung transplantation. One is overventilation of the recipient's remaining emphysematous lung with consequent compression and underventilation of the transplant which is receiving the bulk of pulmonary blood flow. This ventilation-perfusion imbalance has been emphasized by Stevens and his colleagues and by Wildevuur and Benfield in their review of the human experience.<sup>10, 12</sup> Simultaneous transplantation of both lungs has been proposed to avoid this ventilation-perfusion imbalance and to remove a potential septic focus. This procedure has been performed in monkeys<sup>9</sup> and man,<sup>3, 5, 7</sup> but it is generally believed that dogs with bilaterally denervated or transplanted lungs cannot sustain a normal ventilatory pattern and will succumb.<sup>1, 2, 6, 9</sup> Although bilateral lung transplantation in man has many theoretic advantages, the procedure must be investigated experimentally. The present report shows that bilateral transplantation in the dog need not produce inadequate ventilation and provides a convenient laboratory model for further investigation.

## Methods

Fifteen pairs of mongrel dogs weighing 20–25 Kg. were lightly anesthetized with pentobarbital. Cuffed endotracheal tubes were placed, and preoperative spirometers were obtained on all recipient animals while spontaneously breathing room air. After mobilization of the donor left lung, the left thoracotomy was closed and the donor was turned from the right to the left lateral decubitus position. The right lung was then transplanted by standard techniques.<sup>11</sup> The recipient right thoracotomy was closed, the animal turned, and its left lung removed. The donor was exsanguinated. The donor heart and previously mobilized left lung were rapidly removed. The hilar structures were trimmed, and the lung transplanted into the recipient.

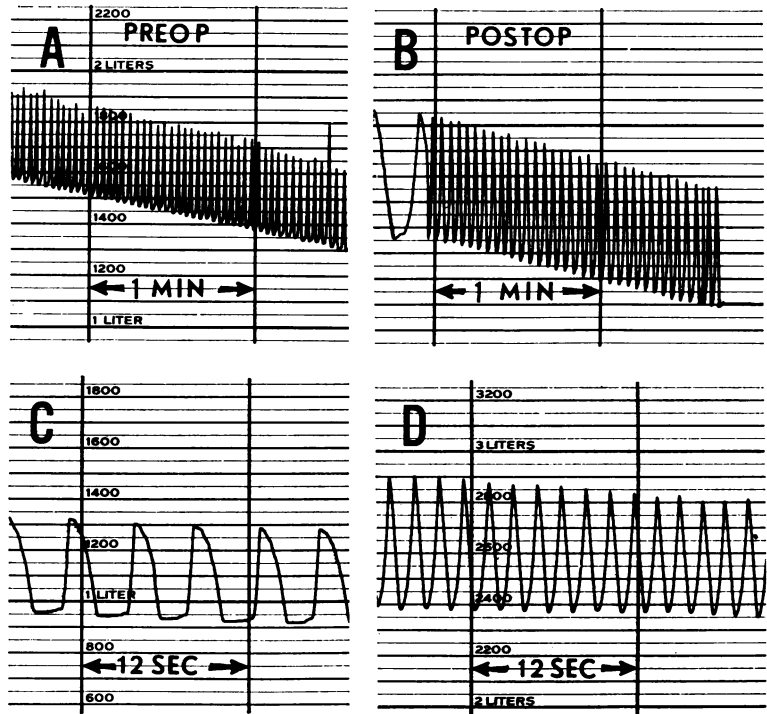
Within 1 hour of completing the operation, 13 recipient dogs were breathing spontaneously. At this time, the endotracheal tubes were connected to spirometers containing room air. Arterial and venous blood were analyzed for oxygen tension, carbon dioxide tension, and pH. Determinations were repeated after extubation which was usually accomplished less than 2 hours after operation. Thereafter the dogs were placed in an oxygen enriched (40%) atmosphere overnight and provided with standard postoperative care. Blood gas values were determined daily. Complete post-mortem examinations were performed. Sec-

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FIG. 1. Spirograms from dogs undergoing bilateral simultaneous lung transplantation. All traces were made with the animal breathing room air. A and B are from one dog before and immediately after operation. C and D are post-operative traces from two other recipient animals.



tions of the lungs were stained with hematoxylin and eosin after formalin inflation and immersion.

### Results

Three animals died from technical mishaps. Two never breathed spontaneously probably because of anesthetic overdosage or air embolization. The remaining 10 dogs resumed spontaneous ventilation with a normal rate, depth, and pattern (Fig. 1). In most instances the ventilatory pattern and depth was indistinguishable from that recorded preoperatively, although the rate was in general slightly faster.

All ten dogs that resumed this normal pattern of ventilation awoke from anesthesia, and were able to walk, eat, and carry out other normal functions without dyspnea or apparent distress. The animals survived from 2 to 5 days, deaths being preceded by 4–24 hours of dyspnea, tachypnea, cough and cyanosed mucous membranes.

Blood gas values postoperatively in surviving animals fell within the normal range for dogs breathing room air. The arterial oxygen tensions ranged from 65–95 mm. Hg except terminally when they were significantly lower. The carbon dioxide tensions of arterial blood were 31 to 39 mm. Hg and the pH 7.38–7.48. Venous oxygen tensions were 37–46 mm. Hg. Preoperative mean pulmonary artery pressures were 12–17 mm. Hg, and postoperatively were 16–17 mm. Hg. Postoperative respiratory rates in surviving dogs varied between 14 and 40 breaths per minute. A decreased oxygen tension (10% oxygen) or an increased carbon dioxide tension (5% CO<sub>2</sub>) in the inspired gas produced an increase in the rate and depth of respiration in 4 animals tested.

At postmortem, lung changes were consistent with allograft rejection and pneumonia. Manifestations of the former included perivascular infiltrations of mono-

nuclear cells and proteinaceous alveolar exudates containing large numbers of desquamated alveolar lining cells and mononuclear cells.

### Discussion

Nakae and colleagues, and Haglin and Lillehei have shown that denervation or transplantation of both lungs in primates does not produce ventilatory abnormalities that prevent survival.<sup>5, 7, 9</sup> Bilateral pulmonary denervation in the dog, however, has been thought to produce an abnormal ventilatory pattern which is fatal.<sup>1, 2, 6, 9</sup> Lower and associates also found abnormalities in respiratory patterns of dogs undergoing total cardiopulmonary allotransplantation although the animals lived as long as 5 days after the procedure.<sup>8</sup> More recently other authors have reported protracted survival in dogs after staged bilateral re-plantation or bilateral simultaneous denervation of the lungs, although these authors also noted ventilatory abnormalities with a prolonged inspiratory phase and a slow rate of breathing.<sup>4, 13</sup>

The present experiments show that pulmonary innervation is not essential for adequate spontaneous ventilation in dogs and establishes the feasibility of one-stage bilateral lung transplantation in this convenient laboratory animal. This should provide the opportunity to evaluate experimentally the physiologic and immunologic aspects of bilateral lung transplantation that must be explored before this procedure is utilized in patients.

### Summary

Fifteen dogs underwent allotransplantation of both lungs at one operation. Ten recovered from anesthesia, breathed spontaneously, were able to walk and eat without dyspnea, had normal rates and patterns of ventilation, and had normal arterial oxygen and carbon dioxide tensions and pH while breathing room air. These 10 animals had mean pulmonary artery pres-

ures of 16–19 mm. Hg after operation and survived 2 to 5 days without respiratory assistance. Deaths resulted from allograft rejection and pneumonia.

### Addendum

Since submission of the present report, Alican and colleagues have described successful one-stage re-plantation of both lungs in the dog.<sup>1A</sup>

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