

TITLE: REINNERVATION OF THE LUNGS AFTER TRANSPLANTATION
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Introduction: The advent of combined heart and lung transplantation for patients with severe congenital or acquired cardiopulmonary disease raises many questions regarding the respiratory function of the transplanted lung. The Breuer-Hering (B-H) inflation reflex was used to test peripheral nerve function, degeneration and neural regeneration in rhesus monkeys surviving orthotopic heart-lung (HL) transplantation.

Methods: Five control, six HL autotransplant, and two HL allotransplant rhesus monkeys were studied. Two animals were sequentially studied; once preoperatively (control) and three times postoperatively after HL autotransplantation. These two animals were therefore part of the control and autotransplant groups. The surgical technique used for transplantation has been previously described. In order to test for the Breuer-Hering inflation reflex all animals were induced with methohexital (10mg/kg) and succinylcholine (5mg), tracheally intubated and given manual ventilation until spontaneous respirations resumed. Anesthesia was maintained using inspired concentrations of 50% nitrous oxide and .75-1.5% halothane. A percutaneous femoral artery catheter was placed and arterial blood gases were obtained to insure adequate respiratory gas exchange and a light level of anesthesia prior to testing. Transpulmonary pressure (TPP) was measured with a differential transducer (Statham PM5) which received pressures from an airway catheter and an esophageal balloon. To test the B-H inflation reflex, successive graded inflations of room air were delivered with a 100 ml syringe, beginning with 20 ml and increasing by 10 ml increments to 100ml. Each inflation volume was held until the animal's first respiratory effort as indicated by TPP monitoring. The reflex response was quantitated in each test period by the slope of regression line fit through the data points comparing the natural logarithm of induced apnea (seconds) versus TPP (cmH₂O). By this analysis, smaller slope values indicated a stronger reflex response, i.e. a greater apnea period induced by a generated TPP. Statistical methods utilized linear regression analysis with a level of significance at $p < .05$.

Results: All regression lines generated r values which were significant ($p < .05$). All control animals had a measurable B-H reflex demonstrating a wide range of response with regression line slopes $= 1.9 \pm 1.3$ (mean \pm SD). All six autotransplant animals studied 1.9 to 17.7 months postoperatively

demonstrated a B-H reflex with regression line slopes $= 3.7 \pm 2.3$ (mean \pm SD). The two HL autotransplant animals who were studied sequentially, showed no reflex response in the early postoperative period at .5 and . months after surgery, but recovered reflex activity when studied at later dates (Figure). The two HL allotransplant animals studied also demonstrated a B-H reflex response in the late postoperative period.

Discussion: This study documents that reinnervation of lung tissue can occur after transplantation. The regeneration of the Breuer-Hering reflex and other important reflexes (e.g. cough reflex) may play a vital role in the long term survival of heart-lung transplant recipients.

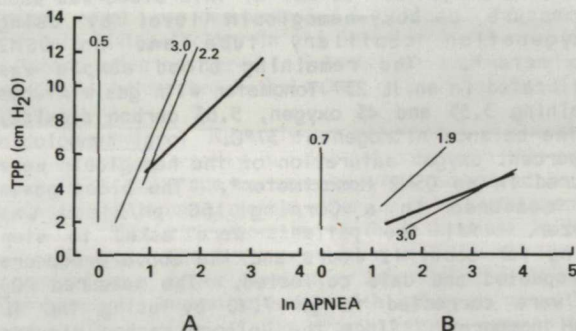


Figure: Data shown in A and B were obtained from sequential testing of two HL autotransplant monkeys. The heavy line in each graph indicates the B-H reflex response as controls before surgery (slopes $= 2.86$ and 1.18 respectively). Other lines show results of reflex testing after surgery, with numbers indicating time from operation in months.

Reference:

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