

Title: THE EFFECT OF HYPOPHYSECTOMY, THYROIDECTOMY AND REPLACEMENT THERAPY BY CORTISOL AND ADRENOCORTICOTROPIN ON OVINE FETAL LUNG STRUCTURE

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**Introduction.** Functional maturational changes in the fetal lung are thought to be controlled in part by the endocrine system of the fetus. Cortisol, epinephrine, thyroxine, prolactin, and prostanooids have been shown to have an effect on biochemical maturation in the developing lung. Recent studies have demonstrated that hypophysectomy in fetal lambs during the second trimester of pregnancy reduced the concentration of saturated phospholipids and lung distensibility at term when compared with controls.<sup>1</sup> These changes were reversed by an infusion of adrenocorticotropin 1-24 (ACTH) prior to delivery. This study reports the structural changes seen in the lung of fetuses subjected to hypophysectomy and subsequent replacement therapy with ACTH and cortisol prior to delivery.

**Methods.** Twenty-two single lamb fetuses were hypophysectomized at 99-122 days gestation by a previously described cryosurgical technique.<sup>2</sup> Four fetuses were thyroidectomized in addition. Sixteen of the fetuses had hindlimb venous catheters placed at term (148-150 days). After recovery, 10 of these fetuses, including the thyroidectomized animals, received an infusion of ACTH 5 µgm/hr for 84 hours. The remaining 6 catheterized fetuses received an infusion of cortisol at 1 mg/hr for 72 hours. After the infusion, the fetuses were delivered by hysterotomy and the caudal lobe of the right lung was prepared for light microscopy. Those hypophysectomized fetuses not receiving ACTH or cortisol were sacrificed at 148-155 days as were a group of term control unoperated fetuses (N=6) and preterm control unoperated fetus (N=4). The preterm control fetuses were sacrificed at 123, 130, 139, and 146 days, respectively. Four animals were randomly selected from each term group for analysis.

Group	N	
1	4	Control, Term
2	4	Hypophysectomy
3	4	Hypophysectomy and ACTH
4	4	Hypophysectomy and Cortisol
5	4	Hypophysectomy, Thyroidectomy and ACTH

Morphometric analysis of the lungs was carried out at 600x and included measurement of minimum interalveolar wall thickness, numerical density of Type I and Type II pneumocytes in parenchyma, and volume density of septal tissue and air spaces within the lung. Ten microscopic fields were analyzed at random for each fetus. The results were compared by the Newman-Keuls Multiple Range test for statistical significance.

**Results.** In the hypophysectomized untreated fetuses, all of the features measured in the right caudal lobe were different from those of the control term animals. In these animals, the alveolar wall was thicker, the numerical density of Type I pneumocytes was less and of Type II pneumocytes was more and the volume density of septal tissue was greater than controls. The hypophysectomized animals treated with either cortisol or ACTH were different from the hypophysectomized untreated group, but there was no difference between these treatment groups. Each showed a decrease in interalveolar wall thickness and volume density of lung tissue when compared with the hypophysectomized untreated group. Treatment caused an increase in numerical density of Type I pneumocytes and a reduction in Type II, so that by our measurements, lung structure was not different in the hypophysectomized treated groups from term control animals. Thyroidectomy had no effect on lung structure in that the lungs of the hypophysectomized ACTH treated group were similar to those which in addition underwent thyroidectomy.

**Conclusion.** After hypophysectomy during the second trimester of fetal life, lung structure at term is abnormal. The abnormalities are corrected by an infusion of ACTH or cortisol. The structure of the lung in the hypophysectomized untreated animals is similar to that of the most immature preterm control fetus that was analyzed (123 days). In addition, lung structure in both hypophysectomized treated groups is similar to the mature lung of the control term animals. This suggests that hypophysectomy impairs structural maturation of the fetal lung and that maturation can be accelerated by a relatively brief infusion of cortisol or ACTH at term. It is concluded that lung structure as well as biochemistry is under fetal endocrine control.

**References.**

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