APOPTOSIS IS INCREASED IN LAMBS VENTILATED WITH NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE

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Introduction
Preterm infants who require mechanical ventilation with supplemental oxygen for twenty-eight days often develop chronic lung disease (CLD). The pathology of CLD is characterized in part by thick, cellular mesenchyme in the future alveolar walls, thereby preventing efficient gas exchange. Several studies have shown that nasal continuous positive airway pressure (NCPAP) moderates the severity of CLD. Therefore, we hypothesized that, compared to conventional ventilation, NCPAP increases apoptosis of mesenchymal cells of the immature lung.

Methods
We managed two study groups of preterm lambs for 72 hours. One group was managed by conventional ventilation (CV), and the second was ventilated via NCPAP. To measure apoptosis we used the following analyses: quantitative histology to measure distal airspace wall thickness, real-time PCR to measure p53, immunohistochemistry and immunoblot to measure caspase-3 (a key apoptotic protein), and TUNEL staining to determine the apoptotic index.

Results
Compared to CV, NCPAP results in thinner distal airspace walls, increased mRNA levels of p53 and its downstream targets, increased protein levels of caspase-3, and increased TUNEL staining and significant increase in apoptotic index.

Conclusion
NCPAP permits apoptosis to occur, allowing the mesenchyme to thin for optimized gas exchange through a narrow air/blood interface. Hence, there is normal alveolar formation. Our results represent the first molecular explanation for the beneficial effect of NCPAP on alveolar formation via apoptotic remodeling of the interstitium. These studies illustrate the detrimental effects on lung development by CV, a method still used in 80% of the newborn intensive care units in the United States. Because NCPAP mitigates the injuries sustained by the premature lung, it could be an alternative ventilation method that would prevent the incidence and severity of CLD.