Response to the Letter to the Editor. The Relevance of Animal Models to Bronchopulmonary Dysplasia

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Dr. Frank correctly points out the difficulty in extrapolation of animal model derived data to disorders affecting preterm infants because neither initial pathogenetic mechanism, clinical intervention technique, pharmacologic treatment, nor species specific metabolic maturation necessarily mimics response to disease or treatment in human infants.

Although the term neonatal guinea pig has lung development in terms of alveolar wall thickness that is similar to adult values, and "alveolarization and lung remodelling" has occurred ontogenically earlier than in the human preterm infant, oxygen-induced injury in this species has mimicked bronchopulmonary dysplasia in human infants (1). Some biochemical responses, but certainly not all, have been shown by Frank *et al.* (2) to resemble those of the adult guinea pig, yet these authors have failed to evaluate species-specific protease elaboration in neonatal and adult animals, including man.

Although total lung lavage elastase in neonatal guinea pigs exposed to FiO_2 .21 exceeded total elastase activity found in FiO_2 > .9 exposure; metalloelastase activity was significantly elevated in the higher oxygen-exposed guinea pig neonates. That metalloelastase activity was elevated is possibly species-specific for the neonatal guinea pig, as elastase activity in pulmonary effluent from human neonates was elevated in infants developing bronchopulmonary dysplasia. Current investigations have documented that lung effluent elastase from preterm infants is mostly neutrophilic in origin. Using immunoprecipitation of pulmonary effluent elastase to monospecific antineutrophilic elastase (kindly provided by Dr. Charles Cochrane, La Jolla, CA), we have found distinct precipitin bands in tracheal fluids containing >15 μg elastase/mg albumin using double diffusion immunoprecipitation assays. Further characterization of high oxygen exposed human infant tra-

cheal effluent with diisopropylfluoridate or 1,10 phenanthroline before incubation with succinyl (ala)₃ paranitroanilide provided further evidence that this protease is a serine elastase (2).

The findings of serine elastase in bronchoalveolar lavage of a majority of adults with adult respiratory distress syndrome (3, 4), as well as in infants with neonatal respiratory distress syndrome and among infants developing bronchopulmonary dysplasia suggests that there may be similar pathogenetic mechanisms operative in the genesis of pulmonary response to the initial pulmonary injury caused by the initial insult or immaturity or to techniques of therapy (mechanical ventilation and high concentrations of oxygen), or both.

The finding of elevated serine elastase levels in the pulmonary effluent of neonates with acute and chronic lung disease may be a useful marker to the extent of lung injury resulting from surfactant deficiency or other lung diseases and current methods of therapy.

REFERENCES AND NOTES

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