Lung effects of inhaled corticosteroids in a rhesus monkey model of childhood asthma.

BACKGROUND: The risks for infants and young children receiving inhaled corticosteroid (ICS) therapy are largely unknown. Recent clinical studies indicate that ICS therapy in pre-school children with symptoms of asthma result in decreased symptoms without influencing the clinical disease course, but potentially affect postnatal growth and development. The current study employs a primate experimental model to identify the risks posed by ICS therapy.

OBJECTIVE: To (1) establish whether ICS therapy in developing primate lungs reverses pulmonary pathobiology associated with allergic airway disease (AAD) and (2) define the impact of ICS on postnatal lung growth and development in primates.

METHODS: Infant rhesus monkeys were exposed, from 1 through 6 months, to filtered air (FA) with house dust mite allergen and ozone using a protocol that produces AAD (AAD monkeys), or to FA alone (Control monkeys). From three through 6 months, the monkeys were treated daily with ICS (budesonide) or saline.

RESULTS: Several AAD manifestations (airflow restrictions, lavage eosinophilia, basement membrane zone thickening, epithelial mucin composition) were reduced with ICS treatment, without adverse effects on body growth or adrenal function; however, airway branching...
abnormalities and intraepithelial innervation were not reduced. In addition, several indicators of postnatal lung growth and differentiation: vital capacity, inspiratory capacity, compliance, non-parenchymal lung volume and alveolarization, were increased in both AAD and Control monkeys that received ICS treatment.

CONCLUSIONS AND CLINICAL RELEVANCE: Incomplete prevention of pathobiological changes in the airways and disruption of postnatal growth and differentiation of airways and lung parenchyma in response to ICS pose risks for developing primate lungs. These responses also represent two mechanisms that could compromise ICS therapy's ability to alter clinical disease course in young children.