Susceptibility to Lower Respiratory Infections in Childhood is Associated with Perturbation of the Cytokine Response to Pathogenic Airway Bacteria - DTU Orbit (08/11/2017)

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BACKGROUND: Neonatal colonization of the airways with respiratory pathogens is associated with increased risk of lower respiratory infections (LRI) in early childhood. Therefore, we hypothesized that children developing LRI have an aberrant immune response to pathogenic bacteria in infancy. OBJECTIVE: To characterize in vitro the early life systemic immune response to pathogenic bacteria and study the possible association with incidence of LRI during the first 3 years of life. METHODS: The Copenhagen Prospective Study on Asthma in Childhood2000 (COPSAC2000) is a clinical birth cohort study of 411 children born of mothers with asthma. LRI incidence was prospectively captured from 6-monthly planned visits and visits at acute respiratory episodes. The in vitro systemic immune response to H. influenzae, M. catarrhalis and S. pneumoniae was characterized by the production of TNF-α, IFN-γ, IL-2, IL-5, IL-10, IL-13, and IL-17 in peripheral blood mononuclear cells isolated at age 6 months from 291 infants. Data were analyzed by Poisson regression against incidence of LRI in infancy. RESULTS:: A multivariable model including all cytokine responses from the three different bacterial stimulations significantly identified children at risk of LRI (p=0.006). The immune response pattern associated with LRI was characterized by perturbed production of several cytokines rather than production of one specific cytokine, and was independent of concurrent asthma. TNF-α and IL-5 were key drivers but did not explain the entire variation in LRI susceptibility. CONCLUSIONS: Children at risk of future LRI present a pertubed systemic immune response upon exposure to common airway pathogens in early life.

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