Pathogenic bacteria colonizing the airways in asymptomatic neonates stimulates topical inflammatory mediator release.

**Rationale:** Bacterial colonization of neonatal airways with the pathogenic bacterial species, *Moraxella catarrhalis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*, is associated with later development of childhood asthma.

**Objectives:** To study a possible association between colonization with pathogenic bacterial strains and the immune signature of the upper airways in healthy neonates.

**Methods:** A total of 20 cytokines and chemokines were quantified in vivo in the airway mucosal lining fluid of 662 neonates from the Copenhagen Prospective Study of Asthma in Childhood 2010 birth cohort. Colonization of the hypopharynx with *M. catarrhalis*, *S. pneumoniae*, *H. influenzae*, and *Staphylococcus aureus* was assessed simultaneously. The association between immune signatures and bacterial colonization or noncolonized controls was analyzed using conventional statistical methods supplemented by a multivariate approach for pattern identification.

**Measurements and Main Results:** Colonization with *M. catarrhalis* and *H. influenzae* induced a mixed T helper cell (Th) type 1/Th2/Th17 response with high levels of IL-1 beta (*M. catarrhalis*, $P = 2.2 \times 10^{-12}$; *H. influenzae*, $P = 7.1 \times 10^{-10}$), TNF-alpha (*M. catarrhalis*, $P = 1.5 \times 10^{-9}$; *H. influenzae*, $P = 5.9 \times 10^{-7}$), and macrophage inflammatory protein-1 beta (*M. catarrhalis*, $P = 1.6 \times 10^{-11}$; *H. influenzae*, $P = 2.7 \times 10^{-7}$). *S. aureus* colonization demonstrated a Th17-promoting profile with elevated IL-17 levels ($P = 1.6 \times 10^{-24}$). *S. pneumoniae* colonization was not significantly associated with any of the mediators.

**Conclusions:** *M. catarrhalis* and *H. influenzae* colonization of the airways of asymptomatic neonates is associated with an inflammatory immune response of the airway mucosa, which may result in chronic inflammation.