

Correspondence

The first rhinovirus-wheeze acts as a marker for later asthma in high-risk children

To the Editor:

We thank Bønnelykke et al¹ for the interesting article on the association between early-life respiratory infections and subsequent asthma. They suggest that the important risk factor for asthma is the underlying susceptibility to triggers instead of the specific triggering agent. We agree with the idea of the host-dependent susceptibility. On the contrary, we suggest a trigger dependence so that the rhinovirus (RV) itself would act as an important early marker uncovering early the underlying susceptibility to asthma by manifesting expiratory wheezing. Childhood asthma risk assessment has traditionally relied on clinical risk factors such as atopic characteristics, wheezing frequency and severity, as well as parental asthma.

The link between early wheezing and subsequent asthma can generally be investigated in 2 types of high-risk cohorts: early wheezing children from atopic families and/or children hospitalized for severe early wheezing. In the former, the findings related to RV etiology of wheezing have been controversial. Two studies showed an increased risk for school-age asthma when the children suffered from RV-induced wheezing during the first (risk ratio, 3; 95% CI, 1-5)² or the first 3 years of life (odds ratio [OR], 10; 95% CI, 4-22),³ whereas no risk was found by Bønnelykke et al¹ (OR, 0.6; 95% CI, 0.3-2 when adjusted for the total no. of respiratory episodes). In hospitalized nonselected children, the RV-associated risk has been clearer. The increased risk for the initiation of regular asthma control therapy was shown already at the first wheezing episode (hazard ratio, 4; 95% CI, 2-8)⁴ and the high RV load markedly exposed to relapse.⁵ Also, hospitalization for RV-induced bronchiolitis was associated with increased risk of school-age asthma (OR, 4; 95% CI, 1-20).⁶

Like Bønnelykke et al¹ stated, the underlying susceptibility rather than the particular triggering agent might be the true asthma risk factor. The RV-associated risk has been explained by the increased susceptibility to lower airway RV infections in individuals with pronounced atopic characteristics (allergen specific IgE sensitization, blood eosinophilia, atopic eczema, maternal atopic eczema, and/or increased IL-4, IL-5, and IL-13 responses in airway secretions), damaged airway epithelium, as

well as decreased interferon $\alpha/\beta/\gamma/\lambda$ and IL-10 responses in airway secretions or cells.⁵ These data support the marker value of the RV-induced early wheezing by uncovering the underlying asthma susceptibility in the sensitized and/or hospitalized children. We suggest focusing on the first wheezing episode because RV-sensitive viral diagnostics is widely available, and RV serves as an effective marker already in these children. On the contrary, the slow development of allergic sensitization, especially aeroallergen sensitization, decreases the value of atopic characteristics in asthma risk indices during early life.^{4,6,7} This suggestion could also provide a novel approach into the mechanisms underlying childhood wheezing and asthma, and would thus encourage to find future therapeutic interventions to prevent asthma.

Minna Lukkarinen, MD

Tuomas Jartti, MD

From the Department of Pediatrics, University of Turku and Turku University Hospital, Turku, Finland. E-mail: mimapo@utu.fi.

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