consequence of a subtle alteration of the sleep structure by an abnormally high sympathetic activity.

C. Vernet*, S. Redolfi^{*,#}, V. Attali^{*,#}, E. Konofal*, A. Brion*, E. Frija-Orvoen*, M. Pottier*, T. Similowski[#] and I. Arnulf^{*,#}

*Sleep Disorders Unit, UMR 975, National Reference Centre for Narcolepsy and Hypersomnia, and [#]Dept of Respiratory and Intensive Care Medicine and ER10 Pierre and Marie Curie University, Pitié-Salpêtrière Hospital, Assistance Publique Hôpitaux de Paris, Paris, France.

Correspondence: I. Arnulf, Unité des Pathologies du Sommeil, Hôpital Pitié-Salpêtrière, 47–83 Boulevard de l'Hôpital, 75651 Paris Cedex 13, France. E-mail: isabelle.arnulf@psl.aphp.fr

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Viral wheezing is virus specific and not just host specific

To the Editors:

In a recent issue of the *European Respiratory Journal*, STRIPPOLI *et al.* [1] reported their interesting findings on exclusive viral wheezing *versus* allergic wheezing in a large population-based, prospectively followed cohort including 4,102 children at 1 yr and 1,858 children at 9 yrs of age. The parents reported current wheezing in 36, 20, 16 and 16% of the children at age 1, 4, 6 and 9 yrs, respectively. The study showed considerable age-related, parent-reported changes in the relative importance of triggers for wheezing in children. The proportion of infection decreased constantly from 94.1% (at age 1 yr) to 81.0% (at age 9 yrs) and the proportion of allergic wheeze increased constantly from 7.5% (at age 1 yr) to 62.4% (at age 9 yrs). The proportion of exercise as a trigger for wheezing was rather similar at all ages, being lowest (35.5%) at age 1 yr and highest (48.6%) at age 6 yrs.

The association between exercise and allergens as triggers for wheezing was significant at age 1, 4 and 6 yrs, and between exercise and infection at age 1, 6 and 9 yrs. Conversely, allergens and infection were not associated at any age; the association was even negative (OR 0.54; $p=0.051$) at age 6 yrs. Thus, the authors confirmed positive associations between exercise and allergens, and between exercise and infection as triggers for wheezing, but there were no positive associations between allergens and infection at any age. The authors concluded that exclusive viral wheezing and allergen-induced, multiple-trigger wheezing are distinct disease entities presenting in genetically different children [1].

The findings are in agreement with those from post-bronchiolitis studies [2], and with clinical experience as well. If bronchiolitis is defined as wheezing-associated respiratory infection at age <24 months, post-bronchiolitis wheezing during subsequent viral infections is common. In long-term, prospective post-bronchiolitis studies, 60% of the former bronchiolitis patients

have wheezed at age 2–3 yrs and 15–40% have had doctor-diagnosed asthma at school age [2]. However, if bronchiolitis has been caused by respiratory syncytial virus (RSV) [2], or has taken place at age <6 months when RSV is the predominant causative agent [3], later asthma seems not to be substantially more common than in the non-selected population. Doctor-diagnosed asthma was present at age 6.5 yrs in 12.7% of the 166 children hospitalised for bronchiolitis at age <6 months. The figure was 8.2% in the former RSV patients *versus* 24% in the former non-RSV patients [3].

Asthma in parents and atopy in infants are the most strong and consistently documented risk factors for later chronic asthma after bronchiolitis or early-life wheezing [2]. In addition, the virus that is associated with the first wheezing episode may play an important role, either by modifying the course or outcome of early-life wheezing, or by picking up those who are prone to asthma and actually have their first asthma episode in infancy. Rhinovirus-induced wheezing, in particular, seems to be associated with atopy, eosinophilia and later asthma [4]. Bocavirus is nearly equally as common as RSV and rhinovirus in wheezing infants and young children, but its role as an independent aetiological agent in children with respiratory infection and its association with later outcomes are still unknown [5]. Thus, children with viral wheezing, even those with exclusively viral wheezing, merely form a genetically heterogeneous, rather than a genetically homogenous, group. In future studies, the group of children with viral wheezing should be analysed as stratified into virus-specific categories allowing the evaluation of the interaction between viral and genetic factors, such as atopy or components of innate immunity.

The observation of STRIPPOLI *et al.* [1] that there was no association between allergens and symptomatic infections as triggers for wheezing in children is important and provides evidence that exclusive viral wheezing is its own disease entity

with its own genetics. However, the great majority of viral infections are nonsymptomatic and wheezing may be the only symptom of respiratory viral infection. Prospective post-bronchiolitis follow-up studies with virus-specific diagnoses and virus-specific outcomes available have provided evidence that viral wheezing is also a virus-specific phenomenon, not only a host-specific phenomenon. There may be different viruses that trigger wheezing in children with exclusively viral wheezing and in children with allergic wheezing.

M. Korppi

Paediatric Research Center, Tampere University and University Hospital, Tampere, Finland.

Correspondence: M. Korppi, Paediatric Research Center, Tampere University Hospital, Tampere 33140, Finland. E-mail: matti.korppi@uta.fi

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