The most effective management strategy for viral infections is prevention through vaccines, as reported in a pilot study of herpes zoster vaccination in 10 adult SLE patients older than 50 years of age,[12] but the efficacy and safety of this live-attenuated virus vaccine in a large SLE population is unknown.

In conclusion, lupus in children has a higher susceptibility to HZI and is characterized by a shorter disease duration, disease activity and lower frequency of postherpetic neuralgia than in adults with SLE. Both groups have a comparable and good overall outcome.

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HUMAN RHINOVIRUS TYPES AND ASSOCIATION WITH RESPIRATORY SYMPTOMS DURING THE FIRST YEAR OF LIFE

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Abstract: Human rhinoviruses (HRV) cause respiratory infections and are associated with asthma development. We assessed HRV prevalence, types and association with respiratory symptoms in the first year of life in 20 unselected infants. HRV was detected in 32% of 825 weekly nasal swabs. Seventy-four different types of all three species were identified. HRV presence and related respiratory symptoms are highly heterogeneous.

Key Words: rhinovirus, respiratory tract infection, infant, birth cohort

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Human rhinoviruses (HRV) are the most common respiratory viruses identified in humans with respiratory infections,[1] and they play a major role in respiratory morbidity of children.[2,3] HRV-induced wheezing during early life is strongly associated with the later development of asthma.[4] Based on their genetic divergence, HRVs are divided into 3 species: HRV-A, HRV-B and HRV-C, of which HRV-A and HRV-C are thought to cause most severe symptoms.[5] For each HRV species, various types are known.

Despite the high frequency of HRV infections, detailed information is lacking on prevalence of HRV types and their association with presence and severity of respiratory symptoms, especially in early infancy of otherwise healthy children. Therefore, we analyzed weekly nasal swabs for HRV presence, sequenced positive samples for HRV typing and compared the results with respiratory symptoms.

METHODS

In a subsample of 20 healthy infants (9 female, 11 male) nested in the prospective Basel–Bern-Infant-Lung-Development cohort study,[6] we analyzed the presence of HRV RNA by one-step real-time polymerase chain reaction in nasal swabs collected weekly during the first year of life. HRV-positive samples were further sequenced to determine HRV types (for method see Tapparel et al[7]). Signs of respiratory symptoms (cough, wheeze and breathing difficulties) were assessed based on a standardized symptom score by weekly telephone interviews with the parents.[6] The study was approved by the Ethics Committee Bern, Switzerland and written informed consent was obtained from the parents.

RESULTS

Prevalence of HRV Species and Types

HRV was detected in 266 of 831 nasal swabs (32%). HRV-A and HRV-C were almost equally frequent (38% and 39%, respectively), followed by HRV-B (12%). Ten percent of the samples were untypable (because of poor sample quality or undetectable viral load). In total, 74 different HRV types were identified (30 HRV-A, 8 HRV-B and 36 HRV-C). Twelve HRV types of all 3 species were particularly frequent and found in 5 or more samples: A78 (detected in 17 samples), A16 (in nine samples), B6 (in 8 samples), A56, A89 (both in 7 samples), A101, C1, C9 (all in 6 samples), A12, C22, C26 and C39 (all in 5 samples). Those HRV types were identified in samples of 1 (A12), 3 (B6, A89, C1), 4 (A16, A56,

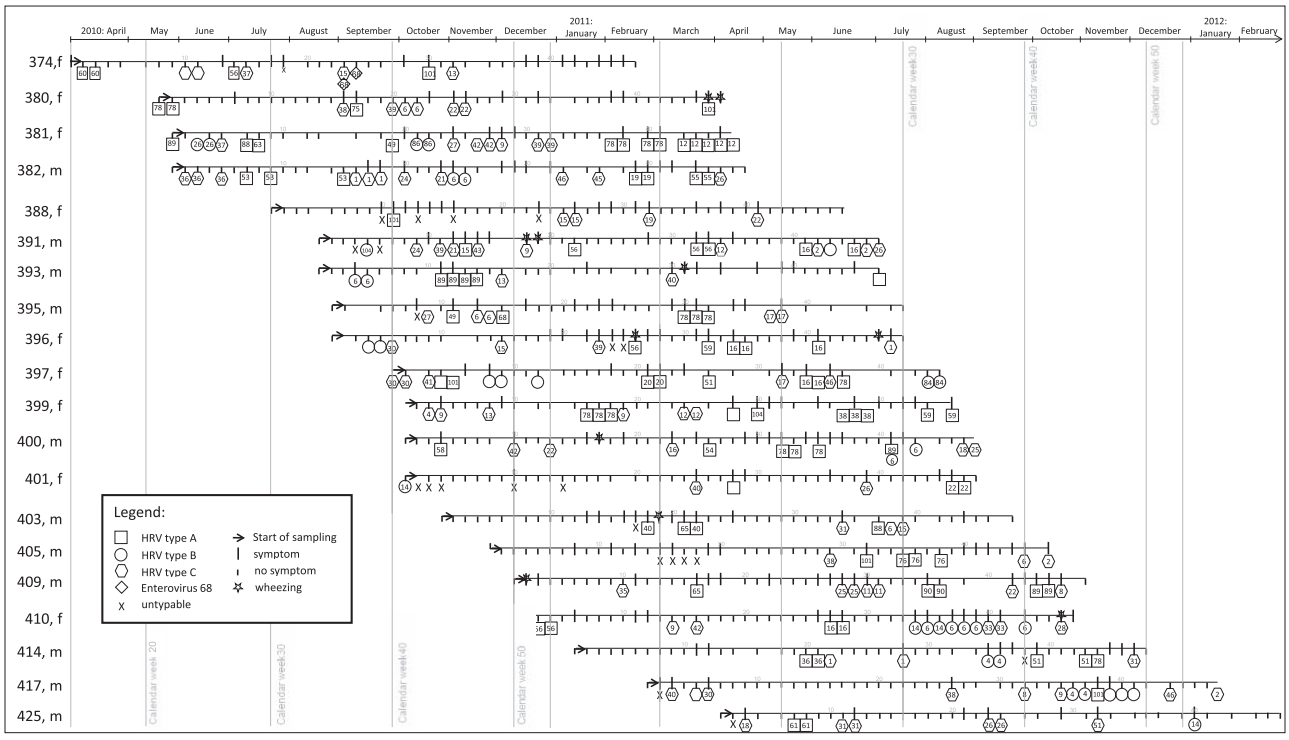

FIGURE 1. Presence of HRV in nasal swabs during the first year of life of 20 children. Arrows stand for sampling start; full upright lines indicate presence of respiratory symptoms, and half upright lines indicate that no symptoms were present in that particular week; squares show infection with HRV-A, circles infection with HRV-B, hexagons infection with HRV-C and rhombus infections with enterovirus 68. × shows infection with an untypable HRV type; stars indicate reported wheezing; f stands for female and m for male infants.

C22, C26, C39), 5 (C9), 6 (A101) or 7 (A78) infants (for details see Fig., Supplemental Digital Content 1, http://links.lww.com/INF/C142). The infective period lasted between 1 and 5 positive samples based on our weekly sampling. The seasonal prevalence of the 3 HRV species was not different. In total, we detected 55 HRV-positive samples during spring (March–May), 68 during summer, 74 during fall and 31 during winter months.

Association of HRV Prevalence and Respiratory Symptoms

In total, half of HRV-positive episodes were accompanied by respiratory symptoms, with slight differences among species: 53% of HRV-A [95% confidence interval (CI) = 42–63%], 42% of HRV-B (CI = 25–61) and 51% of HRV-C (CI = 40–61) positive episodes were symptomatic (Fig., Supplemental Digital Content 1, http://links.lww.com/INF/C142). Wheezing was reported 11 times in the context of HRV detection with the types A40, A56, A101, C1, C9, C28 and C40. The 3 most frequently detected types (A78, A16, B6) were symptomatic in 53%, 75% and 75% of the HRV-positive samples, respectively. Overall, the association between HRV types and respiratory symptoms was highly heterogeneous without any recognizable pattern.

DISCUSSION

During the first year of life of 20 unselected infants, we found 74 different HRV types of all 3 HRV species. We found HRV-A and HRV-C almost equally often and fewer HRV-B. Despite differences in study design and sampling procedure this distribution is similar to those found by others.[5,8] Others have studied the presence of HRV in nasal lavages during scheduled and unscheduled sick visits from otherwise healthy infants of a high-risk birth cohort study[5] or the presence of rhinoviruses in nose–throat swabs of healthy children <5 years with symptoms of an acute respiratory illness.[8] We are thus confident that our results are also representative of other populations of this age group.

The lower detection frequency of HRV-B is either because of lower prevalence (32 HRV-B types identified vs. 80 HRV-A and 54 HRV-C) or its different virus characteristics. Nakagome et al[9] recently showed that HRV-B types isolated from clinical samples have lower replication rates in differentiated primary epithelial cells compared with HRV-A and HRV-C types.

Each infant in our study had at least 9 HRV-positive samples and 4 different HRV types identified during her or his first year of life. In total, we found 74 different HRV types showing a high variability and dynamic pattern of HRV. The lack of a clear association between specific HRV types and respiratory symptoms might relate to this high variability and/or other factors influencing respiratory symptoms (eg, concomitant pathogens, such as bacteria or other respiratory viruses, or individual immune responses).

The strengths of our study are an unbiased selection of the infants and the weekly sampling, including assessment of respiratory symptoms. Mothers were recruited before birth and infants were not selected based on health problems or respiratory symptoms giving a completely unbiased view on HRV presence in early infancy. Despite the large sample size of 831 samples and because of the high number of different HRV types, no pattern for association of HRV types with respiratory symptoms was detected. Thus even larger studies seem to be necessary to draw firm conclusions on respiratory symptoms induced by particular HRV types.

We confirm data from other studies[5,10] showing that the HRV population in the human airway is highly dynamic and rapidly

changing. This means that in vitro studies using single lab strains indeed may add important mechanistic knowledge but never represent the complex in vivo situation.

For now, we conclude that the presence of different HRV species and types in the airways during infancy is highly heterogeneous and dynamic, that about half of the HRV infections in early life are not accompanied by respiratory symptoms and no clear association between HRV types in inducing respiratory symptoms exists. Each infant included in our study had at least 9 HRV-positive samples and 4 different HRV types identified just during its first year of life. This shows that HRV infections and HRV-associated symptoms in early infancy, and their potential role in asthma development, are rather complex.

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Authors contribution: L.M. analyzed the data and drafted the manuscript. I.M. analyzed the data. C.T. and L.K. took care of the RT-PCR and sequencing part. U.F., N.R., L.K. and P.L. designed the study. I.M., C.T., L.K., M.P.A., E.K., U.F., N.R. and P.L. revised the manuscript critically. All authors read and approved the final manuscript.

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THE SPECTRUM OF *NOCARDIA* LUNG DISEASE IN CYSTIC FIBROSIS

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Abstract: We reviewed all cases of *Nocardia* infection in cystic fibrosis patients at 2 centers. Eight of 200 patients had *Nocardia* in sputum. Four developed severe lung disease, including 3 with associated allergic bronchopulmonary aspergillosis; 4 remained clinically stable. *Nocardia* is often associated with significant lung disease in cystic fibrosis, possibly associated with allergic bronchopulmonary aspergillosis or steroids.

Key Words: nocardiosis, cystic fibrosis, aspergillus, lung transplant, steroids

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Nocardiosis in cystic fibrosis (CF) is possibly associated with increasing length of survival, chronic antibiotic therapy, a changing pulmonary microbiome or improving diagnosis.[1]

Pulmonary *Nocardia* infection in CF patients was first described 20 years ago. Its role as a causative agent for either acute or chronic pulmonary disease is debated, and a recent report suggested that no treatment is required.[1] In our experience, *Nocardia* infection in CF can sometimes lead to inexorable pulmonary deterioration and even lung transplantation.

We did a retrospective chart review from 2002 through2013, at 2 CF centers in Israel: the Graub CF Center at Schneider Children's Medical Center of Israel and the CF Center at Meyer Children's Hospital, Rambam Medical Center. All patients met the CF Foundation Consensus Panel criteria for CF diagnosis. Sputum was acquired at least twice annually for Ziehl–Neelsen staining and culture on blood agar for 3 weeks. If found positive, cultures were subsequently taken at every clinic visit, that is, every 1–2 months. We considered *Nocardia* to be eradicated if 3 consecutive sputum cultures were negative.

The study was approved by the hospitals' ethics committees.

RESULTS

We reviewed charts of 200 CF patients aged 2 months to 63 years. Eight (4%) had at least 1 positive sputum culture for *Nocardia*. Findings are summarized in Table 1.

Two patterns of *Nocardia* infection were observed: (1) patients 1–4 experienced a complicated clinical course with respiratory deterioration leading to the decision to treat the infection; patients 1–3 also had pulmonary nodules consistent with *Nocardia* lung disease on chest computerized tomography (CT); (2) patients 5–8 had a more gradual deterioration in their pulmonary disease. In patients 5 and 8, no other pathogens were identified despite pulmonary symptoms. This led to the decision to treat the *Nocardia*. In patient 6, there was an associated decrease in lung function, which improved once *Nocardia* was eradicated. Only patient 7 had no treatment as there appeared to be no associated clinical decline.

When *Nocardia* was repeatedly cultured, with clinical symptoms but without an aggressive course, trimethoprim–sulfamethoxazole (TMP/SMX) single drug therapy was instituted. In cases with a more fulminant clinical course, particularly when resistance to TMP/SMX was shown on susceptibility studies, multidrug therapy including intravenous (IV) meropenem or oral linezolid was instituted for several months.

Case Presentations

Patient 1, a 55-year-old female, was diagnosed with CF at 41 years with diffuse bronchiectasis, recurrent major hemoptysis and