Risk of herpes zoster in children with asthma

Chung-Il Wi, M.D.,1 Bong-Seong Kim, M.D.,1,2 Sonia Mehra, M.D.,1 Barbara P. Yawn, M.D., M.Sc.,3 Miguel A. Park, M.D.,4 and Young J. Juhn, M.D., M.P.H.5

ABSTRACT

Background: There is literature that indicates the association of asthma with an increased risk of common and serious microbial infections. We recently reported an increased risk of vaccine-preventable diseases, e.g., herpes zoster (HZ) among children with asthma, defined by predetermined asthma criteria. Little is known about whether this association is persistent if the asthma status is defined by different asthma criteria, e.g., the Asthma Predictive Index, given the heterogeneity of asthma.

Objective: To assess the consistency of the association between asthma and the risk of HZ in children.

Methods: This is a population-based case-control study based on all pediatric patients with HZ between 1996 and 2001 in Olmsted County, Minnesota, and 1:1 age- and sex-matched controls without a history of HZ who were enrolled in our previous study. The original Asthma Predictive Index criteria was operationalized by two or more wheezing episodes in a year for the first 3 years of life plus one of the major (physician-diagnosed asthma for a parent or physician-diagnosed eczema for a patient) or two of the minor criteria (physician-diagnosed allergic rhinitis for a patient, wheezing apart from cold, or eosinophilia [≥4%]). Data were fit to traditional logistic regression models to calculate odds ratios and 95% confidence intervals.

Results: Of the original cohort (n = 554), 95 (17%) did not meet the enrollment criteria for this study, which left 459. Of the 221 patients, 53% were female, with a mean (standard deviation) age of 9.7 ± 4.2 years. The risk of HZ was increased in children with asthma defined by the API controlling for a varicella vaccine history and atopic status (adjusted odds ratio 2.56 [95% confidence interval, 1.08–6.56]).

Conclusions: The association between asthma and increased risk of HZ in children and adolescents is consistent, independent of asthma definitions. Asthma might be an important clinical condition to be considered in HZ vaccine studies.

(Accession to this article from Merck. The remaining authors have no conflicts of interest to declare pertaining to this article)

From the 1Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, Minnesota, 2Department of Pediatrics, Ganganegu Asan Hospital, University of Ulsan College of Medicine, Ganganegu, South Korea, 3Department of Research, Olmsted Medical Center, Rochester, Minnesota, 4Division of Allergic Diseases, Mayo Clinic, Rochester, Minnesota, and 5Department of Pediatric and Adolescent Medicine/Internal Medicine, Mayo Clinic, Rochester, Minnesota.

This work was supported by a grant from the National Institute of Allergy and Infectious Diseases (R21 AI101277) and Scholarly Clinician Award from the Mayo Foundation. Also, this study was made possible by using the resources of the Rochester Epidemiology Project, which is supported by the National Institute on Aging of the National Institutes of Health under Award R01AG034676.

Presented at Pediatric Academic Societies, Vancouver, Canada, May 3–6, 2014.

B.P. Yawn is a consultant for Merck and GlaxoSmithKline and has received grants from Merck. The remaining authors have no conflicts of interest to declare pertaining to this article.

Supplemental data available at www.IngentaConnect.com

E-mail address: Juhn.Young@mayo.edu

Copyright © 2015, OceanSide Publications, Inc., U.S.A.
We hypothesized that the association between asthma and the increased risk of HZ is consistent, independent of asthma criteria (consistency). To test this hypothesis, as a follow-up study to the original study, which showed an increased risk of HZ among children with asthma defined by the PAC, we sought to determine whether asthma defined by different criteria, e.g., API, is still associated with an increased risk of HZ in children. This study was approved by the institutional review board for human subject research at the Mayo Clinic and the Olmsted Medical Center.

METHODS

Study Setting

Olmsted County, Minnesota, is an excellent setting to conduct a population-based epidemiologic study because medical care is virtually self-contained within the community. In addition, when patients register with any health care provider in the community (e.g., as a newborn), they, or their parents or legal guardian, are asked to grant or refuse authorization of use of their medical records for research. Authorization is granted by more than 95% of all individuals.21 Medical records research by using the geographically defined population of Olmsted County is possible through the Rochester Epidemiology Project (REP), which has been continuously funded by the National Institutes of Health and has been maintained since 1960.22–25 All clinical diagnoses given to an Olmsted County resident who visits nearly any health care facility in the county are electronically indexed to the individual by using a unique REP patient identifying number, and information from every episode of care is contained within the REP data base. By using REP resources, a previous study demonstrated that incidence rates of asthma for this community are similar to other communities.26

Study Design and Subjects

This is a geographically defined population-based case-control study based on all pediatric patients with HZ between 1996 and 2001 in Olmsted County, Minnesota, who were enrolled in our previous study. Details of study subjects were previously described.8,27,28 Briefly, HZ cases were initially identified by the International Classification of Diseases, 9th Revision (ICD-9) codes (053.xx), and medical records for each potential subject were reviewed to verify that the subject was indeed a new case of HZ, based on predetermined criteria for HZ. Confirmation required a characteristic rash (i.e., vesicular rash on a dermatome) and signs or symptoms of pain or itching at the rash site, in addition to a physician’s diagnosis of HZ. Exclusion criteria included a lack of authorization for the use of medical records for research, nonresidence in Olmsted County, Minnesota, and another diagnosis that possibly explained the rash, e.g., a culture positive for herpes simplex. Their corresponding 1:1 age- and sex-matched controls without a history of HZ as of the index date were identified from Olmsted County residents. In addition to those for the original study, we also excluded children whose medical records were unavailable to ascertain asthma status by the API (e.g., adopted children or first registration in the clinic after the age of 3 years). Pertinent information on sociodemographic and clinical characteristics of subjects collected for the original study were used in this present study.

Ascertainment of Asthma Status by the API, PAC, and Physician Diagnosis

We conducted comprehensive medical record reviews to determine asthma status by applying (1) the API criteria based on the first 3 years of life (original API), (2) API criteria based on the entire follow-up duration beyond the first 3 years of life (API ever), (3) PAC, and (4) a physician diagnosis of asthma documented in the medical records. The API is summarized in Table 1, and the operational details for applying the API were reported in our recent study.20 We applied two separate API criteria based on the duration of follow-up, as described above (original API versus API ever). The PAC is summarized in Table 2. Briefly, the PAC was developed to be applied to retrospective studies that concerned asthma epidemiology by the asthma researchers, Yunginger and Reed.29 To our knowledge, the PAC is the only predetermined criteria that can be applied to medical records retrospectively.

| Table 1  | API criteria |
|----------|--------------|
| **Major Criteria** | **Minor Criteria** |
| 1. Physician-diagnosed asthma for parents | 1. Physician-diagnosed allergic rhinitis (or hay fever) for patient |
| 2. Physician-diagnosed eczema (or atopic dermatitis) for patient | 2. Wheezing apart from cold |
|            | 3. Eosinophilia (≥ 4%) |

Positive API: Early frequent wheezing (<3 years of life) plus at least one of the major criteria or two of three minor criteria.
without using ICD codes for asthma. Since its development, it has shown high reliability (0.72–0.92) and excellent construct validity to predict various risk factors for asthma. The onset date of asthma (asthma index date) by the PAC was defined as the earliest constellation of symptoms found in the medical record that met the PAC for asthma regardless of physician diagnosis of asthma. Because most subjects with probable asthma by the PAC (85%) that became definite asthma over time, we combined both probable and definite asthma.

**Statistical Analysis**

The primary aim of the analysis was to determine the association between asthma defined by various criteria and the risk of HZ. Data were fit to multivariate logistic regression models to calculate ORs and their corresponding 95% CIs for asthma status defined by each definition (i.e., original API, API ever, PAC, and ICD-9 code) in relation to the risk of HZ controlling for pertinent covariates and confounders such as a varicella vaccine history and atopic status, defined as the presence of sensitization against an aeroallergen or a food allergen. We used the Greenland entry criteria ($p < 0.20$, based on univariate analysis). All analyses were performed by using the JMP statistical software package (version 9.0.1; SAS Institute, Inc., Cary, NC).

**RESULTS**

Of the original 554 subjects, 95 children (56 cases and 39 controls) were excluded (7, withdrawal of research authorization; 11, adoption; 77, unable to apply the API due to insufficient information during the first 3 years of life), and the comparison of basic characteristics between the included and excluded children is summarized in Supplemental Table 1. Overall, the excluded and included subjects were similar except for white race (82% versus 93%; $p = 0.001$). Characteristics of the subjects with HZ and the controls are summarized in Table 3. Of the remaining 221 subjects, 53% were female and 94% were white. The mean (SD) age at diagnosis of HZ was 9.7 ± 4.2 years. The onset age of
primary HZ in children with asthma defined by original API tended to be younger than those without asthma among subjects with HZ only (10.4 ± 4.1 years versus 8.6 ± 4.2 years; \( p = 0.092 \)).

### Asthma Defined by Different Asthma Criteria and the Risk of HZ

Results for the association between asthma and HZ are summarized in Table 3. Seventeen of the 221 subjects (7.7%) had asthma by the original API before the index date of HZ compared with 8 of the 238 controls (3.4%) (unadjusted OR 2.40 [95% CI, 1.01–5.67]; \( p = 0.041 \)). Similarly, asthma status defined by all other criteria before the index date was associated with the increased risk of HZ. The results of this present study confirmed the original study findings on the relationship between asthma defined by the PAC and an increased risk of HZ.8 In addition, the direction of the association was consistent, despite the definition of asthma status by four different criteria that controlled for all pertinent covariates. The association between asthma status defined by other criteria and the risk of HZ except a physician diagnosis of asthma that only showed borderline significance. Atopic status was significant or approached statistical significance in multivariate models. A history of varicella vaccination was consistently associated with a decreased risk of HZ. Inhaled corticosteroid use was not associated with the risk of HZ.

### DISCUSSION

Analysis of our study results demonstrated that asthma status defined by different criteria was consistently associated with an increased risk of HZ in children. These results helped affirm the association between asthma and an increased risk of HZ. The results of this present study confirmed the original study findings on the relationship between asthma defined by the PAC and an increased risk of HZ. In addition, the direction of the association was consistent, despite the definition of asthma status by four different criteria that controlled for all pertinent covariates. Atopic status was similarly associated with the increased risk of HZ, although the association only approached to sta-

### Table 3  Characteristics of HZ for cases and controls and factors associated with risk of HZ in children

| Variables                              | Controls (\( n = 238 \)) | Cases (\( n = 221 \)) | OR for HZ (95% CI) | \( p \) Value |
|----------------------------------------|--------------------------|------------------------|-------------------|---------------|
| Age, mean (SD), y                      | 9.7 ± 4.3                | 9.7 ± 4.2              | 1.00 (0.96–1.04)  | 0.900         |
| Female, no. (%)                        | 125 (52.5)               | 118 (53.4)             | 1.03 (0.72–1.49)  | 0.852         |
| White, no. (%)                         | 210/228 (92.1)           | 196/209 (93.8)         | 1.29 (0.62–2.71)  | 0.496         |
| Maternal education, no. (%)            |                          |                        |                   |               |
| Non–high school graduation             | 8/107 (7.5)              | 12/106 (11.3)          | Referent          |               |
| High school graduation                 | 30/107 (28.0)            | 31/106 (29.3)          | 0.69 (0.25–1.92)  | 0.475         |
| Some college                           | 50/107 (46.7)            | 49/106 (46.2)          | 0.65 (0.25–1.74)  | 0.391         |
| College graduation                     | 19/107 (17.8)            | 14/106 (13.2)          | 0.49 (0.16–1.52)  | 0.215         |
| Family history of asthma, no. (%)      | 72 (30.3)                | 73 (33.0)              | 1.14 (0.77–1.69)  | 0.522         |
| History of asthma before the index date, no. (%) |          |                        |                   |               |
| Original API                           | 8 (3.4)                  | 17 (7.7)               | 2.40 (1.01–5.67)  | 0.041         |
| API ever                               | 17 (7.1)                 | 29 (13.1)              | 1.96 (1.05–3.68)  | 0.033         |
| PAC                                    | 40 (16.8)                | 62 (28.1)              | 1.93 (1.24–3.04)  | 0.004         |
| ICD-9 codes                            | 32 (13.5)                | 45 (20.4)              | 1.65 (1.00–2.70)  | 0.048         |
| Atopic status (aeroallergen or food allergen sensitization), no. (%) | 5/238 (2.1)             | 13/221 (5.9)           | 2.91 (1.02–8.31)  | 0.037         |
| Varicella vaccination, no. (%)         | 32 (13.5)                | 16 (7.2)               | 0.50 (0.27–0.94)  | 0.030         |
| Tobacco smoke exposure, no. (%)        | 14 (5.9)                 | 12 (5.4)               | 0.91 (0.42–2.03)  | 0.834         |
| Regular use of ICS, no. (%)            | 3/28 (10.7)              | 4/54 (7.4)             | 0.67 (0.14–3.21)  | 0.686         |
| Presence of comorbidities, no. (%)#    | 21 (8.8)                 | 21 (9.5)               | 1.09 (0.58–2.05)  | 0.801         |
| Psychological, social, behavioral problem, no. (%) | 21 (8.8)                 | 19 (8.6)               | 0.97 (0.51–1.86)  | 0.932         |

ICS = inhaled corticosteroid.

#Comorbid conditions were based on the Advisory Committee on Immunization Practices–recommended pneumococcal vaccine–eligible conditions.

#\( p \) value < 0.05 in bold.
tistical significance. Varicella vaccine was consistently protective against HZ, which confirmed our previous study finding. Although 95 children were excluded from the original study, it is unlikely to significantly influence the results and our interpretation of the results because the subjects included and those excluded were similar except race. These results helped establish consistency and coherence in causal inference between asthma and the risk of HZ in children, and are particularly important given the reported heterogeneity of asthma.31–34 Overall, analysis of the results indicated that asthma may have the potential impact on a non–airway-related infection such as HZ.

We recently reported an increased risk of HZ among adults with asthma compared with those without asthma.35 This study finding was corroborated by the two recent studies that indicated associations of asthma with the increased risk of HZ.36,37 The mechanisms that underlie the potential association between asthma and the risk of HZ in children, and are particularly important given the reported heterogeneity of asthma.31–34 Overall, analysis of the results indicated that asthma may have the potential impact on a non–airway-related infection such as HZ.

| Variables                        | Adjusted OR* | 95% CI      | p Value#   |
|----------------------------------|--------------|-------------|------------|
| A history of asthma by original API | 2.56         | 1.08–6.56   | 0.032      |
| Atopic status                    | 2.71         | 0.99–8.65   | 0.053      |
| Varicella vaccination            | 0.46         | 0.23–0.86   | 0.015      |
| A history of asthma by API ever  | 1.98         | 1.01–3.81   | 0.033      |
| Atopic status                    | 2.85         | 1.04–9.07   | 0.041      |
| Varicella vaccination            | 0.48         | 0.25–0.90   | 0.023      |
| A history of asthma by PAC       | 1.81         | 1.15–2.88   | 0.011      |
| Atopic status                    | 2.36         | 0.85–7.59   | 0.101      |
| Varicella vaccination            | 0.50         | 0.26–0.93   | 0.028      |
| A history of asthma by ICD-9     | 1.44         | 0.86–2.43   | 0.16       |
| Atopic status                    | 2.46         | 0.87–8.01   | 0.09       |
| Varicella vaccination            | 0.50         | 0.26–0.94   | 0.03       |

*Adjusted for atopic status, history of varicella vaccination, and history of asthma by each criteria.
# p value < 0.05 in bold.
and minor criteria in the API may affect the results of study. For example, in this retrospective study, eosinophilia data were not available for all the subjects. Eosinophilia was defined by $\geq 4\%$ of the total white blood cells in the test performed before the age of 1 year because blood specimens of the original API study were obtained at the age of 1 year (mean $[SD]: 10.9 \pm 0.6$ months).\textsuperscript{13} The original API study reported that only 10$\%$ of the subjects had eosinophilia and that eosinophilia was seldom used for diagnosing asthma because it is not a specific marker for asthma, particularly in patients with mild asthma.\textsuperscript{47,48} Further, the proportion of missing eosinophilia data in the present study was not different between the HZ group and the control group (which were 85$\%$ versus 83$\%$ respectively), which indicates nondifferential misclassification bias. Thus, we believe it is unlikely to influence our study results.

Our study has important strengths. This is a population-based study design, which minimizes a selection bias. In addition, ascertainment of asthma status by using the API was performed independent of asthma status by a physician diagnosis of asthma, which minimized an observational bias. Our study setting has unique advantages, including a self-contained health care environment and a medical record linkage system that links patients and their medical records to health care providers.

In conclusion, asthma is consistently associated with an increased risk of HZ in children and adolescents, despite ascertainment of asthma status by different criteria. The mechanisms that underlie this association should be explored in future studies.

ACKNOWLEDGMENTS

We thank the staff of the Pediatric Asthma Epidemiology Research Unit for research support. We thank Elizabeth Krusemark for her administrative assistance.

This publication was made possible by CTSA Grant Number UL1 TR000135 from the National Center for Advancing Translational Sciences (NCATS), a component of the National Institutes of Health (NIH). Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NIH.

REFERENCES

1. Azad MB, Coneys JG, Kozyrskyj AL, et al. Probiotic supplementation during pregnancy or infancy for the prevention of asthma and wheeze: Systematic review and meta-analysis. BMJ 347: f6471, 2013.
2. Centers for Disease Control and Prevention. Vital signs: Asthma prevalence, disease characteristics, and self-management education: United States, 2001-2009. MMWR Morb Mortal Wkly Rep 60:547–552, 2011.
3. Lethbridge-Cejku M, Vickerie J. Summary health statistics for U.S. adults: National Health Interview Survey, 2003. National Center for Health Statistics. Vital Health Stat 10(225). 2005. Hyattsville, Maryland.
4. Stanton MW. The High Concentration of US Health Care Expenditures. 2006. Available online at http://www.ahrq.gov/research/ria19/expendria.htm; accessed May 19, 2012.
5. Schiller JS, Lucas JW, Perego JA. Summary health statistics for U.S. adults: National Health Interview Survey, 2011. National Center for Health Statistics. Vital Health Stat 10(256). 2012. Hyattsville, Maryland.
6. Asher MI, Montefort S, Bjorksten B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC phases one and three repeat multicounty cross-sectional surveys. Lancet 368:733–743, 2006.
7. Juhn YJ. Risks for infection in patients with asthma (or other atopic conditions): Is asthma more than a chronic airway disease? J Allergy Clin Immunol 134:247–257, quiz 258–259, 2014.
8. Kim BS, Mehra S, Yawn B, et al. Increased risk of herpes zoster in children with asthma: A population-based case-control study. J Pediatr 163:816–821, 2013.
9. Juhn YJ, Kita H, Yawn BP, et al. Increased risk of serious pneumococcal disease in patients with asthma. J Allergy Clin Immunol 122:719–723, 2008.
10. Capili CR, Hettinger A, Rigelman-Hedberg N, et al. Increased risk of pertussis in patients with asthma. J Allergy Clin Immunol 129:957–963, 2012.
11. Frey D, Jacobson R, Poland G, et al. Assessment of the association between pediatric asthma and Streptococcus pyogenes upper respiratory infection. Allergy Asthma Proc 30:540–545, 2009.
12. Bjur KA, Lynch RL, Fenta YA, et al. Assessment of the association between atopic conditions and tympanostomy tube placement in children. Allergy Asthma Proc 33:289–296, 2012.
13. Castro-Rodriguez JA, Holberg CJ, Wright AL, and Martinéz FD. A clinical index to define risk of asthma in young children with recurrent wheezing. Am J Respir Crit Care Med 162(pt. 1):1403–1406, 2000.
14. National Asthma Education and Prevention Program. Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report 2007. J Allergy Clin Immunol 120(suppl.):S94–S138, 2007.
15. Ater D, Bar BE, Fireman N, et al. Asthma-predictive-index, bronchial-challenge, sputum eosinophils in acutely wheezing preschoolers. Pediatr Pulmonol 49:952–959, 2014.
16. Castro-Rodriguez JA, Sardon O, Perez-Yarza EG, et al. Young infants with recurrent wheezing and positive asthma predictive index have higher levels of exhaled nitric oxide. J Asthma 50:162–165, 2013.
17. Moeller A, Diefencheler C, Lehmann A, et al. Exhaled nitric oxide distinguishes between subgroups of preschool children with respiratory symptoms. J Allergy Clin Immunol 121:705–709, 2008.
18. Guilbert TW, Morgan WJ, Zeiger RS, et al. Atopic characteristics of children with recurrent wheezing at high risk for the development of childhood asthma. J Allergy Clin Immunol 114:1282–1287, 2004.
19. Brand PL, Luz Garcia-Garcia M, Morison A, et al. Ciclesonide in wheezy preschool children with a positive asthma predictive index or atopy. Respir Med 105:1588–1595, 2011.
20. Wi CI, Park MA, and Juhn YJ. Development and initial testing of Asthma Predictive Index for a retrospective study: An exploratory study. J Asthma 26:1–8, 2014.
21. Yawn BP, Yawn RA, Geier GR, et al. The impact of requiring patient authorization for use of data in medical records research. J Fam Pract 47:361–365, 1998.
22. Kurland LT, and Molgaard CA. The patient record in epidemiology. Sci Am 245:54–63, 1981.
23. Rocca WA, Yawn BP, St Sauver JL, et al. History of the Rochester Epidemiology Project: Half a century of medical records.
linkage in a US Population. Mayo Clin Proc 87:1202–1213, 2012.
24. St Sauver JL, Warner DO, Yawn BP, et al. Why patients visit their doctors: Assessing the most prevalent conditions in a defined American population. Mayo Clin Proc 88:56–67, 2013.
25. St Sauver JL, Grossardt BR, Yawn BP, et al. Use of a medical records linkage system to enumerate a dynamic population over time: The Rochester epidemiology project. Am J Epidemiol 173:1059–1068, 2011.
26. Yawn BP, Wollan P, Kurland M, and Scanlon P. A longitudinal study of the prevalence of asthma in a community population of school-age children. J Pediatr 140:576–581, 2002.
27. Yawn BP, Saddier P, Wollan PC, et al. A population-based study of the incidence and complication rates of herpes zoster before zoster vaccine introduction. Mayo Clin Proc 82:1341–1349, 2007.
28. Yawn BP, Itzler RF, Wollan PC, et al. Health care utilization and cost burden of herpes zoster in a community population. Mayo Clin Proc 84:787–794, 2009.
29. Yunginger JW, Reed CE, O’Connell EJ, et al. A community-based study of the epidemiology of asthma. Incidence rates, 1964–1983. Am Rev Respir Dis 146:888–894, 1992.
30. Beard CM, Yunginger JW, Reed CE, et al. Interobserver variability in medical record review: An epidemiological study of asthma. J Clin Epidemiol 45:1013–1020, 1992.
31. Haldar P, Pavord ID, Shaw DE, et al. Cluster analysis and clinical asthma phenotypes. Am J Respir Crit Care Med 178:218–224, 2008.
32. Moore WC, Meyers DA, Wenzel SE, et al. Identification of asthma phenotypes using cluster analysis in the Severe Asthma Research Program. Am J Respir Crit Care Med 181:315–323, 2010.
33. Fitzpatrick AM, Teague WG, Meyers DA, et al. Heterogeneity of severe asthma in childhood: Confirmation by cluster analysis of children in the National Institutes of Health/National Heart, Lung, and Blood Institute Severe Asthma Research Program. J Allergy Clin Immunol 127:382–389.e1–13, 2011.
34. Lazic N, Roberts G, Custovic A, et al. Multiple atopy phenotypes and their associations with asthma: Similar findings from two birth cohorts. Allergy 68:764–770, 2013.
35. Juhn YJ, Kwon HJ, Bang DW, et al. Asthma as an unrecognized risk factor for Herpes zoster in adults: a population-based case-control study. J Allergy Clin Immunol 133(suppl 2), AB 243, 2014.
36. Esteban-Vasallo MD, Dominguez-Berjon MF, Gil-Prieto R, et al. Sociodemographic characteristics and chronic medical conditions as risk factors for herpes zoster: A population-based study from primary care in Madrid (Spain). Hum Vaccin Immunother 10:1650–1660, 2014.
37. Forbes HJ, Bhaskaran K, Thomas SL, et al. Quantification of risk factors for herpes zoster: Population based case-control study. BMJ 348:g2911, 2014.
38. Yoo KH, Jacobson RM, Poland G, Weaver A, Lee L, Chang T, Juhn YJ. Asthma status and waning of measles antibody levels. Pediatr Infect Dis J 33:1016–1022, 2014.
39. Gershon AA, Gershon MD, Breuer J, et al. Advances in the understanding of the pathogenesis and epidemiology of herpes zoster. J Clin Virol 48(suppl. 1):S2–S7, 2010.
40. Santillan Salas CF, Mehra S, Pardo Crespo MR, and Juhn YJ. Asthma and severity of 2009 novel H1N1 influenza: A population-based case-control study. J Asthma 50:1069–1076, 2013.
41. Kloepfer KM, Olenec JP, Lee WM, et al. Increased H1N1 infection rate in children with asthma. Am J Respir Crit Care Med 185:1275–1279, 2012.
42. ANZIC Influenza Investigators, Webb SA, Pettila V, et al. Critical care services and 2009 H1N1 influenza in Australia and New Zealand. N Engl J Med 361:1925–1934, 2009.
43. Jain S, Kamimoto L, Bramley AM, et al. Hospitalized patients with 2009 H1N1 influenza in the United States, April-June 2009. N Engl J Med 361:1935–1944, 2009.
44. Centers for Disease Control and Prevention. What Parents Need to Know about Enterovirus D68. Available online at http://www.cdc.gov/features/evd68/; accessed November 17, 2014.
45. Wark PA, Grissell T, Davies B, et al. Diversity in the bronchial epithelial cell response to infection with different rhinovirus strains. Respiratory Research 14:180–186, 2009.
46. Owens B. Rare enterovirus continues to circulate in North America. Lancet 384:1250, 2014.
47. McGrath KW, Icitovic N, Boushey HA, et al. A large subgroup of mild-to-moderate asthma is persistently noneosinophilic. Am J Respir Crit Care Med 185:612–619, 2012.
48. Bousquet J, Chanez P, Lacoste JY, et al. Eosinophilic inflammation in asthma. N Engl J Med 323:1033–1039, 1990.