Respiratory Infections in Adults with Atopic Disease and IgE Antibodies to Common Aeroallergens

Aino Rantala1, Jouni J. K. Jaakkola1,2,3, Maritta S. Jaakkola1,3,4 *

1 Center for Environmental and Respiratory Health Research, University of Oulu, Oulu, Finland, 2 Public Health, Institute of Health Sciences, University of Oulu, Oulu, Finland, 3 Respiratory Medicine Unit, Department of Medicine, Oulu University Hospital, Oulu, Finland, 4 Respiratory Medicine Unit, Institute of Clinical Medicine, University of Oulu, Oulu, Finland

Abstract

Background: Atopic diseases, including allergic rhinitis, allergic dermatitis and asthma, are common diseases with a prevalence of 30–40% worldwide and are thus of great global public health importance. Allergic inflammation may influence the immunity against infections, so atopic individuals could be susceptible to respiratory infections. No previous population-based study has addressed the relation between atopy and respiratory infections in adulthood. We assessed the relation between atopic disease, specific IgE antibodies and the occurrence of upper and lower respiratory infections in the past 12 months among working-aged adults.

Methods and Findings: A population-based cross-sectional study of 1008 atopic and non-atopic adults 21–63 years old was conducted. Information on atopic diseases, allergy tests and respiratory infections was collected by a questionnaire. Specific IgE antibodies to common aeroallergens were measured in serum. Adults with atopic disease had a significantly increased risk of lower respiratory tract infections (LRTI; including acute bronchitis and pneumonia) with an adjusted risk ratio (RR) 2.24 (95% confidence interval [CI] 1.43, 3.52) and upper respiratory tract infections (URTI; including common cold, sinusitis, tonsillitis, and otitis media) with an adjusted RR 1.55 (1.14, 2.10). The risk of LRTIs increased with increasing level of specific IgE (linear trend P = 0.059).

Conclusions: This study provides new evidence that working-aged adults with atopic disease experience significantly more LRTIs and URTIs than non-atopics. The occurrence of respiratory infections increased with increasing levels of specific IgE antibodies to common aeroallergens, showing a dose-response pattern with LRTIs. From the clinical point of view it is important to recognize that those with atopies are a risk group for respiratory infections, including more severe LRTIs.

Conclusion:

This study provides new evidence that working-aged adults with atopic disease experience significantly more LRTIs and URTIs than non-atopics. The occurrence of respiratory infections increased with increasing levels of specific IgE antibodies to common aeroallergens, showing a dose-response pattern with LRTIs. From the clinical point of view it is important to recognize that those with atopies are a risk group for respiratory infections, including more severe LRTIs.

Methods

Study design

We applied a population-based cross-sectional study design. A random sample of adults 21 to 63 years of age living in Pirkanmaa were drawn using the national population registry, which has full coverage of the population. The Pirkanmaa Hospital District is a geographically defined administrative area in South Finland with a population of 440,913 in 1997 when this study started. A total of...
1016 subjects (response rate 80%) answered the questionnaire. After excluding six persons older than 64 years and two with incomplete questionnaire, our study population included 1008 subjects. Of these, 73.2% gave a serum sample. This population was collected to form the control population of the Finnish Environment and Asthma Study (FEAS), a population-based occupational and work environment, 5) home environment, and 6) dietary questions. The parts of the questionnaire that were used in these were studied as indicators of atopic propensity. These were assessed as indicators of atopic propensity. The determinants of interest were atopic disease and specific IgE antibodies to common aeroallergens or a combination of these. These were assessed as indicators of atopic propensity. The questionnaire also inquired the following questions: Have you ever undergone allergy testing, such as skin prick tests or allergy-antibody tests? and Did these tests reveal any allergies (i.e. were the results positive)?

We performed a systematic literature search of Ovid Medline database with free text (“Atopy” OR “Allergic disease” OR “Allergic patient” OR “Allergic” OR “Immunoglobulin E”) AND with Mesh term “Respiratory tract infections”. We limited the search for English language and human studies. The search produced altogether 262 articles from which three studies [6–8] fulfilled the following criteria: it (i) was a longitudinal/cohort study or case-control study and (ii) reported on relations between atopic diseases and/or specific IgE antibodies and occurrence of respiratory infections. We further searched the reference lists of recent review articles as well as relevant articles identified in our search.

**Systematic literature search**

We studied the relations between atopic disease per se as well as in combination with measured specific IgE antibodies and occurrence of respiratory tract infections by estimating risk ratios (RR) with 95% confidence intervals (CI) from generalized linear model applying PROC GENMOD (SAS v9.3, SAS Institute Inc., Cary, NC, USA) using Poisson regression. The occurrence of infections was compared between subjects with one or several atopic diseases and subjects without any of the atopic diseases (the reference category). Specific IgE was expressed as a Phadiatop score reflecting the IgE antibody levels to common aeroallergens, and the risk of infections among those with higher scores was compared with the score 0 (the reference category). Sex, age, education (as an indicator of socio-economic status), personal smoking, and exposure to SHS in the home or at work were adjusted for as covariates. We tested the adjusted linear trend of the risk of URTIs and LRTIs according to levels of specific IgE based on binomial proportion and their standard errors derived from Poisson regression (proc genmod identity link). In addition, we performed the main analyses stratified by gender which we present in Tables S1, S2 and S3. However, these should be interpreted with caution as this stratification reduces the numbers in specific cells.

**Results**

**Characteristics of the study population**

Table 1 presents characteristics of the total study population and stratified by gender. The prevalence of allergic rhinitis, dermatitis and asthma (previous or current) in this working-aged population was 21.6% (n = 210), 34.1% (n = 344) and 7.5% (n = 76), respectively.

**Association between atopic disease and IgE antibodies**

The proportion of subjects with atopic disease increased significantly with higher IgE levels (i.e. Phadiatop scores 1–6) (Cochran-Armitage Trend Test: P<0.001). The risk of atopic disease was observed to increase with Phadiatop score showing a dose-response pattern: adjusted RR 1.36 (95% CI: 1.01, 1.82) for score 1–2, 1.93 (1.44, 2.57) for score 3–4, and 1.91 (0.77, 4.73) for score ≥4 (Table 2). The RR of atopic disease related to the different Phadiatop scores were slightly higher among men than among women (Table S1).
Atopic disease and the risk of respiratory infections

Results in Table 3 show that subjects with atopic disease experienced more commonly both LRTIs and URTIs in the past 12 months compared to subjects with no atopic disease (12.2% vs. 5.9% and 24.3% vs. 13.3%, respectively). Atopic disease was related to an increased risk of both LRTIs (adjusted RR = 2.24, 95% CI: 1.43, 3.52) and URTIs (adjusted RR = 1.55, 95% CI: 1.29, 1.82). The risk of LRTIs was higher among men than among women.

We also analyzed the risk of infections according to the different atopic diseases (Table 5). Asthma and dermatitis significantly increased the risk of LRTIs (adjusted RR = 4.69, 95% CI: 2.64, 8.35 and RR = 1.82, 95% CI: 1.08, 3.07, respectively) and dermatitis significantly increased also the risk of URTIs (adjusted RR = 1.62, 95% CI: 1.16, 2.26). In addition, the RR of both LRTIs and URTIs related to rhinitis were increased, but these did not reach statistical significance.

**Specific IgE antibodies and the risk of respiratory infections**

The risk of LRTIs increased with increasing specific IgE measured as Phadiatop score (adjusted linear trend \( P = 0.059 \)) suggesting a dose response pattern with specific IgE. The risk of URTIs was also the highest among those with Phadiatop score of more than 4, although the 95% CIs of the adjusted RRs included unity and the trend was not linear (adjusted linear trend \( P = 0.555 \)) (Table 6). The RR of LRTIs seemed to be higher among men than women with the Phadiatop score 3–4, although the numbers in specific cells were small (Table S3). The risk of LRTIs and URTIs related to rhinitis were increased, but these did not reach statistical significance.

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**Table 1.** Characteristics of the total study population and stratified by gender, The Finnish Environment and Asthma Study (FEAS).

| Characteristic            | Female N (%) | Male N (%) | All N (%) |
|---------------------------|--------------|------------|-----------|
| Age (years)               |              |            |           |
| 21–29                     | 89 (16.5)    | 59 (12.6)  | 148 (14.7)|
| 30–39                     | 133 (24.6)   | 150 (22.4) | 283 (26.3)|
| 40–49                     | 150 (27.8)   | 126 (26.9) | 276 (27.4)|
| 50–59                     | 126 (23.3)   | 138 (29.5) | 264 (26.2)|
| 60–64                     | 42 (7.8)     | 40 (8.6)   | 82 (8.1)  |
| Education*                |              |            |           |
| No vocational schooling   | 91 (17.0)    | 74 (15.9)  | 165 (16.5)|
| Vocational course         | 64 (11.9)    | 51 (10.9)  | 115 (11.5)|
| Vocational institution    | 134 (25.0)   | 154 (33.1) | 288 (28.7)|
| College-level education   | 167 (31.1)   | 118 (25.3) | 285 (28.4)|
| University or corresponding | 81 (15.1) | 69 (14.8)  | 150 (15.0)|
| Smoking^b                 |              |            |           |
| No                        | 340 (63.1)   | 182 (39.0) | 522 (51.9)|
| Ex                        | 90 (16.7)    | 132 (28.3) | 222 (22.1)|
| Current                   | 109 (20.2)   | 138 (29.5) | 247 (24.2)|
| SHS in the workplace      | 37 (7.4)     | 103 (23.3) | 140 (14.8)|
| SHS in the home           | 26 (4.8)     | 29 (6.3)   | 55 (5.5)  |

Abbreviations: N, number; SHS, secondhand tobacco smoke.

*aInformation on education was missing for 5 subjects.

*bInformation on smoking was missing for 2 subjects.

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**Table 2.** Association between specific IgE antibody levels and atopic disease, The Finnish Environment and Asthma Study (FEAS).

| Phadiatop score | Subjects with atopic disease | Subjects with no atopic disease | RR (95% CI) | RR* (95% CI) |
|----------------|-----------------------------|-------------------------------|-------------|--------------|
|                | N (%)                       | N (%)                         |             |              |
| Total^b        | 350                         | 378                           |             |              |
| 0              | 227 (64.9)                  | 315 (83.3)                    | 1           | 1            |
| 1–2            | 58 (16.6)                   | 46 (12.2)                     | 1.33 (1.00, 1.78) | 1.36 (1.01, 1.82) |
| 3–4            | 60 (17.1)                   | 16 (4.2)                      | 1.89 (1.42, 2.51) | 1.93 (1.44, 2.57) |
| >4             | 5 (1.4)*                    | 1 (0.3)                       | 1.99 (0.82, 4.83) | 1.91 (0.77, 4.73) |

Abbreviations: CI, confidence interval; IgE, immunoglobulin E; N, number; RR, risk ratio.

^bCochran-Armitage Trend Test, 2-sided \( P \) value < 0.001.

^cRisk ratios adjusted for sex, age, education, smoking and SHS exposure (work/home).

^dTotal number of atopic and non-atopic subjects having Phadiatop result.

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increased in such subjects with an adjusted RR of 1.28 (95% CI: 0.80, 2.05), although this did not reach statistical significance (Table 4).

**Discussion**

**Main Findings**

The results of our large population-based study show that working-aged adults with atopic disease experience consistently more of both LRTIs and URTIs compared to adults with no atopic disease. Subjects with asthma were at the highest risk of LRTIs, experiencing about four times more LRTIs than those without asthma. The risk of infections was even higher when the subject with atopic disease reported positive allergy tests. Furthermore, the risk of infections seemed to increase according to increasing levels of specific IgE, suggesting a dose-response pattern and supporting the hypothesis that allergies are linked to increased susceptibility to infections. The risk of LRTIs and URTIs was also related to atopic dermatitis and allergic rhinitis, although the 95% CI of the latter effect estimate included unity. It is known that atopic diseases share similar impaired immunological mechanisms that may increase susceptibility to respiratory infections [5,19]. It is possible that dermatitis is a more consistent manifestation of atopic constitution and therefore the association with respiratory infections could be stronger compared to rhinitis.

Recently, we published from the Finnish Environment and Asthma Study including the incident (new) cases that respiratory infections were a strong determinant for adult-onset asthma [20]. The strongest risk was seen in those who had atopic disease and had experienced LRTIs during the last 12 months. Taking together the findings of these two studies, it seems that persons with allergy are more prone to respiratory infections and more susceptible to the effects of LRTIs on the risk of asthma.

The mechanisms underlying the susceptibility to microbial infections observed in this study among atopic subjects are poorly understood. Allergic patients typically present a Th2 polarization and hence it is suggested that the protective Th1 response is reduced. In addition, Th2-driven responses are believed to impair the innate immunity mediated host defense responses against microbial infections [3]. Th2-mediated cytokines, such as IL-4 and IL-13, induce airway inflammation that facilitates microbial attachment to the airway epithelia. In addition, IgE antibodies have been shown to suppress neutrophil adhesion that is an important feature of innate immune responses [21]. The present results show that atopic disease and increased levels of specific IgE are significantly related to the risk of both LRTIs and URTIs. We found that those atopic persons who have high IgE level could have stronger inflammation e.g. in airways leading to even stronger susceptible to infections.

**Table 3.** Risk of respiratory infections in the past 12 months in subjects with atopic disease and those with no atopic disease, The Finnish Environment and Asthma Study (FEAS).

| Infection | Subjects with atopic disease | Subjects with no atopic disease | RR (95% CI) | RRb (95% CI) |
|-----------|------------------------------|--------------------------------|-------------|-------------|
| Totalc | 441 (12.2) | 526 | 2.08 (1.34, 3.23) | 2.24 (1.43, 3.52) |
| LRTIs | 54 (12.2) | 31 (5.9) | 2.15 (1.37, 3.35) | 2.32 (1.47, 3.66) |
| Pneumonia | 3 (0.7) | 2 (0.4) | 1.79 (0.30, 10.71) | 2.10 (0.33, 13.18) |
| URTIs | 107 (24.3) | 70 (13.3) | 1.82 (1.35, 2.46) | 1.55 (1.14, 2.10) |
| Common cold | 172 (39.0) | 152 (28.9) | 1.35 (1.09, 1.68) | 1.30 (1.04, 1.62) |
| Sinusitis | 77 (17.5) | 47 (8.9) | 1.95 (1.36, 2.81) | 1.57 (1.08, 2.26) |
| Otitis media | 24 (5.4) | 12 (2.3) | 2.39 (1.19, 4.77) | 2.28 (1.12, 4.61) |

Abbreviations: CI, confidence interval; LRTI, lower respiratory tract infections; N, number; RR, risk ratio; URTI, upper respiratory tract infections.

a1 infection. Common cold 2 infections.
bRR adjusted for sex, age, education, smoking and SHS exposure (work/home).
cTotal number of atopic and non-atopic subjects. Information on infections was missing for 41 subjects.

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**Table 4.** Risk of lower respiratory tract infections and upper respiratory tract infections during the past 12 months among subjects having atopic disease and high specific IgE level or positive allergy tests, The Finnish Environment and Asthma Study (FEAS).

| Atopic manifestation | Lower respiratory tract infections | Upper respiratory tract infections |
|----------------------|------------------------------------|-----------------------------------|
|                      | N | RR (95% CI) | RRb (95% CI) | RR (95% CI) | RRb (95% CI) |
| Atopic disease with positive allergy tests | 199 | 2.56 (1.55, 4.23) | 2.79 (1.66, 4.70) | 1.77 (1.23, 2.57) | 1.42 (0.97, 2.07) |
| Atopic disease with high specific IgE levelb | 119 | 2.14 (1.15, 3.96) | 2.23 (1.19, 4.18) | 1.52 (0.95, 2.41) | 1.28 (0.80, 2.05) |

Abbreviations: CI, confidence interval; N, number; RR, risk ratio.
aRisk ratios adjusted for sex, age, education, smoking and SHS exposure (work/home).
bHigh specific IgE level = Phadiatop score 1–6.
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We found that the association between atopy and lower respiratory infections seemed to be stronger among men than women. However, the present sex stratified results should be interpreted with caution as the numbers in specific cells are small due to the stratification.

Validity of results

The study population was randomly selected from a defined geographic area and the response rate was high (80%). Thus, our results are well generalizable and any major selection bias is unlikely.

Information on the atopic disease was based on reporting allergic rhinitis, allergic dermatitis or asthma diagnosed by a doctor in the questionnaire. Self-reported atopic diseases could include some misclassification, especially if the access to health care system was compromised and related to environmental and dietary conditions that determine their occurrence. The Finnish health care system has a high coverage for the entire population and the majority of the individuals with atopic diseases are likely to receive medical attention. Diagnosis of asthma is further enhanced by reimbursement of medication by the National Social Insurance Institution, which is a strong incentive for an appropriate clinical diagnosis. In addition, we used measurements of specific IgE in combination with reported diseases to strengthen the definition of atopic disease and the risk of both URTIs and LRTIs were increased in this group. Specific IgE antibodies were measured from serum samples using a validated commercial UniCAP system [18]. This method is easier to conduct in a standardized way than skin testing. Phadiatop includes in Finland the following aeroallergens: birch, timothy grass, mugwort, cat, dog, horse, Dermatophagoides pteronyssinus, and Aspergillus fumigatus. The selection of this panel reflects well the most common or otherwise important aeroallergies in Finland. The sensitivity of Phadiatop has been between 0.93 and 0.99 and the specificity between 0.87 and 0.94 by using a clinical diagnosis of atopy as the gold standard [13,18]. In our own study, we found a dose-response pattern in increasing risk of atopic disease with increasing level of specific IgE.

Information about the frequency and type of respiratory infections during the past 12 months was assessed based on reporting in the questionnaire. Although there may be some misclassification, in our opinion it is likely to be non-differential or atopic subjects tend to assume infections as exacerbations of their allergic symptoms and both of these would lead to underestimation of the real effect. We did not have data on specific infectious

| Table 5. Risk of respiratory infections in the past 12 months according to different atopic diseases, The Finnish Environment and Asthma Study (FEAS). |
|---------------------------------|------------------|------------------|------------------|------------------|------------------|
|                                | Lower respiratory tract infections | Upper respiratory tract infections |
|                                | N   | RR (95% CI) | RR* (95% CI) | RR (95% CI) | RR* (95% CI) |
| Totalb                          | 967 | 1             | 1             | 1             | 1             |
| Non-atopic                      | 526 | 1             | 1             | 1             | 1             |
| Asthma                          | 73  | 4.66 (2.65, 8.20) | 4.69 (2.64, 8.35) | 1.85 (1.10, 3.11) | 1.62 (0.96, 2.74) |
| Rhinitis                        | 210 | 1.12 (0.43, 2.88) | 1.24 (0.48, 3.23) | 1.38 (0.78, 2.46) | 1.21 (0.68, 2.17) |
| Dermatitis                      | 337 | 1.69 (1.01, 2.81) | 1.82 (1.08, 3.07) | 1.93 (1.39, 2.67) | 1.62 (1.16, 2.26) |

Abbreviations: CI, confidence interval; N, number; RR, risk ratio.  
*aRisk ratios adjusted for sex, age, education, smoking and SHS exposure (work/home).  
bInformation on infections was missing for 41 subjects.  
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Table 6. Risk of lower and upper respiratory tract infections (≥1 infection) in the past 12 months according to the levels of specific IgE antibodies, The Finnish Environment and Asthma Study (FEAS).

| Specific IgE | N   | Subjects with infections, n (%) | RR (95% CI) | RR* (95% CI) |
|-------------|-----|-------------------------------|-------------|-------------|
| Total       | 700 | 40 (7.7)                      | 1           | 1           |
| Lower respiratory tract infections | 519 | 10 (9.7) | 1.26 (0.63, 2.52) | 1.26 (0.63, 2.54) |
| 0–1         | 103 | 10 (9.7) | 1.78 (0.89, 3.55) | 1.80 (0.89, 3.65) |
| ≥2          | 5   | 1 (20.0)* | 2.60 (0.36, 18.88) | 3.40 (0.44, 26.38) |
| Upper respiratory tract infections | 519 | 103 (19.9) | 1          | 1          |
| 0–1         | 103 | 20 (19.4) | 0.98 (0.61, 1.58) | 1.04 (0.64, 1.68) |
| ≥2          | 73  | 12 (16.4) | 0.83 (0.46, 1.51) | 0.85 (0.46, 1.56) |

Abbreviations: CI, confidence interval; IgE, immunoglobulin E; n, number; RR, risk ratio.  
*aRisk ratios adjusted for sex, age, education, smoking and SHS exposure (work/home).  
Pvalue for the adjusted linear trend test: * 0.059, ** 0.555.  
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agents, but this information is not so relevant from the public health preventive point of view. We collected data concerning different types of infections, including common cold, tonsillitis, sinusitis, otitis media, acute bronchitis or pneumonia, but our main analyses concentrated on LTRIs and URTIs, as it seems plausible that people are able to recall well if they have had a severe respiratory infection, such as acute bronchitis or pneumonia, or a milder upper respiratory infection, although the exact diagnosis may be more difficult to remember.

In the multivariate analyses, all the relations were adjusted for a number of potential confounders to eliminate these factors as explanations for our results.

Synthesis with previous knowledge

In our systematic literature search, no previous population-based study addressing the relations between atopic disease and respiratory infections covering the working aged adults could be identified. Only a few studies had addressed this question in children or young adults. Cirillo and co-workers [7] found in Italian Navy soldiers (with the mean age of 22.7 years) that those with allergic rhinitis had a higher rate of infections. The risk of severe respiratory infections (among which they included middle ear infections, paranasal sinusitis and lower airway infections) was higher than the risk of mild infections. Their results are thus consistent with ours covering adult age. We found that allergic rhinitis was a weaker risk factor for infections than asthma or allergic dermatitis. The Italian study did not address these other forms of allergic diseases. Another Italian study of 3–6 years old children referred to an outpatient clinic reported a higher occurrence of respiratory infections among allergic compared to non-allergic children [6]. Kvaerner and co-workers [8] studied the occurrence of URTIs in a population-based cross-sectional study of Norwegian children aged 4 to 5 years and found that infections were associated with atopic disease. A British study followed for 3–4 months 76 cohabiting couples, one having atopic asthma and the other being healthy, and took repeatedly nasal samples for rhinovirus analysis [22]. They did not find differences in rhinovirus-related URTIs, but asthmatics were more likely to have LRTIs. In addition to studies focusing on respiratory tract infections, a population-based case-control study using registries as sources of information found increased risk of serious pneumococcal disease (including sepsis, meningitis and pneumonia) in both children and adults with atopic disease other than asthma [23]. Association between levels of specific IgE antibodies and respiratory infections has not been studied previously.

Conclusions

We present here new evidence that working-aged adults with atopic disease are more susceptible to both LRTIs and URTIs than adults with no atopic disease. In addition, the occurrence of respiratory infections increased with increasing levels of specific IgE antibodies to common aeroallergens, showing a dose-response pattern with LRTIs. From the preventive and clinical point of view it is important to recognize that those with atopes are a risk group for respiratory infections, including more severe lower respiratory infections. Relevant questions for the future are to study whether effective treatment of allergic diseases could prevent respiratory infections, and to consider if all those with atopic diseases should be subject to preventive measures, such as vaccinations.

Supporting Information

Questionnaire S1 The parts of the questionnaire that were used in this study, The Finnish Environment and Asthma Study (FEAS).

Table S1 Association between specific IgE antibody levels and atopic disease stratified by gender, The Finnish Environment and Asthma Study (FEAS).

Table S2 Risk of respiratory infections in the past 12 months in subjects with atopic disease and those with no atopic disease stratified by gender, The Finnish Environment and Asthma Study (FEAS).

Table S3 Risk of lower and upper respiratory tract infections (≥1 infection) in the past 12 months according to the levels of specific IgE antibodies stratified by gender, The Finnish Environment and Asthma Study (FEAS).

Author Contributions

Conceived and designed the experiments: MSJ [JKJ]. Analyzed the data: AR. Contributed reagents/materials/analysis tools: JJKJ. Wrote the paper: AR [JKJ MSJ].

References

1. Pawanker R, Canonica GW, Holgate S, Lockey R (eds) World Allergy Organization. White Book on Allergy 2011–2012 Executive Summary.
2. Kay AB (2001) Allergy and allergic diseases. First of two parts. N Engl J Med 344(10): 78–87.
3. Ciprandi G, Passalacqua G (2008) Allergy and the nose. Clin Exp Immunol 153 Suppl 1: 22–26.
4. Gilmore MI (2012) Influence of air pollutants on allergic sensitization: the paradox of increased allergies and decreased resistance to infection. Toxicol Pathol 40(6): 312–314.
5. Mrabet-Dahbi S, Maurer M (2010) Does allergy impair innate immunity? Leads and lessons from atopic dermatitis. Allergy 65(11): 1351–1356.
6. Ciprandi G, Tosca MA, Fasce L (2006) Allergic children have more numerous and severe respiratory infections than non-allergic children. Pediatr Allergy Immunol 17(5): 389–391.
7. Cirillo I, Marangoni G, Klever C, Ciprandi G (2007) Allergic patients have more numerous and prolonged respiratory infections than non-allergic subjects. Allergy 62(9): 1057–1060.
8. Kvaerner KJ, Naftad P, Jaakkola JJ (2000) Upper respiratory morbidity in preschool children: a cross-sectional study. Arch Otolaryngol Head Neck Surg 126(10): 1201–1206.
9. Jaakkola JJ, Iermomimou A, Jaakkola MS (2006) Interior surface materials and asthma in adults: a population-based incident case-control study. Am J Epidemiol 164(6): 742–749.
10. Jaakkola JJ, Jaakkola N, Pipari R, Jaakkola MS (2002) Pets, parental atopy, and asthma in adults. J Allergy Clin Immunol 109(5): 784–788.
11. Jaakkola JJ, Miettinen P (1995) Type of ventilation system in office buildings and sick building syndrome. Am J Epidemiol 141(8): 755–765.
12. Jaakkola JJ, Pipari R, Jaakkola MS (2003) Occupation and asthma: a population-based incident case-control study. Am J Epidemiol 158(10): 981–987.
13. Jaakkola MS, Iermomimou A, Jaakkola JJ (2006) Are atopic and specific IgE to mites and molds important for adult asthma? J Allergy Clin Immunol 117(3): 642–648.
14. Jaakkola MS, Jaakkola JJ (1999) Office equipment and supplies: a modern occupational health concern? Am J Epidemiol 150(11): 1223–1228.
15. Jaakkola MS, Nordhamn H, Pipari R, Uutti J, Laatikainen J, et al. (2002) Indoor dampness and molds and development of adult-onset asthma: a population-based incident case-control study. Environ Health Perspect 110(5): 543–547.
16. Jaakkola MS, Pipari R, Jaakkola N, Jaakkola JJ (2005) Environmental tobacco smoke and adult-onset asthma: a population-based incident case-control study. Am J Public Health 93(12): 2055–2060.
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17. Piipari R, Jaakkola JJ, Jaakkola N, Jaakkola MS (2004) Smoking and asthma in adults. Eur Respir J 24(5): 734–739.
18. Paganelli R, Ansotegui IJ, Sastre J, Lange CE, Roovers MH, et al. (1998) Specific IgE antibodies in the diagnosis of atopic disease. Clinical evaluation of a new in vitro test system, UniCAP, in six European allergy clinics. Allergy 53(8): 763–768.
19. Grove DJ, Reid JG, Forbes IJ (1975) Humoral and cellular immunity in atopic eczema. Br J Dermatol 92(6): 611–618.
20. Rantala A, Jaakkola JJ, Jaakkola MS (2011) Respiratory infections precede adult-onset asthma. PLoS One 6(12): e27912.
21. al-Mohanna F, Parhar R, Kawaasi A, Ernst P, Sheth K, et al. (1993) Inhibition of neutrophil functions by human immunoglobulin E. J Allergy Clin Immunol 92(5): 757–766.
22. Corne JM, Marshall C, Smith S, Schreiber J, Sanderson G, et al. (2002) Frequency, severity, and duration of rhinovirus infections in asthmatic and non-asthmatic individuals: a longitudinal cohort study. Lancet 359(9309): 831–834.
23. Jung JA, Kita H, Yawn BP, Boyce TG, Yoo KH, et al. (2010) Increased risk of serious pneumococcal disease in patients with atopic conditions other than asthma. J Allergy Clin Immunol 125(1): 217–221.