Original Article

Increase in Allergic Sensitization in Schoolchildren: Two Cohorts Compared 10 Years Apart

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What is already known about this topic? Allergic sensitization is the cornerstone in allergic diseases and a major risk factor for asthma and allergic rhinitis.

What does this article add to our knowledge? High incidence and low remission of allergic sensitization among schoolchildren explain the increased prevalence by increasing age. Both incidence and prevalence increased significantly compared with a cohort examined identically 10 years earlier.

How does this study impact current management guidelines? As a consequence of increasing incidence and prevalence of allergic sensitization, the prevalence of allergic diseases may continue to increase in the population.

BACKGROUND: Time trends of incidence of allergic sensitization are unknown and recent trends of prevalence and risk factors are lacking.

OBJECTIVE: To estimate the incidence, prevalence, remission, risk factors, and time trends for allergic sensitization among schoolchildren followed from age 7 to 8 years to age 11 to 12 years.

METHODS: In 2006, all children in grades 1 and 2 aged 7 to 8 years in 2 municipalities in northern Sweden were invited to a questionnaire survey and to skin prick testing to 10 common airborne allergens. The cohort was reexamined in 2010, with additional blood sampling for specific IgE. Participation rates were 90% (n = 1700) at age 7 to 8 years and 85% (n = 1657) at age 11 to 12 years. The results were compared with a cohort examined by identical methods 10 years earlier.

RESULTS: The prevalence of positive skin prick test result to any allergen increased from 30% at age 7 to 8 years to 41% at age 11 to 12 years ($P < .001$). The cumulative 4-year incidence was 18%, while remission was low. Sensitization to pollen and furred animals was most common. A family history of allergy was significantly associated with incident sensitization, whereas the presence of furred animals at home was negatively associated. The prevalence at age 7 to 8 years and at age 11 to 12 years and the 4-year incidence were all significantly higher compared with the cohort examined 10 years earlier.

CONCLUSIONS: The prevalence of allergic sensitization increased by age as a consequence of a high incidence and a low remission. The trends of increasing incidence and prevalence among schoolchildren imply future increases in the prevalence of allergic diseases. **(J Allergy Clin Immunol Pract 2016;■:■-■)**

Key words: *Allergic sensitization; Prevalence; Incidence; Risk factors; Longitudinal study; Schoolchildren*

Allergic diseases among children are important issues of public health.[1] The prevalence of asthma and rhinitis has increased particularly in high-income countries in recent decades, and developing countries seem to follow.[2] The prevalence may have leveled in some countries with a high prevalence, although results are ambiguous.[3-5] Studies of prevalence trends and incidence of allergic sensitization have a high clinical relevance because allergic

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Abbreviations used
OLIN- Obstructive Lung diseases In Northern Sweden
OR- Odds ratio
RR- Risk ratio
SPT- Skin prick test

sensitization is a major risk factor for development[6,7] and persistence of asthma from childhood through adolescence.[8] However, few studies have investigated trends in the prevalence of allergic sensitization by using objective methods, and existing studies are not consistent.[3,4,9-14]

The prevalence of allergic sensitization to airborne allergens increases with age during childhood and adolescence as a consequence of high incidence and low remission.[15-17] Among adults, incidence is low and remission substantial.[18] A family history of allergy is consistently reported as a risk factor for allergic sensitization,[17,19,20] as is male sex if sex difference is recognized.[21] A protective effect of rural living,[22] having older siblings,[23] growing up on a farm,[24,25] and having furry animals at home has been found in some, but not all studies.[17,26]

When studying incidence, it is vital to examine the same study population repeatedly with identical methods. Despite existing objective methods such as skin prick test (SPT) and specific IgE, large population-based cohort studies of allergic sensitization are scarce,[15-17] and very few studies have investigated risk factors based on incident cases. We have previously reported a major increase in the prevalence of allergic sensitization at age 7 to 8 years in 2 population-based cohorts examined 10 years apart.[13] We also have reported about the high incidence of allergic sensitization during school age.[17] To our knowledge, no study comparing incidence over time has been published.

The aim of the present study was to determine the prevalence, incidence, and remission of allergic sensitization and to identify risk factors for incidence in a population-based cohort of children followed from age 7 to 8 years to age 11 to 12 years. These results were compared with a cohort investigated with identical methods in the same geographic area 10 years earlier.[17]

METHODS

Study population

Within the Obstructive Lung diseases In Northern Sweden (OLIN) studies, 2 pediatric longitudinal cohort studies are ongoing. The OLIN pediatric cohort II was recruited in 2006 when all children in grades 1 and 2, aged 7 to 8 years in 3 municipalities, Kiruna, Luleå, and Piteå, were invited to participate in a questionnaire study about asthma and allergy. The children in Kiruna and Luleå were also invited to skin prick testing, and 1700 (90% of invited) participated.[13] The cohort was reexamined in 2010 when all children in grades 5 and 6 now aged 11 to 12 years were reinvited using identical methods, and 1657 (85% of invited) participated in SPT.[13] In total, 1450 children participated in SPT both at age 7 to 8 years and at age 11 to 12 years. In addition, at age 11 to 12 years, all children in Kiruna and a random sample of children in Luleå were invited to blood sampling for IgE, and 696 (71%) participated.[27] Participation rates did not differ by municipality and sex. For comparisons of time trends of incidence and prevalence at age 11 to 12 years, the OLIN pediatric cohort I, which was recruited in 1996 and described below, was used (Figure 1).

Consent for SPT was obtained from children and parents. The studies were approved by the regional ethics review board at Umeå University.

Questionnaire

The study questionnaire included the International Study of Asthma and Allergy in Childhood questionnaire[28] and additional questions about physician diagnoses, use of medication, symptoms and risk factors for allergic sensitization, asthma, rhinitis, and eczema, and has been described previously.[13,29,30] The questionnaire was distributed by the teachers and completed by the parents.

Allergic sensitization

SPTs were carried out between February and April at all surveys by a limited number of experienced and specifically trained staff following the European Academy of Allergy and Clinical Immunology recommendations.[31] The tests were performed on the volar aspect of the forearm by using a lancet with a 1-mm tip. The tested allergens were birch, timothy, mugwort, dog, cat, horse, *Dermatophagoides farinae*, *D pteronyssinus*, *Cladosporium*, and *Alternaria* (Soluprick, ALK, Hørsholm, Denmark). The potency of the extracts was 10 HEP, except the 2 moulds, which were 1:20 w/v. Histamine 10 mg/mL and glycerol were used as positive and negative controls. A *positive reaction* was defined as a mean wheal diameter of 3 mm or more after 15 minutes.

Serum samples were collected at the occasion of the SPT.[27] Total IgE and specific IgE levels against the same allergens as at SPT, except *Alternaria*, were measured by the Immuno CAP system (Thermo Fisher, Uppsala, Sweden). IgE concentrations of 0.35 IU/mL or more were considered positive.

The OLIN pediatric cohort I

The OLIN pediatric cohort I was recruited 10 years earlier, in 1996, and has been investigated using identical methods as the OLIN pediatric cohort II described above (Figure 1). We have previously in detail reported about the prevalence and incidence of allergic sensitization in this cohort.[13,17,29] Briefly, participation in SPT at age 7 to 8 years was 2148 (88% of invited) and at age 11 to 12 years was 2155 (88% of invited); 1870 children participated at both occasions. At age 11 to 12 years, a random sample in Luleå and all children in Kiruna were invited to blood sampling, and 845 (78%) children participated. Specific IgE levels to birch, timothy, cat, and dog were measured by the Immuno CAP system (Pharmacia Upjohn, Uppsala, Sweden).[32]

Definitions

Any positive SPT: A positive reaction to any of the tested allergens.
Any pollen: A positive reaction to birch, timothy, or mugwort.
Any animal: A positive reaction to cat, dog, or horse.
Any mite: A positive reaction to D farinae or D pteronyssinus.
Any mould: A positive reaction to Cladosporium or Alternaria.
Additional sensitization: Any positive SPT result while negative to the specific allergen at age 7 to 8 years and positive SPT result to the specific allergen at age 11 to 12 years, that is, an already sensitized individual developing further sensitization toward the specific allergen during the study period.

Information about potential risk factors was obtained from the questionnaire at age 7 to 8 years. The following definitions were used: