Ann Allergy Asthma Immunol xxx (2017) 1–5

Contents lists available at ScienceDirect

Natural history of skin prick test reactivity

A 20-year prospective study of a random population sample of children and adolescents

Jesper Schou Nielsen, MD [*]; Howraman Meteran, MD [*]; Charlotte Suppli Ulrik, MD, DMSci [†,‡]; Celeste Porsbjerg, MD, PhD [*,‡]; Vibeke Backer, MD, DMSci [*,‡]

[*] *Respiratory Research Unit, Bispebjerg University Hospital, Copenhagen, Denmark*
[†] *Department of Pulmonary Medicine, Hvidovre Hospital, Hvidovre, Denmark*
[‡] *Institute of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark*

ARTICLE INFO

Article history:
Received for publication January 25, 2017.
Received in revised form April 10, 2017.
Accepted for publication May 1, 2017.

ABSTRACT

Background: Allergic reactions to airborne allergens may have important consequences for affected individuals and are believed to be unstable through life, although evidence from longitudinal studies is limited.

Objective: To assess changes in skin prick reactivity during 20 years in a random population sample of children and adolescents in relation to symptoms of rhinitis.

Methods: A total of 983 individuals, aged 7 to 17 years, were randomly selected in 1986 and invited to 4 examinations during a 20-year period. During each examination, a skin prick test was performed using common local aeroallergens (ie, birch, grass, mugwort, horse, dog, cat, house dust mite [*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*] and 2 molds [*Alternaria iridis* and *Cladosporium herbarum*]).

Results: The prevalence of allergy to any tested allergen peaked at the ages of 13 to 23 years. Rates of sensitization were variable. In the group of individuals tested more than once (n = 592), 16% developed sensitization during the study period and 9% became desensitized. In the group of individuals tested at all 4 examinations (n = 148), 34% developed sensitization and 22% became desensitized. In the group who developed sensitization, 55% had rhinitis, 17% had asthma, and 70% had eczema. In the group who became desensitized, 30% had rhinitis, 10% had asthma, and 50% had eczema.

Conclusion: This 20-year prospective study found that sensitization is common, but its prevalence in individuals is also variable over time. Furthermore, through puberty and early adulthood a large number of individuals develop sensitization and a smaller number become desensitized. In addition, we found that symptoms of rhinitis rarely preceded sensitization.

Introduction

Allergy to airborne allergens is an increasing health problem[1–3] and is associated with poor quality of life,[4] primarily caused by an increase in symptoms in the upper and lower airways. Left untreated, allergies can result in an worsening of asthma symptoms,[5] worsening of allergic rhinitis, and development of rhinosinusitis with polyposis[6] and can lead to an exacerbation of atopic dermatitis.[7,8] It has been estimated that improved treatment of allergic diseases in the skin and respiratory system can reduce the financial costs related to allergic diseases.[9]

An important tool in diagnosing an allergy is the skin prick test (SPT).[10,11] However, our knowledge of changes over time in reactivity and the clinical implications of sensitization to the different groups of aeroallergens (ie, pollen, fur, house dust mites, and mold) remains limited. The few longitudinal studies completed have mostly observed the study population for a period of 2 to 8 years and found that sensitization is developed through childhood and puberty[12,13] and lost in late adulthood.[14] The aim of the present study was, therefore, to examine the change in SPT reactivity in a random population sample of children and adolescents during a 20-year period.

Methods

Material and Methods

The study participants were randomly selected from the Danish civil registration list based on each potential participant's

Reprints: Howraman Meteran, MD, Bispebjerg University Hospital, Respiratory Research Unit, Bispebjerg Bakke 23, Copenhagen NV, Copenhagen 2400, Denmark; E-mail: hmeteran@gmail.com.

Disclosures: Authors have nothing to disclose.

http://dx.doi.org/10.1016/j.anai.2017.05.001
1081-1206/

year of birth between 1969 and 1979 and the date of birth falling during the first week of each month of the relevant year. Therefore, 983 children and adolescents aged 7 to 17 years from Copenhagen, Denmark, were identified and invited by letter to participate in a study that focused on asthma, allergy, and airway hyperresponsiveness. Participants 18 years or older gave written consent for participation; for participants younger than 18 years, written consent were obtained from the parents. The participants were examined 4 times during a 20-year period (1986, 1992, 1998, and 2006). Mean age when included in 1986 was 12 years.

Of the 983 individuals, 527 (54%) participated in the first examination, and 519 completed an SPT; 662 (67%) participated in the second examination, and all participants completed an SPT; 532 participated in the third examination, and 525 participants completed an SPT; and 297 (30%) participated in the fourth examination, and all participants completed an SPT (Table 1). A total of 835 individuals (85%) completed 1 or more SPT; 200 individuals (20%) completed 1 SPT; 250 individuals (25%) completed 2 SPTs; 237 individuals (24%) completed 3 SPTs; and 148 individuals (15%) completed SPTs in all 4 examinations. Study participants providing data from only 1 SPT were only included in the cross-sectional analyses.

Exclusion Criteria

Participants who were taking medication for asthma or allergies were asked not to use antihistamine for at least 24 hours before the SPT.

Skin Prick Test

SPTs were performed on the volar surface of the forearm with standard dilutions of allergens in 50% glycerol (ALK, Hørsholm, Denmark). The allergens used were birch, grass (timoté), mugwort, horse, dog, cat, house dust mite (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*), *Cladosporium herbarium*, and *Alternaria iridis* (mold) (ALK-Abello, Hørsholm, Denmark).

Histamine hydrochloride (10 mg/mL) in 50% glycerol was used as a positive reference, and a negative reference (50% glycerol) was also included. The reactions were read after approximately 15 to 20 minutes. Double testing was used, so each allergen was tested 2 times at each examination, and reactions were measured as the largest diameter of the wheal for each reaction (D1 and D2). A reaction to each of the allergens was regarded as positive if the mean wheal diameter [(D1 + D2)/2] was at least 3 mm.[15] In case of reaction to the negative reference, a positive result was recorded when the difference between the mean wheal diameter of the reaction to the allergen and that to the negative reference exceeded 3 mm. A positive SPT result was defined as a positive reaction to at least one of the allergens.[15] Sensitization was defined as a positive SPT result.

Longitudinal Analyses

Individuals tested more than once were eligible for partial longitudinal analysis. Changes in sensitization to allergens were noted. Only individuals tested 4 times were eligible for full longitudinal analysis.

Statistical Analysis

The χ^2 test was used to compare the prevalence over time. Descriptive statistics were calculated using SPSS statistical software, version 22.0 (SPSS Inc, Chicago, Illinois). All individuals gave informed consent at each examination, and the local ethics committee in Copenhagen approved the study.

Results

Overall Prevalence of Sensitization

During the 20-year study period, the overall prevalence of sensitization increased from 24% at the first examination to 35% at the fourth examination ($P < .001$) (Fig 1). In the same examinations (ie, the first and fourth), sensitization to pollen increased from 13% to 30% ($P < .001$), with grass being the most common allergen, increasing from 7% to 23% ($P < .001$), birch increasing from 7% to 15% ($P < .001$), and mugwort increasing from 5% to 9% ($P = .03$) (Table 2). Sensitization to animal dander increased from 10% to 17% ($P = .006$), sensitization to house dust mites remained the same (14% vs 13%) ($P = .92$), and sensitization to molds increased from 3% to 6% ($P = .05$) (Fig 1).

Longitudinal Findings

In the group of individuals who had SPTs performed more than once, 16% developed sensitization and 9% became desensitized (Table 3). With respect to the group of individuals who underwent the SPT at all 4 examinations (n = 148 [14% of total cohort]), 34% developed sensitization, with the highest rate of sensitization between the first and second examinations. In terms of desensitization, 22% became desensitized during the study, peaking between the second and third examinations, with 15% becoming desensitized (Fig 2).

Symptoms

Of the 148 individuals participating in all examinations, 47 individuals developed sensitization during the study. Of these, 26 individuals (55%) had symptoms of rhinitis, 8 individuals (17%) had asthma, and 33 individuals (70%) had eczema during the study period. Of the 148 individuals participating in all examinations, 10 individuals lost sensitization during the study; of these, 3 individuals (30%) had rhinitis, 1 individual (10%) had asthma, and 5 individuals (50%) had eczema (Table 4). In this desensitization group, a large number of individuals lost their symptoms of allergic diseases during the study period; 2 individuals (67%) lost symptoms of rhinitis, 1 individual (100%) lost symptoms of asthma, and

Table 1
Characteristics of the 983 Study Participants From the Copenhagen Cohort Who Provided Data on SPT Reactivity From the 4 Examinations

Characteristic	Year				Complete data (n = 148)
	1986 (n = 519)	1992 (n = 662)	1998 (n = 525)	2006 (n = 297)	
Sex, M/F, No.	258/261	321/341	229/296	130/167	62/86
Age for M/F, mean (SD), y	12.1 (2.8)/12.3 (2.9)	18.5 (2.8)/18.7 (2.9)	23.9 (2.9)/23.9 (3.0)	33.2 (2.9)/33.3 (3.0)	21.9 (2.8)/21.9 (2.9)
SPT completed, %	98	100	99	100	100

Abbreviation: SPT, skin prick test.