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Features of sensitization to airborne allergens among extra-european immigrants living in 2 distinct areas of Northern Italy

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SUMMARY

Background: Extra-European immigrants are increasingly seen in allergy clinics. In view of their different genetic background they represent an opportunity to investigate the dynamics of sensitization to airborne allergens. **Objective:** We investigated the pattern of airborne sensitization among allergic extra-European immigrants living in two areas of northern Italy. **Methods:** Extra-European immigrants living in Milan and Verona were compared with age- and sex-matched or allergen-matched allergic Italians. Based on number of sensitizations to airborne allergens, patients and controls were divided into mono-/oligo-sensitized or multi-sensitized (1-3 or > 3, respectively). **Results:** In Milan grass pollen allergy was more frequent among immigrants than in controls (75% vs 49%; $p < 0.01$), whereas ragweed allergy prevailed among Italians (56% vs 20%; $p < 0.001$). In Verona, immigrants were rarely multi-sensitized (21% vs 43%; $p < 0.01$), more frequently sensitized to grass and birch. In both areas immigrants became allergic at a significantly older age than Italian controls ($p < 0.0001$), particularly to grass and mites. Allergy to HDM and ragweed was rare in Central & South Americans, whereas Africans showed the lowest proportion of multi-sensitizations. On average, immigrants became allergic after 2-4 years of stay in Italy. **Conclusion:** Subjects genetically prone to become allergic to a particular allergen get eventually sensitized irrespective of their age when they are exposed to the "right" allergen for a sufficiently long time. The higher proportion of mono-/oligo-sensitized immigrants might reflect a shorter exposure to airborne allergen load in this group.

Introduction

Nowadays immigrants from extra-European countries represent an increasing proportion of patients seen in allergy clinics. Leaving their home countries, these subjects become suddenly exposed to a completely new environment characterized by a different climate, foods, and airborne allergens, and are in most cases exposed to a much higher amount of pollutants. The genetic background dif-

fers profoundly from that of the resident population, particularly if they are from Extra-European countries. In most cases these subjects, which have not been suffering from any allergic disease in their homelands, get sensitized at an adult age after some years of contact with a westernized lifestyle. Thus, allergic extra-European immigrants represent an invaluable opportunity to investigate the differences in sensitization patterns from the resident population. Studies of this sort have not been frequently

carried out before. Those performed in the '90s and at the beginning of the new century highlighted the relevance of the new environment in sensitization process (1-6). Some of these studies underlined the role of poor socio-economic status in the frequent development of hypersensitivity to particular airborne allergens such as house dust mites (7). In 2001 the European Community Respiratory Health Survey (8) found higher rates of asthma in immigrants, although bronchial hyper-responsiveness and atopy were similar to the non-migrant population. However, some data suggested that in general, migrants are more prone to the development of allergies than the local population (9). In a study carried out in northern Italy, immigrants from all Central- and South American countries seemed to show an increased risk of allergy and asthma (10), and a high rate of asthma among immigrants was detected in other countries as well (11). On the other hand, some recent Italian studies have highlighted the increasing prevalence of sensitization to local allergens and of asthma in immigrant children and adults (12, 13). The present study aimed to investigate the pattern of sensitization among extra-European immigrants living in two distinct areas of northern Italy from the allergen point of view.

Methods

Patients and controls

This retrospective study was carried out on allergic extra-European immigrants living in two areas of northern Italy. Those living in the area North of Milan were seen at the allergy centre of the Clinica San Carlo during the last 8 years. This area is characterized by the presence of high concentrations of ragweed pollen. Grass, and birch represent other major causes of seasonal airborne allergy, whereas pellitory, cypress, mugwort, and olive pollen are minor allergens. Patients living in the area of Verona were seen at the allergy centre of Verona General Hospital during the last 5 years. Although sited also in the Po basin and only 150 km away from Milan, Verona is characterized by a very low prevalence of ragweed allergy and a much higher prevalence of olive and cypress pollen allergy due to its closeness to the Garda lake area.

The admission criteria for the study included allergy to airborne allergens and birth outside Europe. Ninety-five patients (mean age 34 years, range 9-64 years; M/F 28/67) eventually entered the study in the area of Milan,

and 75 (mean age 33,4 years, range 9-53 years; M/F 32/43) in the area of Verona. Patients were carefully interviewed in order to ascertain the presence of seasonal and/or perennial respiratory symptoms, including rhinoconjunctivitis with or without asthma. Further, the year of arrival in Italy and the year of appearance of symptoms were investigated.

Italian age- and sex-matched or allergen-matched patients with respiratory allergy, randomly selected among the thousands seen at the same centres during the same period were used as controls.

Skin tests

All patients underwent SPT with the same panel of commercial allergen extracts including pollens (grass, mugwort, ragweed, pellitory, plantain, birch, plane, olive, and cypress), house dust mites, animal dander (cat, dog), and moulds (*Alternaria*, *Aspergillus*, *Cladosporium*, *Candida*) (all by Allergopharma, Reinbeck, Germany). All SPT were performed and read following established methods (14). Since all in-vivo tests were part of the routine evaluation of subjects presenting spontaneously at the clinic for diagnostic and therapeutic purposes, no formal informed consent was required.

Since molecule-based allergy diagnostic assays were not yet available at the time when most patients were visited, in order to avoid the possible interference of plant pan-allergens (profilin and polcalcin) hypersensitivity in the analysis, pollen-hypersensitive patients were divided on the basis of the number of positive skin responses to the allergen sources tested. Those scoring positive for 1-3 seasonal allergen sources were regarded a mono- or oligo-sensitized. Those scoring positive to > 3 allergens were considered multi-sensitized irrespective of the fact that they were really co-sensitized to the different allergen sources or showed co-recognition of a pollen pan-allergen. Previous studies carried out at this allergy centre showed that this is an adequate means to distinguish patients sensitized or not sensitized to cross-reacting pan-allergens (15).

Statistics

Proportions were compared by chi-square test with Yates' correction. Means were compared by two tailed Student's t-test. Probability (p) values < 5% (i.e., < 0.05) were considered statistically significant.

Results

Duration of stay in Italy and disease duration

The median stay in Italy for immigrants from both areas was 8 years (range 1-20 years for Milan; 2-25 years for Verona). The median disease duration was 5 years (range 1-10) for immigrants living in Milan and 4 years (1-29) for those living in Verona. The time between arrival in Italy and the first appearance of allergic symptoms ranged between 0 and 15 years (median 2 years) in Milan and between 0 and 23 years (median 4 years) in Verona. Some patients from the Verona group had been suffering from respiratory allergy before their arrival in Italy.

Prevalence of sensitization to different allergen sources

A comparison between extra-European immigrants (patients) and age- and sex-matched allergic Italians (controls) living in the two areas studied is shown in Table 1. In Milan a similar proportion of multi-sensitized patients was present in the two groups and, among subjects sensitized to 1-3 allergen sources, a similar prevalence of sensitization to mites, animal dander, moulds, and to different pollens (birch, cypress, pellitory, mugwort, plane). In con-

trast, significant differences in the prevalence of allergy to grass and ragweed pollen were observed, the former being much more frequent among immigrants than in Italian controls (49/65 [75%] vs 30/61 [49%], respectively; $p < 0.01$) and the latter being much more frequent among Italians (34/61 [56%] vs 13/65 [20%], respectively; $p < 0.001$).

In Verona, multi-sensitization was significantly less frequent among immigrants than among age- and sex-matched Italian controls (16/75 [21%] vs 32/75 [43%]; $p < 0.01$; Table 1). Among subjects sensitized to 1-3 allergen sources, immigrants showed a significantly higher prevalence of sensitization to grass and birch pollen (Tab. 1), whereas no difference in the prevalence of sensitization to the other airborne allergens was detected.

Comparing the whole populations of patients and controls, immigrants showed a significantly higher prevalence of mono- or oligo-sensitized subjects ($p < 0.05$) and a lower prevalence of mugwort and *Alternaria* sensitization.

Age at onset

As a whole, in the area of Milan extra-European immigrants showed a significantly higher age at onset of allergic symptoms than age- and sex-matched Italian controls

Table 1 - Comparison between allergic extra-European immigrants and age- and sex-matched allergic Italians living in the area of Milan and Verona

	Milan			Verona			MI + VR
	Patients	Controls	p	Patients	Controls	p	
Total	95	95		75	75		
Multi-sensitized	30	34	NS	16	32	< 0.01	
Mono- or pauci-sensitized	65 (68%)	61 (64%)	NS	59 (79%)	43 (57%)	< 0.01	< 0.05
Grass	49 (75%)	30 (49%)	< 0.01	43 (73%)	19 (44%)	< 0.01	< 0.0005
Ragweed	13 (20%)	34 (56%)	< 0.001	0 (0%)	0 (0%)	NS	
Mugwort	0 (0%)	5 (8%)	NS	2 (3%)	4 (9%)	NS	< 0.05
Parietaria	1 (1%)	1 (1%)	NS	5 (8%)	6 (14%)	NS	NS
Birch	9 (9%)	8 (13%)	NS	13 (22%)	2 (5%)	< 0.05	NS
Cypress	2 (2%)	1 (2%)	NS	3 (5%)	6 (14%)	NS	NS
Olive	0 (%)	0 (0%)	NS	12 (20%)	6 (14%)	NS	
<i>Alternaria</i>	0 (0%)	4 (6%)	NS	0	4 (9%)	NS	< 0.05
Mite	19 (20%)	13 (14%)	NS	15 (25%)	16 (37%)	NS	NS
Animals	1 (1%)	4 (6%)	NS	8 (14%)	11 (26%)	NS	NS

(Mean 29.9 [SD 9.4] [Median 30] years vs 24.4 [SD 11.6] [median 24] years, respectively; $p < 0.0001$).

Comparing pauci-sensitized patients and controls hypersensitive to the 3 main airborne allergens present in the area of Milan (grass pollen, ragweed pollen, and house dust mite), immigrants were found to become sensitized to grass pollen and house dust mite at a significantly older age than the Italian allergen-matched controls ($p < 0.001$, and $p < 0.01$, respectively) whereas the age at onset of ragweed allergy was virtually identical in the two groups (table 2).

Also in the area of Verona the mean age at onset of allergic symptoms was significantly higher among immigrants than among age- and sex-matched Italian controls (Mean

29.0 [SD 8.96] [median 29] years vs 24.4 [SD 8.65] [median 24] years; $p < 0.005$). A comparison between subjects pauci-/monosensitized to the 2 major allergens present in the area of Verona is shown in Table 2. Similarly to Milan, immigrants were found to become allergic to grass pollen at a significantly older age than Italian controls ($p < 0.001$), whereas no difference between subjects allergic to mites in the two groups was observed.

Analysis by region of origin of immigrants

The pattern of sensitization of immigrants from the 3 geographic macro-areas of the world is shown in Table 3. The age at onset of allergic symptoms was similar in the three subgroups (data not shown). Immigrants from Central & South America showed a significantly lower prevalence of sensitization to house dust mite than immigrants from Asia and Africa, and a higher prevalence of sensitization to grass pollen than Italian controls. In contrast ragweed sensitization was infrequent in this subgroup. Africans showed a significantly lower prevalence of multi-sensitized subjects than both immigrants from other geographic regions and Italian controls.

Discussion

This is one of the first studies investigating respiratory allergies in immigrants and comparing them with allergies found in the autochthonous population at the level of al-

Table 2 - Comparison between the age at onset of allergic symptoms in extra-European immigrants and allergen-matched Italians sensitized to the most common airborne allergens detected in the two study centers

Allergen	Patients	Controls	
MILAN			
Grass	34,9 (10,8) [34]	21,2 (11,8) [20]	< 0.001
Ragweed	32,8 (10,1) [32]	33,9 (12,8) [34]	NS
Mite	32,5 (12,9) [32]	19,5 (11,5) [18.5]	< 0.01
VERONA			
Grass	29,0 (8,8) [29]	19,9 (6,07) [20]	< 0.001
Mite	26,9 (7,7) [27]	24,3 (7,9) [24]	NS

Figures in brackets are standard deviations. Figures in square brackets are medians.

Table 3 - Pattern of sensitization in extra-European immigrants from different geographical macro-areas of the world, and comparison with Italian age- and sex-matched controls

Origin	No.	Multi-s	Mono/pauci-s	Grass	Mite	Ragweed
C&S America	75	23 (31%)	52	42 (81%)§	7 (13%)*	4 (8%)**
Controls	75	29 (39%)	46	18 (39%)	13 (28%)	17 (37%)
Africa	49	6 (12%)§§	43	30 (70%)	13 (30%)	5 (11%)
Controls	49	21 (43%)	28	15 (54%)	8 (29%)	8 (29%)
Asia	46	17 (37%)	29	17 (59%)	12 (41%)	3 (10%)
Controls	46	16 (35%)	30	16 (53%)	9 (30%)	9 (30%)

Multi-s: Sensitized to > 3 allergen sources. Mono-/pauci-s: sensitized to 1-3 allergen sources.

§ $p < 0.001$ by comparison with Italian controls

** $p < 0.05$ by comparison with immigrants from other macro-areas.*

*** $p < 0.005$ by comparison with the Italian controls*

§§ $p < 0.001$ by comparison with both immigrants from other macro-areas and Italian controls

All ragweed allergic subjects were from the Milan area

lergen source. To this end, two distinct geographic areas from northern Italy that have been both recently involved in intense immigration from extra-European countries but show some significant aerobiological differences, were considered. In order to get a meaningful picture, allergic immigrants were compared both with sex- and age-matched and with allergen-matched Italian controls. The relevance of findings of this study is possibly reduced by the limited number of patients that were studied (n=179); nonetheless, some interesting observations emerged. In contrast with a recent study that found a similar pattern of sensitization among immigrants and the autochthonous population (16), in our series patients were much more frequently sensitized to grass pollen than controls in both areas, whereas they showed a much lower prevalence of ragweed allergy in Milan, an area where ragweed pollen now represents the second cause of respiratory allergy. Further, in both areas immigrants showed a significantly older age at onset of grass pollen allergy than controls. These findings are in keeping with previous observations in Italian patients with birch or ragweed pollinosis living in the area of Milan suggesting that those who are genetically prone to become allergic to a particular allergen get eventually sensitized irrespective of their age when they are exposed to the "right" allergen for a sufficiently long time (17). Grass pollen allergy generally appears at a young age in western countries; the occurrence of grass pollen allergy at a significantly older age in extra-European immigrants might be the result of a delayed exposure to this seasonal allergen. The same phenomenon occurred with mite allergy in the area of Milan, another allergy that is generally found in young people. In contrast, no difference in the age at onset of ragweed allergy was found between patients and controls, most probably because ragweed allergy occurs at older ages in the autochthonous population in this area (17). Frequently, atopic subjects get sensitized to an increasing number of allergen sources with age. Thus, the higher prevalence of mono-sensitized or oligo-sensitized subjects among immigrants, a finding that is in keeping with previous studies (16) might reflect a shorter exposure to airborne allergen load in this group. The prevalence of sensitization to respiratory allergens other than grass and mite was lower in immigrants than in Italian controls, with the notable exception of birch pollen in Verona.

By examining ethnic groups some differences clearly emerged. Most Africans were mono- or oligo-sensitized. Patients from central and south-America showed a high prevalence of grass pollen allergy and a low prevalence of

mite allergy. In Milan, ragweed allergy was consistently less frequent in immigrants from all macro-areas than in their Italian counterparts, although, due to low numbers, statistical significance was observed only in one subgroup. All these differences are likely to reflect the different genetic background of the ethnic groups rather than variable exposure to airborne allergens. Altogether, this study suggests that extra-Europeans who immigrate in westernized countries showing temperate climate, a high prevalence of allergies and high levels of pollution become sensitized following a "sequence" of events, starting with few allergens, grass in most cases, thus reproducing the situation that characterized the autochthonous population about 20-30 years ago. This study represents one further evidence of the relevance of environmental factors on the development of respiratory allergy (18).

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ERRATA CORRIGE

We report that in the article "*Prevalence of allergic disorders in Italy: the Cotignola population study*" published on VOLUME 44 – ISSUE 1/2012, pag. 5-11 is missing table 6 by misprint. We reported the table below

Table 6 - Details on the 207 subjects reporting allergic reactions to insect stings

Feature	Females (%)	Males (%)	Total (%)
Environment where the reaction occurred			
At home	11/91 (12.1%)	1/116 (0.9%)	12/207 (5.8%)
Outdoors	76/91 (83.5%)	108/116 (93.1%)	184/207 (88.9%)
While eating	1/91 (1.1%)	0/116 (0%)	1/207 (0.5%)
While sporting	0/91 (0%)	4/116 (3.4%)	4/207 (1.9%)
While working	3/91 (3.3%)	7/116 (6%)	10/207 (4.8%)
While gardening	1/91 (1.1%)	4/116 (3.4%)	5/207 (2.4%)
Kind of aid received			
E.R.	39/91 (42.9%)	75/116 (64.7%)	114/207 (55.1%)
Family doctor	23/91 (25.3%)	11/116 (9.5%)	34/207 (16.4%)
Other doctor	3/91 (3.3%)	2/116 (1.7%)	5/207 (2.4%)
Other health-care worker	2/91 (2.2%)	2/116 (1.7%)	4/207 (1.9%)
Auto-medication	18/91 (19.8%)	22/116 (19%)	40/207 (19.3%)
No aid	3/91 (3.3%)	3/118 (2.6%)	6/207 (2.9%)
Performance of allergy tests	18/91 (19.8%)	40/116 (34.5%)	58/207 (28%)
Performance of venom immunotherapy	3/91 (3.3%)	21/116 (18.1%)	24/207 (11.6%)