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Is it 'bad hygiene' to inhale pollen in early life?

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1

It is generally believed that allergic sensitization to aero-allergens reflects the degree of exposure, and that applies to pollen sensitivity as well. We have investigated sensitization to a typical Mediterranean tree *Olea europaea* in a population of Israeli Arabs who live in a region in which olive has been cultivated as a crop plant for centuries. Their houses and courtyards are surrounded by olive trees, thus they are massively exposed to olive pollen from their first days of life. We present a study of 86 patients with respiratory allergies from Shefaram, an Arab city situated in the Israeli mountains, in which the population belongs to three subgroups: Druse, Christian and Muslim. The following parameters were assessed: clinical diagnosis; skin prick test (SPT); total and Ole e 1 specific IgE; and HLA class II genomic typing. SPT show that in the study population, prevalence of sensitization to olive pollen was extremely low, especially in the Druse (12%) as compared to that in the Israeli Jewish population that lives in olive tree rich regions (66%).

Total IgE levels were elevated in 35% of the allergic Arabs, while in the Jewish 50–60% of allergic patients have elevated IgE.

The total IgE levels were significantly higher in the Arab patients who had anti-Ole e 1 IgE than in those who had no antiOle e 1 IgE ($P = 0.00$).

HLA class II genomic typing has shown that in Arab allergic patients who were sensitive to olive pollen, phenotypic frequency for DQ2 was high and low for DR4 low, while in those who were not sensitive to olive pollen phenotypic typing for DR4 was high and for DQ2 low.

It therefore appears that DR4 is protective against sensitization to olive pollen, while DQ2 predisposes to it.

Thus, we suggest that the described overall low prevalence of sensitization to olive pollen in a population that is highly exposed, might be due to genetic and also environmental factors such as tolerance or spontaneous desensitization.

Allergy is an ecogenetic disease resulting from the interplay between genetic and environmental factors.

The intriguing question which of these factors is more important in the determination of clinical allergy symptoms is still top priority on the agenda of the international scientific community.

The general feeling being that additional data is needed.

Information coming from a place like Israel could be of special interest since Israel is a melting pot in which people from 100 different ethnic origins arrived at different time points, from different geographic regions, and with different socioeconomic backgrounds.

Presently they live together under the warm Mediterranean sun, surrounded by Mediterranean vegetation, and have a similar life style.

The classic concept maintains that sensitization of allergic patients to pollen parallels the blooming season of each of the species and is positively correlated with the intensity of exposure to the specific pollen.

One should however, keep in mind that since most of allergy research stems from Western Europe, Scandinavia and the USA, this might be

applicable merely to the climate and vegetation in the respective regions.

In our Mediterranean country, some special local situations occur regarding exposure to pollen and sensitization to it.

For example, exposure and sensitization to olive pollen in the Israeli Arab population, which we shall concentrate on in the following presentation:

The Israeli Arab rural population in the Samarian and Carmel Mountains grow olive trees as a crop plant. Their work place, house and courtyard have all been equally imbedded in olive plantations for many years. They inhale olive pollen every year in May–June, day and night, from birth on, during their entire life.

It was our aim to find out whether the continuous and massive exposure of these Arabs to olive pollen affects the prevalence of sensitization to olive in patients with respiratory allergies.

We have studied and published the results of the first group of patients from the Arab town Um-El-Fahem (1); results have shown that the prevalence of sensitization to olive pollen among the Arab patients with clinical hay-fever (14%) was much lower than that known in the Jewish patients that live in olive tree rich regions – Jerusalem or the Jordan Valley (46–66%). The prevalence among Arabs was lower than that of Jewish patients who live in sites where olive trees are rare, and where only few olive trees are close to their home, e.g. in Tel Aviv (34%), and various villages in the Coastal Plain (39%), and even lower than that of the Jews in the Negev desert (29%) where very few olive trees grow.

Recently we studied the Arab population of Shefaram, a town with some 32 000 inhabitants belonging to three different subgroups:

1 17% are Druse, who have lived in the region for hundreds of years.
2 31% are Christians who presumably emigrated to the Galilee during the last century from Lebanon or even earlier from Southern Syria.
3 52% are Muslims, whose origin and time of immigration are difficult to trace, and therefore uncertain.

Patients and Methods

After obtaining their written informed consent 86 patients from the local allergy clinic, with well documented clinical hay-fever, were assessed 90% of patients had rhinitis, 72% conjunctivitis, 53% asthma, and 22% skin symptoms.

Table 1 Distribution of positive skin prick test in 83 allergic Arab patients from Shefaram

	Number	Olive	*Parietaria*	HDM*
Total	83	21%	40%	30%
Druse	34	12%	59%	35%
Christian	22	18%	32%	32%
Muslim	27	30%	33%	30%

*HDM = House dust mites

The symptomatic season for 89% of the patients was mainly spring and early summer.

Each patient underwent a SPT to the allergens most common in the region: House dust mites (HDM) and the pollen of *Olea europaea*, *Parietaria judaica*, *Cupressus sempervirens*, *Quercus alba*, *Atriplex halimus*, *Ceratonia siliqua* and Alternaria.

Results

Skin prick tests

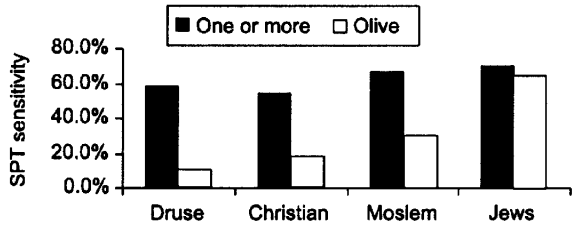
Skin prick tests to the three most relevant allergens (Table 1) showed that 40% of the tested population were sensitive to *Parietaria*, 30% to HDM, and 21% to olive pollen. The distribution of sensitivity to HDM was similar in the three different subgroups of Arabs and was similar to what is known for the Israeli Jewish population. The major sensitivity to *Parietaria* was found in the Druses (59% vs. 32–33% in Christian and Muslim, respectively).

Regarding olive (Fig. 1), the story is different: not only is prevalence of sensitization low (21%), compared to that of the Jewish population (66%), but the distribution of prevalence of positive SPT to olive pollen in the three Arab subpopulations was not the same: it was 12% among the Druse, 18% among the Christian and 30% among the Muslim.

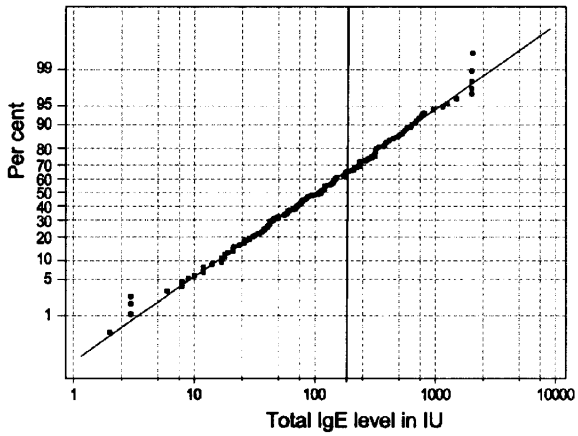
Total and anti-Ole e 1 IgE

In the whole tested Arab patients population with clinical respiratory allergy (Fig. 2) total IgE was elevated (more than 120 IU) in 35% of cases while in the Israeli Jewish population elevated IgE levels occur in 50–60% of patients with respiratory allergies (2).

The lowest IgE levels (Fig. 3) were observed among the Druse, then the Muslim followed by the Christian Arabs.



2 *Figure 1* Prevalence of SPT sensitivity to one or more allergens as compared with prevalence of SPT sensitivity to live for each subgroup. Allergic patients from all the Arab population groups and from the Jewish population have similar prevalence of sensitization to one or more allergens – but the prevalence of sensitization to olive pollen differs between Jews and Arabs and between the different Arab population groups.

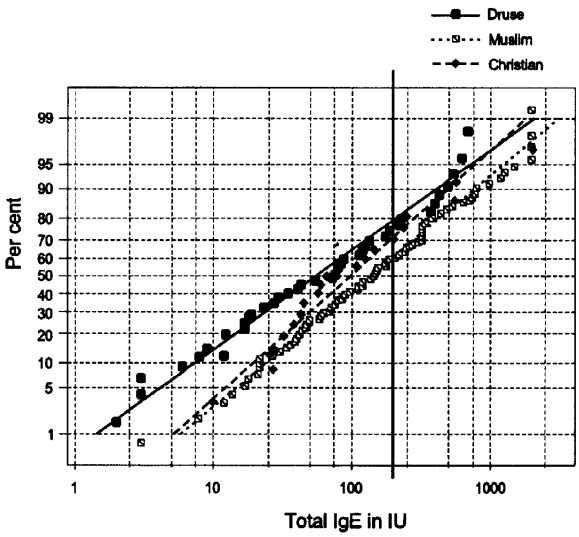


3 *Figure 2* Total IgE levels expressed as a percentage of the total number of tested patients. Total IgE levels were elevated in 35% of the overall allergic Arab population (the vertical line represents the 120 I.U. cut off).

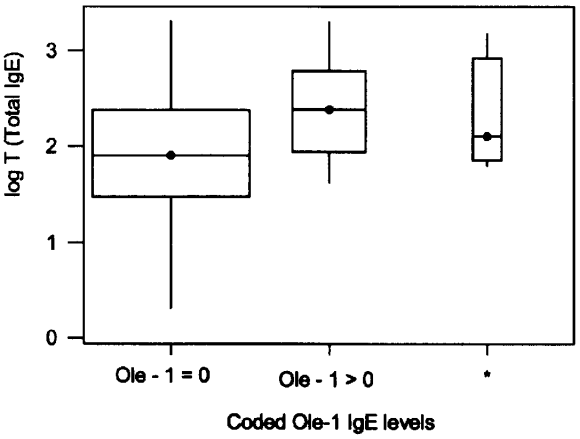
Table 2 Genomic typing of 75 allergic Arab patients from Shefaram

	Olive sensitive	Olive nonsensitive	*P*-value
Druse	(*n* = 1)	(*n* = 33)	
DQ2	0	6%	ns
DR4	0	33%	ns
DR5 (11)	0	60%	ns
Christian	(*n* = 2)	(*n* = 17)	
DQ2	0	35%	ns
DR4	0	41%	ns
DR5 (11)	50%	47%	ns
Muslim	(*n* = 10)	(*n* = 12)	
DQ2	60%	17%	0.07 (0.04)
DR4	10%	66%	0.01 (0.01)
DR5 (11)	40%	16%	ns

Patients who have developed Ole e 1 specific IgE antibodies (Fig. 4) had significantly more total IgE than the patients who have no anti-Ole e 1 IgE at all.



4 *Figure 3* Total IgE levels expressed as a percentage of the total number of tested patients in each subgroup. Total IgE levels were elevated in 20% of the Druse, 30% of the Christian and 40% of the Muslim Arabs.



5 *Figure 4* Boxed plot representation of total IgE by presence of anti Ole-1 specific IgE. In boxed plot analysis it appears that in all Arab tested patients total IgE levels of those who do have specific Ole e 1 IgE antibodies, are significantly higher than total IgE levels of those who do not have specific Ole e 1 IgE antibodies. The significance is: $P = 0.000$. *represents missing values.

HLA class II genomic typing

At genomic typing only patients who had anti-Ole e 1 IgE were counted as olive sensitive.

Table 2 shows that one out of the 34 Druse was olive sensitive. Among the remaining 33 phenotypic frequency for DQ2 is extremely low (6%) and for DR4 it is 33%.

No significant differences were found between the Christian olive sensitive and nonsensitive patients.

Among the 12 Muslims that are nonallergic to olive, the phenotypic frequency for DQ2 is 17% and for DR4 is 66%, while in the 10 olive allergics, the phenotypic frequencies for these antigens are increased for DQ2 (60%) and decreased for DR4 (10%). These differences are significant, and they do reconfirm the results of our previous investigation of the Arab population in Um-El-Fahem.

Discussion

The described low prevalence of sensitization to olive pollen in the Israeli Arab population, especially among the Druse, may result from two factors that also modulate one another.

Genetic

DR4 seems to be a protective class II antigen against sensitivity to olive while DQ2 is a risk factor for it.

Thus, the high prevalence of DR4 and low prevalence of DQ2 among the Druse, and the Muslim, might confer them this resistance against allergenicity of olive pollen.

This genetic trait could have been preserved by intermarriage that is common especially among the Druse.

Cárdaba *et al.* (3) have described similar genetic restriction in the case of sensitization to olive pollen in Spanish populations, and in a study of 22 nuclear olive pollen allergic families (4).

Based on the total IgE *vs* Ole e 1 specific IgE results we could also speculate that there might be a common genetic restriction for total and Ole e 1 specific IgE production in the presented study population.

It is remarkable that total IgE levels are lowest in the Druse and highest in the Muslims, following the same pattern as the SPT and the Ole e 1 IgE levels.

Environmental

The presented Arab population is exposed to a massive olive rain from birth on. Such a continuous exposure has apparently lowered their odds to becoming sensitive to olive allergens as reported recently by Florido *et al.* for the Spanish population in Jaen (5).

This could have happened either by developing tolerance, or spontaneous desensitization.

We therefore raise the following provocative questions:

Is it really 'bad hygiene' to inhale pollen in early life?

Would an early exposure enhance or rather reduce the risk of developing pollen allergy later on?

In order to clarify such matters we need additional data about sensitization to olive pollen in populations that live permanently surrounded by olive trees.

For this, and for many other reasons, the working group on Mediterranean pollinosis has pointed out at the Berlin meeting the urgent need for collaboration between as many as possible 'olive' countries.

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