

Altitude and house dust mites

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The effects of altitude on house dust mites (one of the allergenic components of house dust) and the synthesis of anti-acari IgE antibodies were studied. Flotation extraction, counting, and identification of mites were performed each season for 1 yr on 218 mattress-dust samples taken from the Briançon region in the Alps, 900 to 3170 meters in altitude. Of the total dust samples, 41 were repeatedly positive and 177 repeatedly negative. The percentage of positive samples and the concentration of mites varied inversely with the altitude (40% positive with seven mites per 100 mg of dust at 900 to 1100 m, 14% and 4/100 mg at 1200 to 1350 m, 6% and 2/100 mg at 1400 to 1600 m, and 0% at higher altitudes). Species did not vary with altitude (Dermatophagoides pteronyssinus 17%, Euroglyphus maynei 51%). In contrast, on the plain we found 80% of 77 dust samples positive (88 mites/100 mg of dust, 65% D. pteronyssinus), with the peak in autumn. Total and specific IgE were measured initially and every 3 mo in 42 asthmatic children with positive skin tests to D. pteronyssinus and subjected to a 9-mo stay in Briançon (the highest city in Europe, 1365 m altitude). Geometric mean of initial total IgE (1047 U/ml) dropped to 40% ($p \leq 0.001$); specific IgE to D. pteronyssinus also fell. The value of climate change as a therapeutic modality in asthma is not supported by convincing data but may be attributed in some cases to removal of antigenic stimulation. The decrease in the number of mites and in IgE levels at higher altitudes supports this hypothesis. (J ALLERGY CLIN IMMUNOL 69:290, 1982.)

The physician providing care for a patient with severe asthma in whom all therapeutic measures have failed may be confronted with the alternative of moving the patient to a more favorable climate. Some authors^{1, 2} have reported favorable results from this approach, although it is not supported by convincing data.

One explanation of the possible climatic benefit in allergic asthma is the removal of some allergens from the atmosphere. To clarify this problem, we studied the effects of altitude on house dust mites, which are one of the major allergenic components of house dust in Europe, and on the immunologic responses of asthmatic children allergic to house dust and mites. The children were subjected to a 9-mo stay at Brian-

çon, the highest city in Europe (1365 m), where many asthmatic patients are sent in order to benefit from a more favorable environment.

MATERIALS AND METHODS

Study of mites

Collection of dust. Only beds were examined, since these are the major site of mite infestation.^{3, 4} Samples were collected at the end of each trimester from mattresses in the lowlands of the Southeast of France and from the mountains in the Briançon region (900 to 3170 m). The mattresses were from permanent residences. One hundred milligrams of dust were collected by brushing the surface of each mattress at the seams and buttons and samples were stored at 4° C.

Extraction and counting of mites. The technique used was a flotation method.^{5, 6} The dust was suspended in saturated sodium chloride with five to 10 drops of 4% detergent to facilitate sedimentation. Subsequently, it was shaken and left to settle for 5 min. The supernatant, which contained more than 90% of the total number of mites, was placed in a Petri dish and the mites were removed from the surface. They were counted under binocular control and mounted as microscopic preparations. The variation in mite numbers in two samples collected from the same mattress at the same time was less than 15%. The interobserver error in counting in the same sample was less than 2%.

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Abbreviations used

PRIST:	Paper radioimmunosorbent test
RAST:	Radioallergosorbent test
RH:	Relative humidity
FEV ₁ :	Forced expiratory volume in one second

Identification of species. This was based on the work of Fain,⁷⁻¹⁰ who described the Pyroglyphidae in a series of reference figures, and of Van Bronswijk and Sinha,¹¹ Hughes,¹² Robertson,¹³ Griffiths,¹⁴ and Summers and Price.¹⁵

Patients

Forty-two children were studied (36 boys and six girls, ages 9 to 17 yr), who were not receiving immunotherapy. All 42 were moved from the plains to Briançon and skin tests and IgE antibody assays were performed for each subject. Initial bronchial provocation test to aqueous extract of house dust (Institut Pasteur France) was done in 41 of the children. Increasing doses of antigen were given at 15-min intervals until a 20% or greater fall in FEV₁ was recorded.¹⁶ Intradermal skin tests were positive to house dust extract (Institut Pasteur 1/50,000) in all subjects, and 39 children had tests positive to *Dermatophagoides pteronyssinus* extract (Institut Pasteur 1/50,000). Tests for IgE specific anti-*D. pteronyssinus* and IgE specific anti-house dust were positive and 37 and 32 children, respectively. Forty subjects had positive bronchial provocation tests (provocative dose causing a 20% fall in FEV₁ < 9000 µg cumulated) to house dust, and one test was negative.

Assays of total serum immunoglobulins

Total IgE was measured by the PRIST technique (Pharmacia France) in all children in their first week at Briançon (September) and again at the third, sixth, and ninth months. In 20 of the 42 children chosen at random, IgG, IgA, and IgM were studied by nephelometric technique in September and at 9 mo.

Titration of specific IgE antibodies

These were studied with RAST according to the methods of Ceska et al.¹⁷ Briefly, the extracts of house dust and *D. pteronyssinus* (Institut Pasteur France) were coupled in carbonate buffer to cellulose discs activated by cyanogen bromide, incubated for 3 hr with 50 µl of serial dilutions of serum, washed, incubated overnight with 50 µl of anti-IgE serum labeled by ¹²⁵I (Pharmacia France), and washed again. Radioactivity was measured in counts/minute by a gamma spectrometer. The RAST was considered positive when the radioactivity was double that of a disc incubated with a negative serum. The anti-*D. pteronyssinus* and anti-house dust IgE titers were measured initially and at the third, sixth, and ninth months; the anti-*D. pteronyssinus* IgE titers were measured at the beginning and after a period on the plain and during a second stay at higher altitude.

Skin tests

The intradermal reactions (0.02 ml) with house dust and *D. pteronyssinus* aqueous extracts (1/50,000 and 1/100,000) (Institut Pasteur, Paris, France) were done at the beginning and the end of the stay; readings were made after 15 min, and a wheal and flare response greater than 9 and 20 mm, respectively, was recorded as positive. Mean diameter of the wheal was recorded. The chi square test was used when necessary.

Statistical evaluation

Because the distribution of serum IgE in a population is not unimodal, a logarithmic scale was used. Results were compared by the Student's t test.

RESULTS

House dust mites on the plain and at higher altitudes

The results are shown in Table I. Of the 77 samples (i.e., 77 different mattresses studied at each season of the year) from the plain, 62 were repeatedly positive at each trimester and 15 were repeatedly negative. No mattresses yielded mites intermittently. At altitudes from 900 to 1100 m to 1600 to 3170 m, 41 of 218 samples were repeatedly positive and 177 were repeatedly negative. The percentage of positive samples for mites (80% on the plain) decreased progressively and significantly ($p \leq 0.05$) at higher altitude, with 40% positive at 900 to 1100 m and 0% positive above 1600 m. The mean number of mites per 100 mg of house dust was 88 ± 6 in the 62 positive samples from the plain. At higher altitude, there was not only a reduction in the number of positive samples but also a net decrease in the number of mites in the positive samples. For example, at 900 to 1100 m, the mean number of mites (7 ± 1) was 10 times less than that on the plain.

Mean seasonal number of mites

As shown in Table II, seasonal variations in the number of mites in plain samples were observed, with a maximum in autumn and a minimum in spring ($p \leq 0.05$). In autumn there was 212 ± 16 mites per 100 mg house dust, i.e., nine times more mites than in spring samples (26 ± 2). At higher altitude, peaks were more variable and much less significant, since there was no more than a twofold difference between seasons.

Types and frequency of species

As shown in Table III, *D. pteronyssinus* was the major species recovered on the plain (64%). However, at higher altitudes *Euroglyphus maynei* was more frequent (51%). *D. farinae*, found in nearly 25% of specimens, showed no significant difference between the plain and at higher altitude. Identified

TABLE I. House dust mites on the plain and at higher altitudes

	Positive samples			Total no. of samples each season†
	No. of positive samples	% Positive*	Mites (mean no. $\pm$ SEM per 100 mg of house dust)*	
Plain				
0-300 m	62	80	88 $\pm$ 6	77
Altitude				
900-1100 m	26	40	7 $\pm$ 1	67
1200-1350 m	12	14	4	84
1400-1600 m	3	6	2	52
1600-3170 m	0	0	0	15
Total	41			218

*Significant decrease at high altitude ($p \leq 0.05$).

†Each sample comes from a different mattress studied at each season of the year.

TABLE II. Mites (mean number $\pm$ SEM per 100 mg of house dust) on the plain and at high altitude during seasons

	March	June	September	December	No. of positive samples studied each season
Plain					
0-300 m	26 $\pm$ 2*	64 $\pm$ 5	212 $\pm$ 16*	47 $\pm$ 3	62
Altitude					
900-1100 m	9 $\pm$ 1*	4 $\pm$ 1	11 $\pm$ 1*	5 $\pm$ 1	26
1200-1350 m	3 $\pm$ 1	7 $\pm$ 1*	3 $\pm$ 1	3 $\pm$ 1	12
1400-1600 m	2 $\pm$ 1	3 $\pm$ 1	2	1	3

*Significant variation ($p \leq 0.05$).**TABLE III.** House dust mites on the plain and at high altitude: frequency of recovery for major species of Pyroglyphidae*

	<i>D. pteronyssinus</i> (%)	<i>D. farinae</i> (%)	<i>E. maynei</i> (%)	No. of positive samples studied each season
Plain				
0-300 m	65	21	11	62
Altitude				
900-1600 m	17	24	51	41

**D. pteronyssinus* was more frequent on the plain, whereas *E. maynei* was more frequent at high altitude ($p \leq 0.05$).

species, alone or in association in the samples, did not vary throughout the year. The family Pyroglyphidae represented 97% of the species on the plain and 92% at higher altitude.

In addition, the other minor families found were Acaridae, Glycyphagidae, Cheyletidae, and Tarso-nemidae.

Variations of immunoglobulins

Total IgE fell 40% during the stay at high altitude (Fig. 1), from a geometric mean of 1047 U/ml at the beginning to 603 U/ml after 9 mo. This became significant at 3 mo ($p \leq 0.02$) and became very sig-

nificant at 9 mo ($p \leq 0.001$). One notes the very high initial values of total IgE, above 1000 U/ml, which confirm the atopic syndrome in these asthmatic children. In contrast, IgG, IgA, and IgM did not show significant variations throughout the stay (Table IV). The mean levels of immunoglobulins were normal.

Variations of specific house dust and mite IgE antibodies

RAST done on serum diluted to 1/16 showed a significant drop in specific anti-*D. pteronyssinus* IgE from 3 mo onward to reach a 50% level at 9 mo (Fig. 2). The house dust RAST done at the beginning and

end of the stay with serum diluted either 1/4 or 1/16 also showed a significant fall in specific IgE (Fig. 3).

In four patients, RAST to *D. pteronyssinus* was done at high altitude from September to June during a first stay of 9 mo (Fig. 4, A) and again during a second stay from September to June the following year (Fig. 4, B). Specific IgE decreased at high altitude during the first stay, increased when subjects returned to the plain, and decreased again during the second stay at high altitude in three of the four children.

Skin tests

As shown in Table V, skin tests done for house dust and *D. pteronyssinus* at the beginning and end of the stay did not vary significantly.

DISCUSSION

Dutch authors¹⁸⁻²⁰ working at Davos in the Swiss Alps pointed out that house dust mites decrease in number with altitude, and Ruffi et al.²¹ noted in 1969 that there were no *Dermatophagoides* in house dust of mountain treatment centers for asthma, such as Celerina (1724 m) or Pontresina (1803 m). Some French investigators^{22, 23} confirmed these observations. However, our study is the first systematic observation of mites at different altitudes.

The number of positive dust samples fell by 50% between plain and higher altitude (900 to 1100 m), but even more interesting was the decrease in the number of mites by 90%. Thus the amount of antigen decreased significantly at 1000 m altitude.

Several explanations have been given for this decrease. The main one, agreed to by the majority of authors, is that the climatic conditions at high altitudes are unfavorable to mites, principally because temperature and RH are not high enough. For example, high-altitude conditions are quite different from the 75% to 80% RH and the 25° C temperature known to be optimal for the growth of these mites (75% RH for *D. farinae*²⁴ and 80% for *D. pteronyssinus*²⁵). The temperature is an important factor, since the mites cannot grow below 15° C.²⁶ More important is the RH; there are six times fewer *D. pteronyssinus* at 75% RH than at 80%.²⁵ Experimental data have shown that below the critical equilibrium humidity (<70%) the mite can no longer maintain its body and progressively loses water until it succumbs to desiccation.^{27, 28} When the RH falls to 50% all *D. farinae* die within 11 days.²⁸ *D. pteronyssinus* are less able to withstand a low RH.²⁹ However, in some studies, live mites have been found in mattress dust in reduced numbers when the RH falls below 50%,^{3, 30} which can be explained by the increase in RH that results from regular use.³⁰

The observations of Ordman³¹ in South Africa and

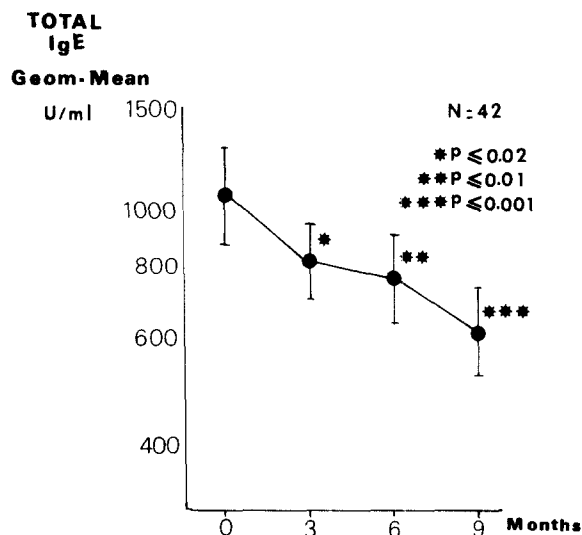


Fig. 1. Graph showing decrease in total IgE concentrations at high altitude with time.

TABLE IV. Concentrations of IgG, IgA, and IgM (mg/100 ml, Mean $\pm$ SEM)

	0 mo		9 mo
IgG	1521 $\pm$ 105		1482 $\pm$ 61
IgA	232 $\pm$ 21	NS	251 $\pm$ 23
IgM	188 $\pm$ 19		174 $\pm$ 19

NS = not significant.

of Gitoh and Rees³² in Kenya confirmed the importance of humidity. In 67 cities situated at the coast and in the interior at higher altitudes, Ordman showed a greater number of mites in the former with two exceptions. He explained this by the presence in the coastal cities of a cold wind and a warm humid breeze in interior cities. These winds modified the climate and consequently the number of mites. Gitoh and Rees showed a great number of *D. pteronyssinus* in mattress dust in Nairobi, despite the altitude of 1650 m. Thus it is not the altitude that influences the proliferation of mites but rather the climatic conditions. Other environmental factors such as the age of the dwelling did not affect the mite population, in agreement with reports from California³³ and from England.^{34, 35}

With regard to seasonal variations in mite populations on the plain, our study is in agreement with the observations of Spieksma et al.³⁶ In addition, Hughes and Maunsell³⁷ in London, Miyamoto and Ouchi³⁸ in Tokyo, and Domrow³⁹ in Brisbane all observed a maximum peak in summer, whereas Sharp and Hara-moto⁴⁰ in Honolulu observed it in winter. However, no previous studies are available on seasonal variations at high altitudes. We have shown few seasonal variations

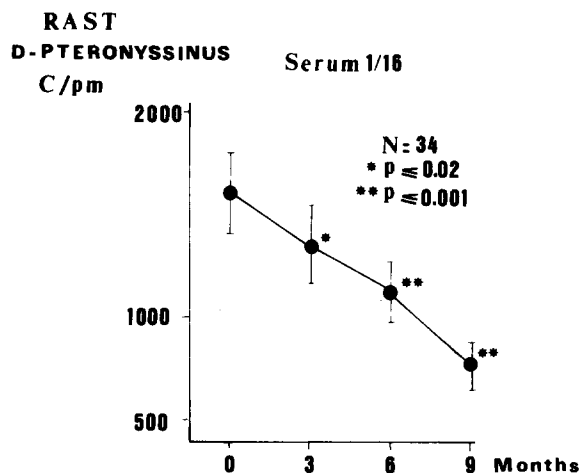


FIG. 2. Graph showing decrease in specific IgE to *D. pteronyssinus* at high altitude with time.

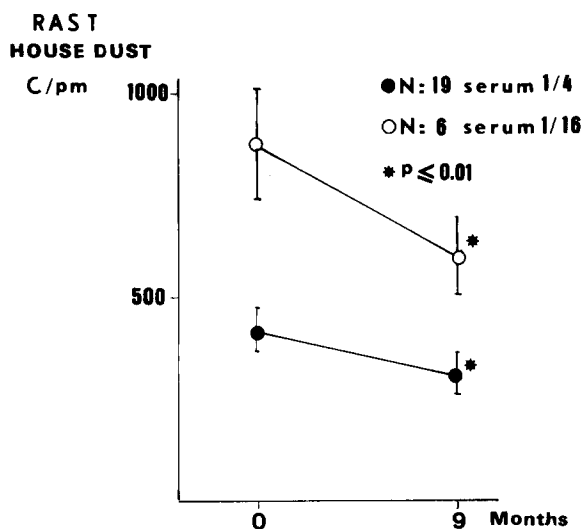


FIG. 3. Graph showing decrease in specific IgE to house dust at high altitude with time.

in the growth of mites (Table II), although such differences between the plain and higher altitude might be explained by the temperature and humidity. To these basic factors must be added the effect of heat on the decreased RH in the houses in relation to the exterior. However, one must take into consideration that peaks shift by one or more months from year to year; for example, Murray and Zuk⁴¹ in Vancouver noted a slight maximal peak in October 1977 and a large maximal peak in July 1978.

With regard to species, it was observed that on the plain *D. pteronyssinus* was the more frequent. This has already been found by other authors in Europe^{25, 34, 42} and in Hawaii.⁴³ *D. farinae*, which is the most common species in the continental U.S.A.^{29, 44} and which we observed to be the second most common on the

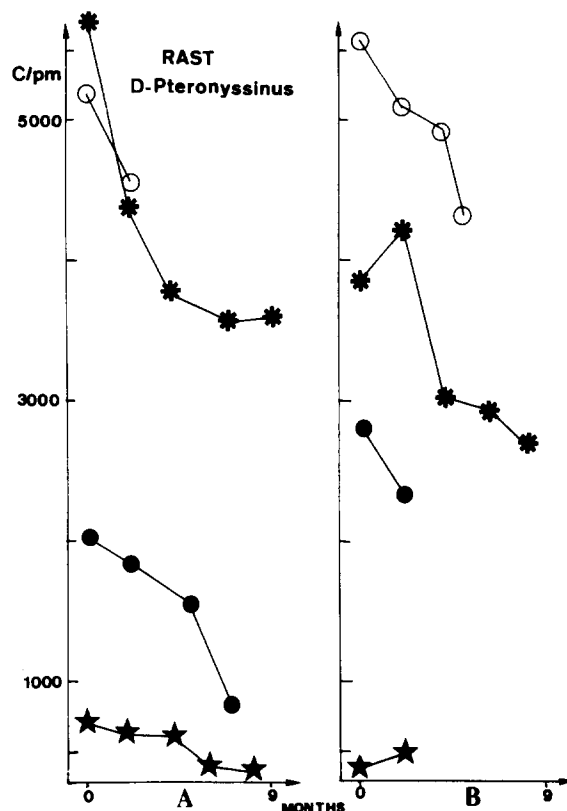


FIG. 4. Graph showing decrease in specific IgE to *D. pteronyssinus* during two stays at high altitude. A, First stay at high altitude from September to June. B, Second stay from September to June the following year.

plain is of variable frequency in Europe, varying from 2% for Spijsma et al.³⁶ to 33% for Mumcuoglu.⁴² For most authors it is the third most common species, the second being *E. maynei*.^{25, 34, 42} At higher altitudes we found *E. maynei* to be the most frequent species (51% compared with 17% for *D. pteronyssinus*). Other studies are not available to corroborate this point. It might be explained by the fact that *E. maynei*, like *D. farinae*, are better adapted to low humidity than is *D. pteronyssinus*.^{11, 29} *D. farinae* is considered a continental species and *D. pteronyssinus* a marine one.

A number of authors have shown that the pollen season increases specific IgE in allergic subjects and that when this allergic stimulation stops, there is a slow decrease.⁴⁵⁻⁴⁷ The progressive and regular fall in anti-*Dermatophagoides* IgE we found can be explained by the decrease or even elimination of this antigenic stimulation, confirming the observations of Cabanieu et al.^{48, 49} This fall in serum IgE antibodies is observed only at high altitudes. On the plain, no significant spontaneous variation in *Dermatophagoides* IgE antibodies was noticed.^{50, 51} Total IgE in our study fell progressively 40% during the 9 mo, whereas total IgG, IgA, and IgM did not vary. It is interesting to speculate

TABLE V. Intradermal skin tests*

	0 mo		9 mo
House dust (1/100,000 w/v)	9.9 ± 0.4 (n = 21)	NS	10.5 ± 0.5 (n = 21)
<i>D. pteronyssinus</i> (1/100,000 w/v)	8.3 ± 1.4 (n = 15)	NS	8.4 ± 1.4 (n = 15)

NS = not significant.

*Data expressed as mean diameter of wheal (mm) ± SEM.

that specific IgE constitutes an important percentage of total IgE antibodies, since it is the case for grass pollen.^{47, 52} This could significantly influence total IgE levels. As for IgG, IgA, and IgM, the percentage of specific antibodies to *Dermatophagoides* is probably too low to produce a variation. In association with the fall in anti-*Dermatophagoides* antibodies, there is an important decrease in anti-house dust IgE. Because *Dermatophagoides* is one of the major components of the house dust antigen, the fall in anti-house dust IgE is understandable. Variations in anti-*Dermatophagoides* and anti-house dust IgE were measured on diluted sera, since the use of pure serum can falsely lower RAST values by the fixation of non-IgE antibodies on the insoluble allergens.

Despite the important fall in circulating specific IgE, the skin tests were not modified. Recently, Lichtenstein⁵³ showed that basophils were functionally saturated when serum IgE reached 10 ng/ml, a modest level. Considering the parallel between mast cells and basophils, one can suggest that despite circulating IgE decrease, the levels of antibodies fixed to the cells would not be very different before and after therapy at higher altitudes and thus the sensitivity of these cells would not be modified. On the other hand, the release of mediators by the target cells under the influence of the antigens depends not only on the sensitization of these cells by antibody but also on other parameters related to cellular reactivity. It is interesting to recall that the basophils of 10% of normal subjects do not release histamine under the influence of anti-IgE serum, although they possess surface IgE.

Thus we have shown that altitude was associated with, and perhaps caused, a progressive fall in house dust mite numbers and a decrease of IgE synthesis in children allergic to these antigens.

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