presence of FcεRI-expressing LC/IDEC, bearing IgE molecules, is a prerequisite to provoking eczematous lesions, observed after application of aeroallergens to the skin of atopic patients, strongly supports this concept. Thereby, IgE receptors are the connecting link between the specificity gaining IgE molecules and the APC. However, FcεRI seems to play the major role in these phenomena. It should be noted that FcεRI expressed on circulating monocytes may have other functions, mainly in regulating their survival and differentiation outcome.[12]

Following the presentation of allergens to T cells, allergen-specific B cells may be activated to produce high amounts of allergen-specific IgE. This IgE may then in turn bind to the FcεRI on the APC, closing a vicious circle of facilitated antigen presentation. The intermittent or continuous supply of aeroallergens or autoantigens to the process of facilitated antigen presentation may define the pathophysiological basis of the recurrent or self-perpetuating course of AD frequently seen in untreated patients. The successful application of aeroallergens such as cat dander in the recently standardized atopy patch test[13] shows that it is possible to elicit eczematous skin lesions by solely external application of aeroallergens to the skin. Based on the facilitated antigen presentation model of AD, the need for an identification of the individual provocation factors in each patient calls for diagnostic procedures based on the allergen-specific IgE. Cat dander, house dust mite allergens and a variety of food allergens may be successfully avoided following a thoroughly undertaken prick test and *in vitro* IgE diagnostic evaluation.

Conclusion

Consequently, AD may represent a paradigm of IgE/FcεRI-mediated, delayed-type hypersensitivity reaction. A similar role could be attributed to other FcεRI-expressing DC in the lung, where such cells may also be considered as putative targets for new therapeutic strategies.

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Why is the prevalence of allergic diseases increasing? A critical assessment of some classical risk factors

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Introduction

Many epidemiological surveys, among which repeated cross-sectional surveys have most validity, have demonstrated a twofold increase in the prevalence of allergic and asthma during the past two decades.[1,2]

The next presentations will deal with newly-identified or suspected risk factors such as repeated childhood infections, the role of the gut flora and the potential protective effect of contact with farm animals.

In this paper, we review some risk factors whose responsibility is often given for granted but which do not actually appear to play a major role in the increase of allergic diseases, namely allergen exposure, air pollution and passive smoking.

Allergen exposure

Among allergens, house-dust mites have been advocated to be responsible for the increasing trend in the prevalence of allergic diseases.[3] We will present the pros and cons of this hypothesis.

- Because of the worldwide energy crisis in the 1970s, there has been a large decrease in the ventilation rate of private houses in Western countries, which could have led to multiplication of house-dust mites. Actually, there is a single study supporting this latter statement.[4] Another hypoth-

esis is that exposure to mite allergens has increased because people, especially children, today spend much more time indoors to watch television.

- Undoubtedly, there is good correlation between exposure to mite allergens and rate of sensitisation to that allergen.[1] Recent studies demonstrate that minute, but repeated, exposures to mite allergens lead to sensitisation.
- The most controversial issue is to know whether there is a causal relationship between exposure to mite allergens and occurrence of respiratory allergic diseases.

Pros

Two cross-sectional surveys, including geographical comparisons, support such a relationship. The first[5] compared the prevalence of allergic rhinitis and asthma in populations living either at sea level (high exposure to mite allergens) or in altitude (very low exposure). The second survey[6] included comparison of populations living either in coastal humid areas or in desert areas. In both instances, the gradient of exposure between exposed or low-exposed areas was very high, greater than 50.

Cons

However, other cross-sectional and two cohort studies led to negative results. Kuehr *et al.*[7] have followed-up a group of 1812 children from age 7 to age 10. They did not demonstrate a link between mite-allergen exposure and incidence rate of asthma, on the one hand, and exercise-induced bronchospasm on the other. More recently, a group of German paediatricians followed-up a group of 4300 newborn babies up to the age of 7.[8] The sensitisation to mite allergens was highly dependent on their exposure in infancy and at the age of 3. However, there was no relationship between exposure to mite allergen and occurrence of asthma. These authors hypothesised that the risk of becoming asthmatic is independent both of the exposure level and the sensitisation to mites. This interpretation, if true, would have very strong negative implications on the feasibility of a primary prevention of allergic diseases. Finally, in the Marseille area, we have studied a group of 157 school children allergic to mites and shown that the prevalence of asthma in these children is independent of their exposure to mite allergens.[9] We proposed to reconcile these discordant results: in situations where the contrast in terms of mite exposure is very strong, such as geographic comparisons between sea level and altitude or coastal versus desert areas, a difference in asthma prevalence can be identified. In contrast, in the other situations where the contrast is much lower, and considering that the threshold, if any, for the development of asthma should be low, then the whole population is exposed to mite allergens,[9] and no difference in asthma prevalence can be identified. In conclusion, in temperate climates where mites are ubiquitous, it seems unlikely that an increase in mite exposure could have induced a significant upward trend in asthma prevalence.

Air pollution

In the past two decades, air pollutants from industrial sources have been drastically reduced whereas air pollutants from vehicle exhausts (nitrogen dioxide, diesel exhaust particulates, ozone) show stable and, in some instances, increasing concentrations. Animal and human experiments have convincingly shown a synergy between air pollutants and allergens.[10] In other words, the risk of developing a sensitisation to an allergen is boosted when the exposure to air pollutants has been performed prior to the exposure to the allergen. However, in the epidemiological setting, the three large surveys published so far have failed to show a relationship between long-term exposure to air pollutants and the risk of being atopic.[11–13]

The relationships between long-term exposure to air pollutants and risk of asthma occurrence are also very controversial. Most published studies do show an increased risk of chronic cough, chest tightness or wheezing in more polluted areas, but not a higher prevalence of asthma[14] or bronchial hyperreactivity.[15] Other cross-sectional[16] or cohort[17] surveys do demonstrate such an association. In such a discussion, two important issues should be kept in mind. First, the definition of asthma is not straightforward. How should we interpret a higher prevalence of cough, chest tightness and wheezing in a polluted area? Does it reflect merely an irritate bronchial response or should it be considered as an asthmatic response? Only carefully planned cohort studies could help to answer this question. Second, an irritant such as air pollutants could trigger wheezing and even asthma attack in an asthmatic individual. Then, when one demonstrates an increased prevalence of asthma in a polluted area, this does not necessarily mean that the prevalence of the disease has increased compared with a low-polluted area. It could also mean that asymptomatic asthma cases have become symptomatic because of chronic exposure to air pollutants and could be identified as such by a survey.

Passive smoking

The relationships between passive smoking and allergic sensitisation are also most controversial, both at the pre-natal and post-natal periods.[18]

Regarding asthma, most prospective or retrospective studies have demonstrated a twofold increase in asthma risk in children exposed to passive smoking, either *in utero* or after birth.[19] As far as post-natal

exposure to passive smoking is concerned, two issues have to be considered. The first, which has been developed in the preceding section, is that passive smoking could act to disclose an asthmatic state that was so far asymptomatic. The second issue lies in the natural history of asthma. Following Martinez *et al.*'s publications,[20] it has become obvious that transient wheezing could occur in non-atopic infants exposed to passive smoking. Because the relationships between passive smoking and asthma are mostly demonstrated in infants and young children, and have a tendency to weaken with increasing age, one cannot discard the hypothesis that passive smoking is responsible for transient wheezing, not for an asthmatic disease. In this field also, prospective long-term studies are clearly needed.

In conclusion, the relevance of such risk factors as allergen exposure, air pollution and passive smoking is far from being clear. Because the implication of such risk factors has enormous social consequences, such a clarification is strongly needed. More carefully designed epidemiological investigations should obviously be performed.

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Fungal allergies

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Introduction

Inhalation of fungal spores may induce a wide range of allergic diseases: rhinitis, dermatitis, allergic bronchitis, asthma, allergic broncho-pulmonary aspergillosis, and even hypersensitivity pneumonitis.

Asexual fungal spores are among the most numerous and diversified airborne microoorganisms that we breathe. Filamentous fungi are disseminating their spores in the air by thousands and, in temperate zones, hundreds of species are continuously invading our environment.

Few surveys are carried out to define the airborne fungal flora in indoor spaces. Results are often incomplete and should require further investigation. As a matter of fact, a lot of mould species grow only on specific media and, depending on the temperature of incubation, the results will be completely biased by the selection. Moreover, sedimentation sampling methods are still currently used too often (contact plates left open); they only give a restricted overview of the mycoflora since numerous species do not grow in these conditions. Furthermore, many researchers do not identify moulds up to species level. And as far as allergy is concerned, specificity is the key element when making a diagnosis.

How many allergenic species are there?

Indoor moulds and their adverse health effects

Indoor moulds grow abundantly in dark, moist, warm and ill-ventilated places. These ideal conditions are found not only under warm and moist climates, but nowadays also in temperate zones. Indeed, excessive insulation after the oil crisis has markedly favoured condensation areas (cold bridges) from cellars to attics, which rapidly become the centre of intensive mycelial growth. A parallel change in lifestyle has led