

Allergologia et immunopathologia

www.elsevier.es/ai



RESEARCH LETTERS

Imported subclinical house dust mite sensitisation in migrants from geohelminth-endemic developing countries

To the Editor:

Migration studies provide information on the role of environmental factors on the development of atopy and respiratory disease. International studies provide strong and objective evidence for an association of atopic disease with westernisation.¹ A metaanalysis has shown higher rates of asthma in immigrants. Immigrants moving to allergy prevalent countries have generally more allergy and asthma comparing both with natives, but also with respect to the prevalence in their countries of origin.²

It has been postulated that parasite-burden in developing countries is inversely associated with atopy and asthma.^{3,4} Furthermore, climatic conditions for a high prevalence of geohelminths parallel those for growth of different house dust mite (HDM) species. Up to now, most immigrant studies on an epidemiological background have addressed prevalence rates of asthma or allergy without taking into account the specific sensitisation to different aeroallergens.

In our study region, HDM sensitisation is infrequent due to a predominantly dry climate. Otherwise, many immigrants come from tropical or subtropical regions, where HDM are the predominant sensitising allergens. We hypothesise that immigrants from these countries, although developing allergic respiratory disease after migrating, could be sensitised to different aeroallergens in comparison to natives. The aim of this study was therefore to compare the sensitisation profile of allergic immigrants proceeding from helminth endemic developing countries regions, with native patients of our region, in which no significant endemic helminth infection is known.

In a mainly dry region (Madrid, Spain), we performed a cross-sectional study of 49 consecutive adult immigrant patients from South-America and the Philippines who attended our Allergy Service for an allergological evaluation of rhinoconjunctivitis or bronchial asthma (RCBA). Patients were included if they had interview based typical rhinitis or rhinoconjunctivitis symptoms and/or bronchial asthma for at least one year. One hundred native RCBA patients in the same age range of 23-63 years served as control group. We asked for the age of migration and onset of RCBA symptoms. Patients were assessed for seasonal and/or perennial symp-

toms. They could be included in both groups, if seasonal exacerbation of perennial symptoms were present.

Skin Prick Tests (SPT) were performed against house dust mites (HDM, *Dermatophagoides pteronyssinus*, *D. farinae*, *Tyrophagus putrescentiae*), animal dander (cat, dog), 5 pollen mixtures of grass, tree and weed pollen and mould (*Alternaria alternata*, *Cladosporium herbarum*). SPT was performed in standard technique and was considered positive with a mean wheal diameter of $\geq 3 \times 3$ mm. Histamine at 1% concentration and saline solution 0.9% (NaCl) were positive and negative controls.

SPT data were analysed separately for HDM, pollen and PMD (group of non-HDM allergens: pollen, mould or dander). Statistical analysis was performed using SPSS 15.0 for Windows Version (SPSS Inc.).

ANOVA and Chi-Square-Test were used for evaluation of significance of means and percentages, respectively.

Forty-four of 49 patients began to suffer RCBA after migrating to our region with a mean latency of 3.8 ± 3.8 years (Fig. 1). Mean age of symptoms initiation was 36.3 ± 11.0 years and 30.6 ± 8.8 years in the control group ($p = 0.005$). 75% were female in immigrant patients and 68% in natives (n.s.). Overall SPT reactivity was higher in immigrants than in native

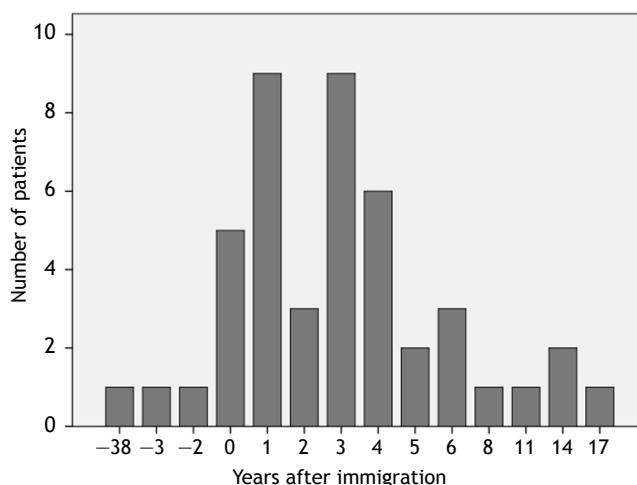


Figure 1. Latency of first Rhinoconjunctivitis or Bronchial Asthma symptoms in immigrants. All, except three patients began to suffer RCBA after migrating to our region with a mean latency of 3.8 ± 3.8 years.

patients (95.5% versus 75.0%; $p = 0.002$). Immigrants claimed perennial symptoms in 25% (natives 56%, $p < 0.0001$) and seasonal symptoms in 75% (natives in other 50%, $p < 0.004$).

The following prevalence rates are described only for sensitised patients with RCBA (in migrants those who initiated their symptoms after migration ($n = 42$)): Rhinoconjunctivitis without bronchial asthma was present in 45.2% of immigrants and 41.3% of natives (n.s.). HDM sensitisation was significantly higher in immigrant patients (50% versus 32%; $p = 0.04$) (Fig. 2). Pollen sensitisation rate was similar in immigrants and natives (90.5% and 90.7%, respectively, $p = 0.6$). Sensitization against PMD was also similar (97.6% and 96%, $p = 0.5$).

Fourteen of 30 (46.7%) immigrant patients with pollen sensitisation associated only seasonal RCBA were also subclinically sensitised to HDM (only 21.7% of native patients with seasonal pollen sensitisation associated RCBA; $p = 0.001$) (Fig. 3).

This study was not designed to gain information about prevalence rates of allergic respiratory disease of immigrants neither compared with the population in their countries of origin, nor with respect to the native population. However, our results corroborate some data of previous epi-

demiological reports and enrich our understanding on the different possible sensitisation profiles due to new or missing environmental factors.

Nearly all adult immigrants began to suffer rhinoconjunctivitis or bronchial asthma (RCBA) after migrating, a fact that corroborates results by other studies⁵. This fact, together with the elevated age of onset of symptoms has already been described previously and favours the hypothesis of environmental factors leading to the appearance of allergic symptoms⁶. We do not know the possible sensitisation profile of these immigrants before their onset of symptoms, or even before migrating. Pollen sensitisation reaches 90% in patients with RCBA, both in immigrants and natives. The higher HDM prevalent rate in immigrants compared to our age-matched control group attracts attention, but even more so does the fact that immigrants show a more than twice higher sensitisation rate against HDM, if only patients with seasonal RCBA were analysed. Due to geographic and climatic conditions, these results are to be interpreted in the special circumstance of a low prevalence of HDM sensitisation in Central Spain. Whereas HDM sensitisation is associated with perennial asthma⁷, seasonal RCBA is mainly related to pollen sensitisation. Therefore, the mentioned subanalysis gives us information about very high subclinical sensitisation prevalence against HDM in immigrants.

If we search for possible explanations, we cannot rule out a possible selection bias, such as different HDM prevalence favouring living conditions. Taking into account the low HDM allergen prevalence in our region and the relatively short time interval between migration and the first symptoms, this possibility seems unlikely. Thus, if we search for environmental factors, we should look at the country of origin: due to climatic conditions, and the fact that most immigrants are those who can afford the step to migration and proceed from urban or semi-urban regions, contact with sufficient sensitising HDM is a possibility, as is the fact that other arthropods, like cockroaches, or geohelminths with known cross-reactivity with HDM could have sensitised our study population in their country of origin⁸. This hypothesis is tempting, as it has been shown that a high parasite burden in developing countries is not only inversely associated with asthma and atopy, but otherwise even in the case of sensitisation, high intensity parasite infection is able to inhibit the risk of wheeze^{3,9}.

Early childhood infections outside the US seem to protect against asthma in a cross-sectional survey comparing native and foreign born immigrants¹⁰. However, immigrants from developing countries can be asymptomatic, even showing positive SPT, but moving to industrialised centres adds a new environmental exposure, to which immigrants do not seem to be protected². Pollen sensitisation in developing countries is not as high as HDM sensitisation, but the inverse situation is given in our area.

Thus, it seems that immigrants have been immunologically primed for HDM or equivalent cross-reacting arthropod-helminth allergens, but possibly environmental and lifestyle factors prevented their expression¹¹. In this respect, if environmental aspects of allergic disease in migrants are discussed, also those *missing* environmental factors should be addressed in future studies. In this study we did not assess prior helminth exposure. It is clear that having evidence of this would strengthen the analysis and is an area of future research. A previous study has shown an increase in skin re-

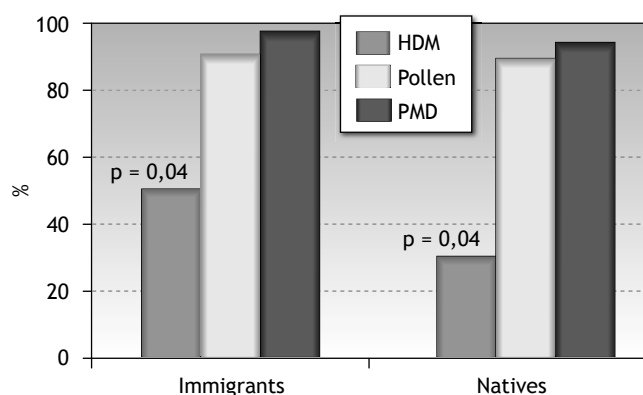


Figure 2. Percentage of specific sensitisation in patients with allergic Rhinoconjunctivitis or Bronchial Asthma (Only patients with positive SPT). HDM: house dust mites. PMD: pollen, mould or dander. p only for significant results.

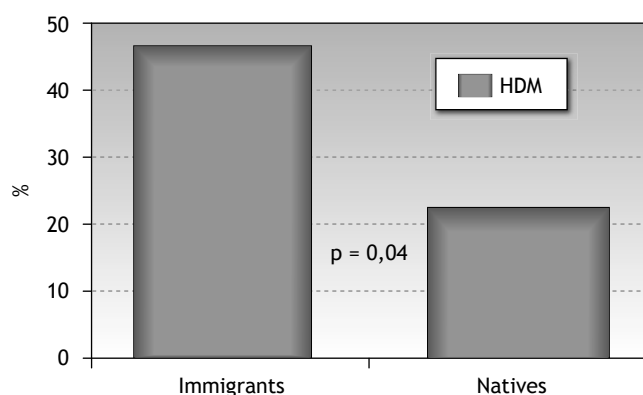


Figure 3. Percentage of mite sensitisation in patients with seasonal Rhinoconjunctivitis or Bronchial Asthma. These pollen-sensitised patients suffered only seasonal symptoms, but subclinical house dust mite (HDM) sensitisation was present.

activity to newly acquired allergens following antihelminthic treatment in migrants from Ethiopia¹². Together with new environmental factors, which are able to enhance sensitisation, like a polluted atmosphere, this could be the cause for the appearance of new respiratory symptoms in a subgroup of our migrant patients. A previous report proposed a differential atopy evaluation when dealing with the relationship between atopy and parasites¹³. Thus, arthropod-parasite related sensitisation, which includes HDM sensitivity, in our migrant population could have a different clinical outcome compared to pollen or other aeroallergen sensitisation, as is shown by our results.

This reasoning is not contrary to the possible implication of genetic factors. Evidence supports an increased susceptibility to allergy and asthma among populations with tropical ancestry¹⁴. The differences in asthma prevalences due to ethnicity could thus be due to a common genetic factor that predisposes to both allergy and resistance to infection¹⁵.

Summarizing, the high prevalence of HDM sensitisation of our migrant patients could be due to previous subclinical sensitisation in their tropical and subtropical countries with more favourable conditions for the presence of different mite species, but other factors have to be taken into account, such as genetic factors, the elevated burden of microbial burden or the higher prevalence of geohelminths, which in turn could be responsible for possible cross-reactive sensitisation against HDM.

References

- Hopkin JM. Mechanisms of enhanced prevalence of asthma and atopy in developed countries. *Curr Opin Immunol* 1997;9: 788-92.
- Rottem M, Szyper-Kravitz M, Shoenfeld Y. Atopy and asthma in migrants. *Int Arch Allergy Immunol* 2005;136:198-204.
- Scrivener S, Yemaneberhan H, Zebeign M et al. Independent effects of intestinal parasite infection and domestic allergen exposure on risk of wheeze in Ethiopia: a nested case-control study. *Lancet* 2001;358:1493-9.
- Cooper PJ. Intestinal worms and human allergy. *Parasite Immunol* 2004;26:455-67.
- Tedeschi A, Barcella M, Bo GA, Miadonna A. Onset of allergy and asthma symptoms in extra-European immigrants to Milan, Italy: possible role of environmental factors. *Clin Exp Allergy* 2003;33: 449-54.
- Dervaderics M, Fust G, Otos M, Barok J, Pataky G. Differences in the sensitisation to ragweed pollen and occurrence of late summer allergic symptoms between native and immigrant workers of the nuclear power plant of Hungary. *Immunol Invest* 2002; 31:29-40.
- AO, Peat JK, Woolcock AJ. Prevalence of atopy, asthma symptoms and diagnosis, and the management of asthma: comparison of an affluent and a non-affluent country. *Thorax* 1999;54: 606-10.
- Yazdanbakhsh M, Kremsner PG, Van Ree R. Allergy, parasites, and the hygiene hypothesis. *Science* 2002;296:490-4.
- Yemaneberhan H, Bekele Z, Venn A, Lewis S, Parry E, Britton J. Prevalence of wheeze and asthma and relation to atopy in urban and rural Ethiopia. *Lancet* 1997;350:85-90.
- Brugge D, Lee AC, Woodin M, Rioux C. Native and foreign born as predictors of pediatric asthma in an Asian immigrant population: a cross sectional survey. *Environ Health* 2007;6:13-20.
- Van Ree R, Yazdanbakhsh M. Allergic disorders in African countries: linking immunology to accurate phenotype. *Allergy* 2007;62:237-46.
- Borkow G, Leng Q, Weisman Z, et al. Chronic immune activation associated with intestinal helminth infections results in impaired signal transduction and anergy. *J Clin Invest* 2000;106:1053-60.
- Daschner A, Cuellar C, Valls A. Towards a differential definition of atopy: *Anisakis simplex* and the relationship between parasites and arthropods in respiratory allergy. *Parasite Immunol* 2008;30:417-24.
- Hagel I, Di Prisco MC, Goldblatt J, Le Souef PN. The role of parasites in genetic susceptibility to allergy: IgE, helminth infection and allergy, and the evolution of the human immune system. *Clin Rev Allergy Immunol* 2004;26:75-83.
- Maizels RM. Infections and allergy – helminths, hygiene and host immune regulation. *Curr Opin Immunol* 2005;17:656-61.

Álvaro Daschner*, Ana Elices, Consolación De Frutos
and Ana Valls
Allergy Department, Hospital Universitario
La Princesa, Madrid, Spain
*Corresponding author.
E-mail: adaschmer@meditex.es (A. Daschner)

Ambroxol-induced systemic contact dermatitis confirmed by positive patch test

To the Editor:

Ambroxol hydrochloride (trans-4-(2-amino-3,5-dibromobenzylamino) cyclohexanol hydrochloride) is a bromexine metabolite¹ (Fig. 1). Both ambroxol and bromexine are well known mucolytics and ambroxol has also been used in clinical

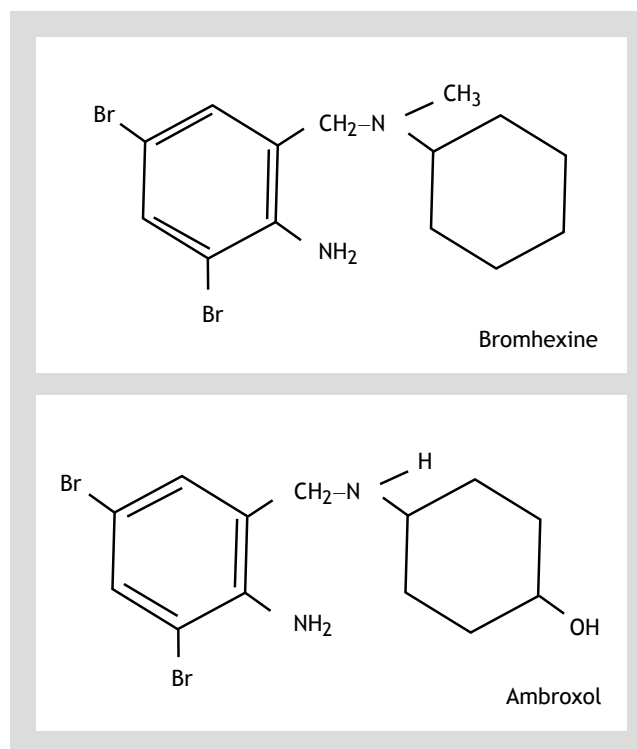


Figure 1. Chemical structures of bromexine and ambroxol.

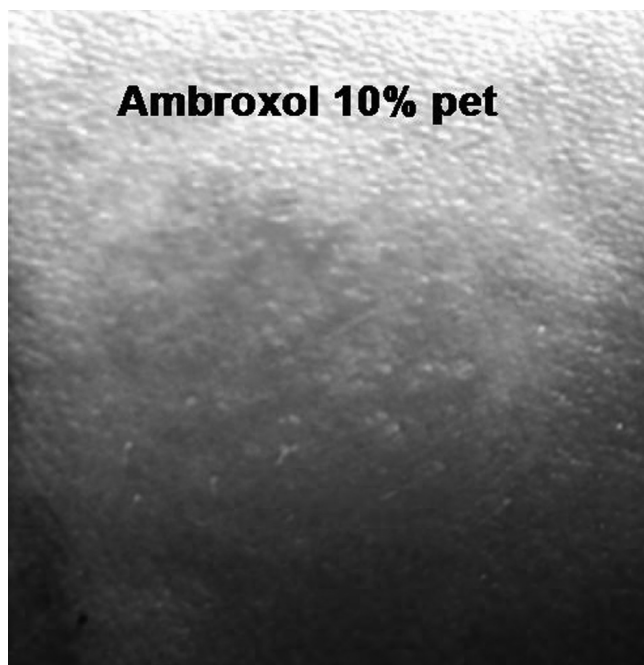


Figure 2. Patch test with ambroxol (10% pet) positive at 96 h (+++).

cal trials for the prevention of chronic bronchitis and respiratory distress syndrome in infant.

A 79-year-old woman presented a maculopapular rash with intense pruritus. She had taken ambroxol, acetaminophen, and codeine for 4 days at doses of 90 mg/day, 1,500 mg/day and 90 mg/day respectively, prescribed for odynophagia. On clinical examination there was a generalised maculopapular exanthematous eruption, with furfuraeous desquamation and intense erythema. The mucosa was spared. She was treated with hydration, antihistamines, and oral corticosteroids and the skin lesions resolved within a week. After this episode the patient tolerated acetaminophen and acetylsalicylic acid. She had no personal and familiar history of atopic diseases.

Patch tests were performed, according to the guidelines of the International Contact Dermatitis Research Group, with the GEIDC standard series, ambroxol (10% pet) and codeine (10% pet).

Positive reaction was found to ambroxol at 48 hours (++) which increased at 96 (+++) (Fig. 2), and negative to codeine and the standard series. Patch tests were negative in 10 controls. The oral challenge was not carried out for ethical reasons.

Delayed reactions to systemic drugs are not rare and patch test is a well-known method for diagnostic confirmation purposed in patients with generalised type IV hypersensitivity reactions.^{1,2} We report a systemic contact dermatitis due to ambroxol, presented as a maculopapular rash and confirmed by patch testing.

Systemic cutaneous reactions by immediate hypersensitivity have been described during the treatment with ambroxol such as urticaria. Delayed reactions to ambroxol such as non-pigmented fixed erythema³ and contact sensitivity to ambroxol have also been reported when administered by

aerosol,⁴ but as far as we know, this is the first case of systemic generalised dermatitis caused when taken orally.

Exanthema induced by bromexine has been reported⁵ and despite the chemical structures being very similar, the absence of cross-reactivity between them has been demonstrated in one case.⁴ More studies should be reported to ascertain it definitely. We did not perform an oral challenge with bromexine because of the possibility of inducing a severe reaction, and because it was not an essential drug for the patient.

References

1. Osawa J, Naito S, Aihara M, Kitamura K, Ikezawa Z, Nakajima H. Evaluation of skin test reactions in patients with non-immediate type drug eruptions. *J Dermatol* 1990;17:235-9.
2. Barbaud A, Reichert-Penetrat S, Tréchet P et al. The use of skin testing in the investigation of cutaneous adverse drug reactions. *Br J Dermatol* 1998;139:49-58.
3. Garcia Puga JM, Thomas Carazo E, Morata Cespedes MC, Caballero Garcia S, Recalde Manrique JM. Non-pigmented fixed drug-induced erythema. *An Esp Pediatr*. 1996;45(6):642-4.
4. Mancuso G, Berdondini RM. Contact allergy to ambroxol. *Contact Dermatitis*. 1989;20(2):154.
5. Anderson JAA, Adkinson NF. Allergic reactions to drugs and biological agents. *JAMA* 1987;258:2891-9.

Susana Monzón^a, María del Mar Garcés^b, Apolinar Lezaun^b, Juan Fraj^b, M. Asunción Domínguez^b y Carlos Colás^b

^aAllergy Department, Consorcio de SALUD, Ejea, Zaragoza, Spain

^bAllergy Service, Hospital Clínico Universitario

"Lozano Blesa", Zaragoza, Spain

E-mail: susanamonzonballarin@hotmail.com

(Susana Monzón Ballarín).

Severe allergy to poultry meat without sensitisation to egg proteins with concomitant Leguminosae allergy. Case report

To the Editor:

The number of known animal food allergens is limited. Although chicken meat is quite a common part of European diet and hen's egg is one of the most frequent allergens in children, severe poultry meat allergy without sensitisation to egg proteins is extremely rare.¹⁻³ Allergy to turkey and duck meat is even more rarely reported and the implicated allergens are poorly characterised.²⁻⁴ In the bird-egg syndrome, sensitisation to chicken feather allergen occurs by the respiratory route and afterwards allergy symptoms appear due to bird meat consumption. The implicated allergen is thought to be alpha-livetin.² We report a clinical case of severe chicken and turkey meat allergy without sensitisation to egg proteins. There was also coexisting Leguminosae allergy.

The particular interest of this case is the need for liver transplantation and use of immunosuppressive therapy in the patient with familial amyloid neuropathy.

Solid organ transplantation with the use of calcineurine inhibitors, especially tacrolimus, is a risk factor for new food allergies and probably for aggravation of the pre-existing food allergy.⁵ For this reason, careful elimination diet and immunosuppression with alternative drugs are very important in the post-operative period.

A 31-year-old Caucasian man, with a diagnosis of familial amyloid neuropathy, proposed for liver transplantation, was referred to our Immunoallergology Department for investigation of food allergy.

At the age of 21 and 23, he experienced generalised pruriginous erythema, laryngeal tightness and sialorrhoea immediately after ingestion of cooked red beans, white beans and black-eyed beans. At the age of 29, the patient developed generalised itch, palmar erythema, laryngeal tightness and dysphagia after ingestion of grilled chicken meat. One year later, he had a similar episode with ingestion of grilled turkey meat and oropharyngeal pruritus and sialorrhoea with ingestion of duck meat.

Following that, the patient eliminated all poultry meat and every type of beans from his diet. He had never had any complaints after ingestion of other legumes (namely soy), tree nuts and cooked or fresh eggs and had not previously ingested goose, pheasant and/or grouse meat.

The patient had symptoms of recurrent nasal obstruction from the age of 20 without seasonal aggravation. There was no contact with birds in the domestic environment and no history of eczema, asthma or drug allergies.

Skin prick tests (SPT) were performed with plastic Morrow-Brown needle (Stallerpoint®, Stallargenes) with extracts of the most common inhalant allergens and commercially available extracts of food allergens in a 0.5% phenolated solution and 50% glycerine (Bial-Aristegui®, Bilbao, Spain). Saline was used as a negative control and 10 mg/mL histamine phosphate as a positive control.

The SPT results were evaluated after fifteen minutes and reactions were considered positive if the largest wheal diameter was 3 mm over the negative control.

Cooked and raw chicken, turkey and duck meat, cooked and raw red and black-eyed beans were tested by prick-to-prick tests.

Serum total and specific IgE were determined by enzyme-immunoassay following the manufacturer's instructions (UniCAP®, Phadia, Uppsala, Sweden). Inhibition study was performed using RAST technique (UniCAP®, Phadia, Uppsala, Sweden) and results were expressed as percentage inhibition. Sodium dodecylsulphate-polyacrylamide gel electrophoresis (SDS-PAGE) Immunoblotting was carried out according to the method of Laemmli.⁶

Skin and serological test results are shown in Table I.

Food challenge was not performed due to the underlying disease and because of the clear clinical data with reproducible symptoms.

RAST inhibition study between rye-grass pollen and bean was positive (91%); the inverse study was negative.

SDS-PAGE Immunoblotting (Fig. 1) showed IgE binding bands of 27, 42 and 70 kDa in both, chicken and turkey raw meat extracts. Regarding turkey meat there was an intense fixation band in the 55 kDa region. The assay with bean extract demonstrated binding bands of 31 kDa.

The patient was instructed about the elimination diet (avoidance of all avian meat, beans, pea and chickpea) and

the use of intramuscular adrenaline Kit. He was submitted to a liver transplantation with a use of cyclosporine as immunosuppressive drug without any complications during one year of follow-up.

Patients with so-called "bird-egg" syndrome exhibit cutaneous and respiratory symptoms after ingestion of egg-yolk and/or inhalation of feathers. In the majority of cases the allergen involved is alpha-livetin (chicken serum albumin) and sensitisation occurs by respiratory route.² Allergy to poultry meat is rare and the implicated proteins are poorly characterised.

We describe a rare case of severe chicken and turkey meat allergy and oral allergy syndrome after ingestion of duck meat. The patient had no sensitisation to egg proteins. IgE-mediated mechanism was confirmed by skin prick, prick-to-prick tests and serum specific IgE measurements.

According to the published results, patients with bird-egg syndrome have specific IgE antibodies against a 70-kDa protein of egg yolk, whereas those who suffer from chicken meat allergy but no feathers or egg allergy show IgE antibodies against several lower molecular weight proteins of chicken meat.^{3,4} Our IgE-Immunoblotting study revealed proteins of 27 and 42 kDa with both chicken and turkey meat^{2,4}. A protein of 55 kDa was only found with the turkey meat extract, a protein with a similar molecular mass was previously reported by Cahen et al.² Although IgE binding has been described at 70 kDa-band in studies with both chicken and turkey meat extracts, this binding was weaker than with sera from patients with bird-egg syndrome.⁴

The results of electrophoresis of various avian meats performed by Kelso et al. showed that duck meat has binding bands (8 kDa, 16 kDa) different from chicken, turkey and goose meat. This fact can probably explain milder symptoms of our patient in exposure to duck meat with negative skin prick-to-prick test results and negative specific IgE measurement.

Legumes are dicotyledonous plants belonging to the Fabales order. This botanical order is formed by three families: *Mimosaceae*, *Caesalpiniaceae* and *Papilionaceae*. Bean (*Phaseolus vulgaris*), chickpea (*Cicer arietinum*) and pea (*Pisum sativum*) belong to the *Papilionaceae* family.⁷ Our patient had anaphylaxis after ingestion of red, white, and black-eyed bean, positive tests with pea and chickpea commercial extracts and elevated specific IgE to chickpea.

According to previously published results in Mediterranean population, about 80% of patients allergic to legumes had sensitisation to pollen; pea and bean were the legumes with more *in vitro* cross reactivity with *Lolium perenne*.⁷

Our RAST inhibition studies with rye-grass pollen and bean extracts showed the existence of cross-reactivity between both allergenic sources and the initial respiratory sensitisation to grass pollen. In the report of Ibanez et al., there was cross-reactivity between pea (*Pisum sativum*) and bean (*Phaseolus vulgaris*) in about 23% of the patients studied.⁷

To our knowledge, there are no reports of cross-reactivity between bean and chickpea (*Cicer arietinum*). SDS-PAGE Immunoblotting performed with bean extract revealed implicated protein of 31 kDa. The protein with similar molecular weight (30 kDa) was previously described for soy (*Glycine max*).⁸

Our patient had no complaints with soy ingestion and had negative skin and serological test results for soy.

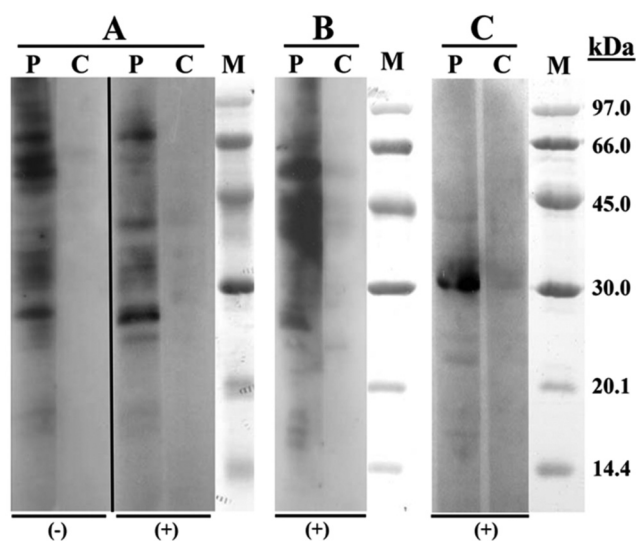
The cross-reactive allergens of Leguminosae family are poorly characterised and the risk of cross-reactivity is hard

Table 1. Skin and serological test results

Commercial allergens	SPT, mm	slgE, kU/L	Commercial allergens	SPT, mm	slgE, kU/L
Negative control	0	—	<i>Plantago lanceolatum</i>	5.5	0.73
Positive control	5.5	—	<i>Artemisia</i>	6.0	0.32
<i>Dermatophagoides pteronyssinus</i>	8.5	3.1	<i>Parietaria judaica</i>	0	NP
<i>Dermatophagoides farinae</i>	7.5	2.0	Latex	0	NP
<i>Acarus siro</i>	0	NP	Feathers mix	0	0
<i>Blomia tropicalis</i>	0	NP	Egg white	0	0
<i>Euroglyphus maynei</i>	0	NP	Egg yolk	0	0
<i>Lepidoglyphus destructor</i>	0	NP	Ovomucoid	0	0
<i>Alternaria alternata</i>	0	NP	Ovalbumin	0	0
<i>Asperillus fumigatus</i>	0	NP	Lentil	0	0
<i>Cladosporium</i>	0	NP	Chickpea	7.0	0.31
<i>Mucor</i>	0	NP	Pea	6.0	0.24
<i>Penicillium</i>	0	NP	Peanut	0	NP
<i>Candida albicans</i>	0	NP	Soybean	0	NP
<i>Trichophyton rubrum</i>	0	NP	Broad bean	0	NP
Grass pollen mix	6.5		Green bean	0	NP
<i>Lolium perenne</i>	7.5	3.52	White bean	5.5	0.20
<i>Phleum pratense</i>	6.5	3.2	Chicken meat	6.0	0.43
<i>Olea europea</i>	7.5	0.84	Turkey meat	0	0.14
<i>Betula</i>	0	NP	Duck meat	0	0

Native food	PPT, mm	Native food	PPT, mm
Chicken meat (cooked)	9.5	Duck meat (cooked)	0
Chicken meat (raw)	8.0	Red bean (raw)	0
Turkey meat (raw)	9.5	Red bean (cooked)	0
Turkey meat (cooked)	9.0	Black-eyed bean (raw)	0
Duck meat (raw)	0	Black-eyed bean (cooked)	0

SPT: Skin Prick Test, mean diameter of the wheal; slgE, serum specific IgE; NP: not performed; PPT: prick-to-prick test, mean.

**Figure 1.** Sodium dodecylsulfate-polyacrylamide gel electrophoresis results. A) Chicken meat extract; B) Turkey meat extract; C) Bean extract. P: patient serum; C: control serum (pool of serum from non-atopic subjects); M: molecular weight marker.

to predict, in any case elimination diet is recommended only for foods with positive clinical data or oral provocation tests. We suggested elimination of beans because of clear clinical data and laboratory results. Pea and chickpea elimination was suggested because of sensitisation, documented by skin prick-to-prick tests in the patient with elevated food allergy risk.

When a patient has allergy to hen's meat without sensitization to hen's egg, the risk of cross-reactivity with other types of poultry meat is increased³. This fact was the reason for a very restrictive diet with elimination of all poultry meat.

It is well recognized that immediate-type hypersensitivity and life threatening food allergy may arise post-liver transplantation in patients treated with tacrolimus and it has been suggested that those at greater risk are patients with a personal history of atopy⁵. The mechanism of this phenomenon is poorly understood. Tacrolimus increases intestinal permeability and probably also antigen transport across gastrointestinal epithelium. Besides, as other calcineurin inhibitors, tacrolimus was associated with suppression of interleukin-2 and interferon-gamma, having no effect on IL-4 and IL-10 (Th2 cytokines). Cyclosporin is significantly less potent than tacrolimus, so the current recommenda-

tions for cases with high risk of food allergy after solid organ transplantation involve dietary manipulations – elimination diet and replacement of tacrolimus by cyclosporine⁵. In this particular case we suggested cyclosporine therapy and a rigorous elimination diet with avoidance of all poultry meat and Leguminosae. The patient had no complications and has been asymptomatic during one year of follow-up.

We describe a rare case of an adult with allergic rhinitis who had serious allergic reactions to various beans and poultry (chicken and turkey). The complexity was increased due to the need for immune suppression for liver transplantation.

References

1. Zacharisen MC. Severe allergy to chicken meat. *WMJ*. 2006; 105(5):50-2.
2. Cahen YD, Fritsch R, Wuthrich B. Food allergy with monovalent sensitivity to poultry meat. *Clin Exp Allergy*. 1998;28:1026-30.
3. Kelso JM, Cockrell GE, Helm RM, Wesley Burks A. Common allergens in avian meats. *J Allergy Clin Immunol*. 1999;104:202-4.
4. Liccardi G, Szépfalusi Z, Noschese P, Nentwich I, D'Amato M. Allergy to chicken meat without sensitization to egg proteins: a case report. *J Allergy Clin Immunol*. 1997;100:577-9.
5. Ozdemir O, Arrey-Mensah A, Sorensen RU. Development of multiple food allergies in children taking tacrolimus after heart and liver transplantation. *Pediatr Transplantation*. 2006;10:380-3.
6. Laemmli UK. Cleavage of structural proteins during the assembly of the head of bacteriophage T. *Nature*. 1970;227:680-5.
7. Ibanez MD, Martínez M, Sánchez JJ, Fernandez-Caldas E. Reactividad cruzada de las legumbres. *Allergol Immunopathol (Madr)*. 2003;31(3):151-61.
8. Pereira M, Belver M, Pasqual C. La importancia alergénica de las legumbres. *Allergol Immunopathol (Madr)*. 2002;30(6):346-53.

Anna Sokolova^a, Ana Célia Costa^a,
Maria Conceição Santos^b, Borja Bartolomé^c
and Manuel Pereira Barbosa^a

^a*Serviço de Imunoalergologia,
Centro Hospitalar Lisboa Norte,
Hospital de Santa Maria, Lisbon, Portugal*
^b*Unidade de Imunologia Clínica,
Instituto de Medicina Molecular,
Faculdade de Medicina de Lisboa, Lisbon, Portugal*
^c*Bial-Aristegui, R&D Department, Bilbao, Spain*

*Corresponding author.

E-mail: asokolova@netcabo.pt (A. Sokolova).

Allergic Rhinitis and Childhood Sleep Disordered Breathing

To The Editor:

Paediatric allergic rhinitis is one of the most common chronic illnesses of childhood. It is typically characterized by sneezing, pruritis, rhinorrhea and congestion. Even mild al-

lergic rhinitis impacts all aspects of sleep, most prominently when uncontrolled. This case illustrates that uncontrolled allergic rhinitis can result in insomnia in a school age child.

Case Report: The patient is a 10 year old Hispanic male with a history of allergic rhinitis (AR) and specific IgE responses to grass, trees and dust mites documented by skin testing. He was well controlled with daily montelukast, and as needed, cetirizine and inhaled nasal corticosteroids. Currently, his mother stopped the montelukast and other medications, after hearing a news report that there were behavioural side effects associated with the montelukast. At the time she stopped the medications, there were no symptoms, changes in sleep or behaviour.

One month later, his sleep pattern dramatically changed. His sleep latency changed from ten minutes to two hours according to his history. Once asleep, he had two to three nocturnal awakenings. There was no associated snoring, nightmares, night terrors or daytime somnolence. His mother denied any changes in social, school or family history. He does not drink caffeinated beverages and has had no recent illness. His current symptoms also include frequent rhinitis, congestion and itchy eyes.

Environmental history: They have no pets or smokers at home. The family uses dust avoidance measures.

His past medical history is notable for normal spirometry, removal of tonsils and adenoids, for habitual snoring and enlarged tonsils in 2006. One nasal polyp was removed at the same time. No sleep study was performed. At the age of 15 months, he had one episode of cold symptoms and wheezing, which was relieved with albuterol. **Family Medical History:** notable for asthma in one parent. **Review of Systems:** He participates in soccer without dyspnoea or cough. His school performance is very good and has not changed since being off montelukast treatment. Notable findings on physical examination include a body mass index of 19. His ear, nose and throat exam revealed boggy pale nasal turbinates and clear nasal discharge. The remainder of his exam was normal. The patient was restarted on inhaled nasal corticosteroids and a second generation antihistamine with complete resolution of his symptoms.

Allergic Rhinitis is one of the most common chronic conditions among children. The disease is associated with both mechanical and inflammatory molecular mechanisms of sleep disordered breathing (SDB).¹ The case report illustrates that while the treatment of AR can contribute to SDB, the lack of treatment also can cause SDB.

Inflammatory cytokines are released as part of the allergic response, and in turn have been associated with suppression of both rapid eye movement (REM) and non-REM sleep. In particular, IL-1, IL-4 and SP can cause increased latency to REM.² Nasal challenges with Substance P can increase nasal airway resistance and latency to REM.³ The patient described was well controlled with montelukast, a leukotriene antagonist. Leukotrienes as key allergic mediators increase vascular permeability, mucus secretion and nasal obstruction. Nasal congestion is directly linked to sleep quality. Nasal congestion caused a 1.8 fold increase in moderate to severe sleep-disordered breathing compared to subjects without this symptom. The peak congestive hours are in the early morning, correlating with enhanced effect on sleep. In studies, mean nasal congestion peaked at 5:00 AM and was associated with a 20% increase in overall symptom intensity.⁴

One month after discontinuation of the montelukast, the patient developed symptoms of SDB. Post-marketing reports of behavioural and sleep disturbances among patients treated with montelukast prompted the parent to discontinue the drug. The published safety and tolerability data in children though, are quite favourable compared to placebo.⁵ A recent analysis of the use of montelukast showed that montelukast is effective in the treatment of allergic rhinitis, in comparison to placebo, but less effective than local application of corticosteroids.⁶ The clinician must balance the potential sleep related adverse side effects of anti-allergy medications, with the symptom control of allergic rhinitis to avoid SDB in this common paediatric disease.

References

1. Ferguson B. Influences of Allergic Rhinitis on sleep. *Otolaryngol Head Neck Surg* 2004;130:617-29.
2. Krouse HJ, Davis JE, Krouse JH. Immune mediators in allergic rhinitis and sleep. *Otolaryngol Head Neck Surg* 2002;126:607-13.
3. Devillier P, Dessanges JF, Rakotosihanaka F et al. Nasal response to substance P and methacholine in subjects with and without allergic rhinitis. *Eur Respir J* 1988;1:356-61.
4. Smolensky MH, Reinberg A, Labrecque G. Twenty four hour pattern in symptom intensity of viral and allergic rhinitis: treatment implications. *J Allergy Clin Immunol* 1995;95:1084-96.
5. McComas J, Noonan G, Philip G. et al. Safety and tolerability of montelukast in patients with seasonal allergic rhinitis: Adults and children as young as 2 years. *Ann Allergy Asthma Immunol.* 2003;90(1):131-51.
6. Nayak AA, Langdon RB. Montelukast in the treatment of allergic rhinitis: an evidence based review. *Drugs* 2007;67(6):887-901.

Amrita Dosanjh
Department of Pediatrics,
University of California-San Diego, USA
E-mail: pulmd@aol.com