antiphospholipid and anticardiolipin antibodies in the acute stage.

Hepatitis A is usually a benign and self-limited disease, but special attention must be paid to its complications when they occur.

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Prick test: A survey and comparison between Iranian allergic children and adults

To the Editor:

Allergic respiratory diseases such as asthma and rhinitis are common disorders which have grown considerably during the past 30 years with no doubt due to the world being more industrialised. Allergic rhinitis (AR) may simply affect man during almost any stages of life. Among causative allergens, aeroallergens have received more attention. It seems rational that recognition of high load responsible aeroallergens using a simple and inexpensive method such as skin prick test (SPT) within each specific area may improve the understanding of the pathologic patterns and ultimately give rise to more efficient treatment protocols.

All of the patients with the diagnosis of AR referred to the Research Center for Allergy & Asthma in Rasoul-e-Akram Hospital in Tehran, Iran between March 2007 and March 2008 were recruited in this cross-sectional study. Patients with a history of immunotherapy, dermographism, chronic steroids use and individuals younger than four years were excluded. After taking written informed consent from patients or guardians, all were provided with the questionnaires for medical records and baseline characteristics (e.g. gender, age, and family history of atopy). Patients were divided into two age categories: children <21 years and adults ≥ 21 years based on the American Academy of Pediatrics limits.[1]

All patients' sera and nasal smear were obtained for measuring the total IgE (ELISA method, Padtan Elm, Iran) and nasal smear eosinophilia (Gimsa staining), respectively. After enrolment, they were subjected to SPT by prick puncture test and the result was carefully graded for the widest wheal diameter [0 (<3 mm); 1+ (3–3.99 mm); 2+ (4–5.99 mm); 3+ (6–8.99 mm); and 4+ (≥ 9 mm or pseudopodia)]. The patients under confounding medication such as antihistamines and topical corticosteroids which interfere with SPT interpretation were asked to withhold them for a certain period based on the allergist's discretion.

Allergenic extracts (Allergopharma, Germany) included pollens (weeds, grass and trees), mites and moulds (*Penicillum Notatum, Aspergillus Fumigates*). Weeds were *Oxe eye daisy, Sorrel, Lambs quar*ter and three weeds mix (*Nettle, English Plantain, Dandelion Taraxacum Vulgare*). Grasses were *Barley, Vernal* and six grasses mix: *Velvet, Orchard, Rye* (*Lolium perennel*), *Timothy, Kentucky Blue and Meadow Fescue*. Tree extracts provided with early boom sing (*Birch, Beech, Oak and Plane*) and mid-boom sing [*Alder, Hazel, Poplar, Elm* (*Ulmus Scabra*) and *Willow*].

To test the differences between parametric and non-parametric variable means in groups of the study, Independent T-test and Mann-Whitney U-test were used, respectively. A Chi^2 statistical test was also used to evaluate the possible statistical differences in the distribution of qualitative variables among different groups of the study. A Spearman's rho test was used to assess the correlations between continuous variables. Receiver operating characteristics (ROC) curve analysis was also performed to evaluate the predictability of positive SPT with total serum IgE and a cut-off point was determined. A 5% probability of a type I error (two-tailed), and a power of 80% were

Table 1 Correlations between dependent and independent variable and predictor groups. (All mentioned data are significantly more frequent in the specific groups, otherwise, determined with NS)

	Sex *(Male vs. female)*		**Age** *(Children vs. adults)*		**Skin test** *Overall (±)*	**Groups**		
Signs	**F > M:** Contact dermatitis, wheal	**M > F:** Nasal polyps	**A > C:** PND	**C > A:** Insect bite allergy, congestion, purulent discharge, diaper rash	*NS.*	**Weed:** Wheal, turbine hypertrophy, bright discharge	**Grass:** Bright discharge	**Tree:** Bright discharge
Aggregators	*NS*		*NS*		*NS*	**Grass:** Indoor, park	**Tree:** Outdoor, diurnal, park	
Seasonal Patterns	*NS*		*NS*		*NS*	**Grass:** Spring, summer	**Tree:** Spring, summer	**Mould:** Spring

A: adults; C: children; F: female; M: male; NS: not significant.

considered in the analysis. All reported *P*-values are two-tailed and a *P*-value of <0.05 was considered significant. The study protocol was approved by the ethics committee of Iran University of Medical Sciences (IUMS thesis record: 4399) and all researchers adhere to the Declaration of Helsinki.

Among a total of 245 patients, there were 118 males (48.2%) and 127 females (51.8%) with a mean age of 26.39 (SD = 11.95) years, ranging from 4 to 65 years. Eighty-four patients (34.3%) were children and 161 patients were adults (65.7%). Asthma was presented in 42 (17.1%) allergic patients and a positive family history of atopy was reported in 179 (73.1%) of the patients. Rhinorrhoea (86%) and sneezing (73%) were the most frequent symptoms in medical records of the patients. Most frequent aggregators were cold weather (61%) and dust (56%), respectively. Overall seasonal pattern was seen in 36% (88) of patients, perennial pattern in 29.38% (72) and 20.81% (51) had perennial pattern with exacerbation in some seasons (mixed). More prevalent signs and symptoms, aggregators and seasonal patterns of exacerbations regarding age, sex, overall SPT results and specific antigenic groups are summarised in Table 1.

Eosinophilia (defined by more than 10% and 4% in adults and children, respectively) was seen in 88 (44%) of nasal smears and it was seen more in males than females [52 (59.1%) vs. 36 (40.9%), $P=0.031$]. Our study revealed that serum IgE level was higher in the positive SPT group in comparison to those with negative SPT (224.14 ± 235.05 vs. 53.57 ± 40.85 IU/ml, $P=0.005$). Regarding patient gender, there was no significant difference in IgE serum level between them. Moreover, no significant differences in the serum level of IgE were observed in different specific antigenic groups except for the positive SPT for mites ($P<0.001$). Also, serum IgE level was significantly correlated to the number of positive tests (Spearman's rho = 0.198, $P=0.002$) and severity of skin response based on diameter of the wheal (Spearman's rho = 0.243, $P<001$). Using ROC curve analysis, we proposed a cut-off point of 57 IU/ml for the total serum IgE to predict positive SPT results [Area under curve (AUC) = 0.815] with a specificity of 86%, sensitivity of 78%, positive predictive value (PPV) of 88%, and negative predictive value (NPV) of 9%.

Positive SPT was seen in 97.1% (238) of patients for at least one antigen while polysensitisation was also very common, observed in 93.7% (230). In particular, 4% (10) of patients were sensitised against one allergen, 27% (66) against 2–5 allergens, 41% (100) against 5–10 allergens, and 26% (64) against >10 allergenic extracts. Surprisingly, 13 patients (7%) were sensitised against all of the 13 antigenic extracts. The highest rates for positive SPT were for pollens (92.7%) followed by mites (64.9%), and moulds (50.2%); and among the pollens, weeds (87.3%), grass (78.8%) and trees (71%) were the commonest. In addition, the most frequent single allergen was weed pollen *Lambs quarter* (74.7% of total patients). There were not any significant difference in positive SPT frequencies of various allergens comparing for age groups and sex except for the grass *Bermuda* which occurred more frequently in females ($P=0.031$). A complete comparison of different variables between the two age groups is shown in Table 2.

Reviewing a relative large number of variables and predictors in our study, pollens constituted the major sensitising allergens, comparable to studies from Kuwait[2] and Turkey[3] with regards to considerably higher sensitising rates in our country [92.7% (our study, Iran) vs. 77.3% (Kuwait) and 44.3% (Turkey)]. Weeds and in particular *Lambs quarter* are heavily loaded out-door aeroallergens responsible for most allergic rhinitis patients in the area studied. As analysed, there were no considerable differences between children and adults. Our study failed to demonstrate a significant relationship between positive reactions and patient's age and gender except for the grass *Bermuda*. Furthermore, we found no statistically significant correlation between patients' sera total IgE and patient age.

Table 2 Comparison between children and adults for various variables

	Children *(n=84)*	Adults *(n=161)*	*P*-value
Serum IgE (IU/ml)	234.32±210.45	211.03±227.65	*NS*
Positive SPT			
Overall	81 (96.4%)	157(97.5%)	*NS*
Pollens	79 (94%)	148(91.9%)	*NS*
Weed	74 (88.1%)	140(87%)	*NS*
Grass	67 (79.8%)	126(78.3%)	*NS*
Tree	58 (69%)	116(72%)	*NS*
Mould	40 (47.6%)	83(51.6%)	*NS*
Mite	48 (57.1%)	111(68.9%)	*NS*
Polysensitisation			
Overall	78 (92.1%)	150(93.2%)	*NS*
2–5 allergens	26 (31%)	39(24.2%)	*NS*
6–10 allergens	31 (36.9%)	68(42.2%)	*NS*
>10 allergens	21 (25%)	43(26.7%)	*NS*
Full[a]	3 (3.6%)	11(6.8%)	*NS*
Eosinophilia	24 (35.5%)	64(48.1%)	*NS*

NS: not significant
[a]Sensitisation against all 13 antigenic extracts.

Our research centre receives allergic patients from almost all parts of the country with the different vegetation, climate and temperature which could design a relatively reliable model for predicting the responsible aeroallergens in a certain area between the Caspian Sea and Persian Gulf. Our result is comparable with studies in four capital cities of Iran conducted in Karaj[4] in the north; Mashhad[5] in the northeast; and Shiraz[6] in the central part, all have semiarid climate with hot summers and cold winters. Higher rates for house dust mites reported from Sistan-Blouchestan[7] province in the southeast may probably be due to the higher humidity which is to be expected as it is located along the Oman Sea. This is in agreement with studies from Thailand[8], and Singapore[9] with high humidity that makes a suitable medium for mites to grow.

Comparable level of serum IgE in positive SPT for mites – despite its low positive rate (64.9% vs. 92.7% for pollens)- may be due to the higher antigenicity of these allergens versus lower spread load. Although total serum IgE level is considered as a non-specific-sensitive diagnostic laboratory aid, our study proposed a cut-off point of 57 IU/ml to predict positive reaction with a considerable sensitivity and specificity. It was also related to the severity of skin response to various allergenic extracts.

Significant casual relationship was found between passive or active smoking and asthma (OR=2.5, CI 95%=1.2–5.05, P=0.008). This simple but real fact reminds one that overlooking such a non-medical cultural point of view may readily fade the effects of specific medical interventional strategies against allergic diseases, even at a national level.

Designation of a proper multidisciplinary strategy demands an exact knowledge about the spread load of the responsible allergens in certain areas according to their considerable variation within a country, besides the vast variety between countries. Moreover, concordance of medical and non-medical strategies may warrant better results controlling the morbidities related to allergic diseases and which put a very heavy financial burden on healthcare systems.

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Sitagliptin Intolerance

To the Editor

In type 2 diabetes mellitus, the actions and secretion of insulin are impaired, as opposed to the absolute deficiency of insulin which occurs with type 1 diabetes mellitus. Type 2 diabetes has traditionally been treated in a stepwise manner.[1] The treatment has started with lifestyle modifications, exercise, and later on, pharmacotherapy with oral and parenteral agents.[3] Sitagliptin is one of the dipeptidyl peptidase-4 (DPP-4) inhibitors which represent a new therapeutic approach.[4] Side effects of sitagliptin include upper airway symptoms mimicking rhinitis. Allergic rhinitis is frequent in the Turkish population (16%).[2] Rhinitis is one of the most frequent and disabling illnesses affecting the general population. The history of symptoms, medication and disease is important to be able to distinguish between allergic or non-allergic rhinitis, and also for diagnosis and treatment.

Fifteen type 2 diabetics were selected from the whole diabetic population admitted and were followed up for blood glucose regulation in 2008–2009 in Fatih University Hospital. Those patients who had unregulated blood glucose with other antidiabetic drugs received sitagliptin for accepted indications. Two diabetics among them developed nasal congestion, postnasal drip, wheezing, and fatigue. There was no accompanying medication associated with nasal and pulmonary symptoms such as ACE inhibitors and/or beta blockers. The Ear-nose-throat and department of pulmonary and allergic diseases consultations revealed no noticeable findings. The symptoms were resolved completely within three days after drug withdrawal for these two patients. The others who received sitagliptin did not have any complaint about medication.

In the first case a 66 year-old woman who was diagnosed with type 2 diabetes mellitus 10 years ago was admitted to the endocrinology clinic with the complaint of postnasal drip, cough and fatigue at the 10th day of sitagliptin use. She had a history of hypertension. She was prescribed sitagliptin for diabetes and followed up for blood glucose regulation. Ten days after initialising the sitagliptin treatment she had symptoms of rhinitis, nasal congestion, postnasal drip, wheezing, and fatigue. She was evaluated for atopic aetiology with skin prick tests. Skin prick tests were negative for mites, moulds, pollens, animal dander and feathers. The symptoms were resolved after the fourth day of drug withdrawal.

In the second case a 52 year-old woman who was followed up with type 2 diabetes mellitus for 25 years presented with the complaints of nasal congestion, postnasal drip, throat pain, cough and fatigue after 15 days using sitagliptin. She had also history of hypertension requiring no medication. She was prescribed sitagliptin for glycaemic control. She did not have any history of atopy. Skin prick tests were also performed for this patient and were negative. The symptoms were resolved after the third day of drug withdrawal. Due to the severity of the symptoms, we were unable to re-introduce the drug to determine whether the symptoms would return.

Type 2 diabetes mellitus is characterised by two major pathophysiological defects: (1) insulin resistance, which results in increased hepatic glucose production and decreased peripheral glucose consumption, and (2) impaired β-cell secretory function.[1]

Dipeptidyl peptidase-4 (DPP-4) inhibitors represent a new therapeutic approach for the treatment of type 2 diabetes.[4] These agents work by inhibiting the DPP-4 enzyme that degrades incretin hormones such as glucagon-like peptide (GLP)-1 and glucose-dependent insulinotropic polypeptide (GIP). Active GLP-1 and GIP stimulate glucose-dependent insulin biosynthesis and release, and GLP-1 also suppresses glucagon release, delays gastric emptying, and increases satiety.[5] In patients with type 2 diabetes, chronic treatment with DPP-4 inhibitors decreased postprandial glucose excursion, fasting plasma glucose, and haemoglobin A1c (HbA1c), and was well tolerated with neutral weight effects and a low incidence of hypoglycaemia and gastrointestinal adverse events relative to placebo.[6]

One of the DPP-4 inhibitors is sitagliptin, which is a potent, competitive, reversible inhibitor of the DPP4 enzyme, and is the first agent in this class to be used.[7]

Medication with DPP-4 inhibitors appears to be reasonably safe.[8] There was also slightly higher incidence of constipation, nasopharyngitis, pharyngitis, pharyngolaryngeal pain, rhinitis, urinary tract infection, myalgia, arthralgia, hypertension, and dizziness.[9] In our cases, these side effects did not occur. Rhinitis and other upper airway symptoms were seen in our two cases although it has been reported that