

**Original Article** 

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# Skin prick test results and prevalence of allergic symptoms in workers exposed to toluene

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**Aim:** To determine the distribution of allergens and allergic symptoms according to occupation groups in those who were exposed to toluene and presented with allergic rhinitis symptoms.

**Materials and methods:** Of the 2005 patients who were administered an allergy test with the prediagnosis of allergic rhinitis, the files of 138 patients who were exposed to toluene were analyzed retrospectively.

**Results:** The mean age of the patients was  $35 \pm 10$  years. Distributions of symptoms and allergens of 57 patients (41.3%) with negative skin prick test and 81 patients (58.7%) with positive skin prick test were analyzed according to occupation groups. There was no significant difference between the groups in terms of symptoms at baseline except for the symptom of runny nose (P > 0.05). The groups were compared in terms of complaints that started at the age of 16 or later, which was found as 76.5% in the positive group and 91.2% in the negative group.

**Conclusion:** The occupation of the patient must be considered in patients who present with allergic symptoms; in particular, patients with negative skin prick test should be investigated in terms of occupational exposure.

Key words: Allergic rhinitis, allergy, toluene, occupational disease

# Toluen maruziyeti olan işçilerde deri prik testi sonuçları ve alerjik semptom sıklığı

**Amaç:** Toluene maruziyetin olduğu mesleklerde çalışan ve alerjik rinit semptomları ile başvuranlarda alerjenlerin ve alerjik semptomların meslek gruplarına göre dağılımının belirlenmesi.

**Yöntem ve gereç:** Alerjik rinit ön tanısıyla başvurup deri prik testi yapılan 2005 hastadan toluene maruziyetin olduğu mesleklerde çalışan 138 hasta retrospektif olarak incelendi.

**Bulgular:** Hastaların yaş ortalaması 35  $\pm$  10 idi. Deri prik testi negatif olan 57 (% 41,3) hasta ve pozitif olan 81 (% 58,7) hastanın semptom ve alerjen dağılımları meslek gruplarına göre analiz edildi. Nazal semptomların sıklığı karşılaştırıldığında burun akıntısı dışında gruplar arası fark bulunmadı. Gruplar şikayetlerin 16 yaş üstünde başlama durumu açısından karşılaştırıldığında pozitif grupta bu oran % 76,5 ve negatif grupta % 91,2 olarak tespit edildi.

**Sonuç:** Alerjik semptomlarla gelen hastalarda mutlaka meslek sorgulanmalı özellikle deri prik testi negatif olan hastalar mesleksel maruziyet yönünden araştırılmalıdır.

Anahtar sözcükler: Alerjik rinit, alerji, toluen, meslek hastalıkları

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# Introduction

Allergic rhinitis (AR) is a symptomatic inflammatory disease of the nose characterized by specific IgE-related hypersensitivity. Its symptoms generally appear after exposure of the nasal mucosa to the allergen (1). Allergic rhinitis is the most common type of allergic disease, with 10%-40% prevalence in the community (2). Factors causing allergic diseases can vary between countries or different parts of a country due to geographic, climatic, occupational or various social conditions (3).

Toluene is the basic component of thinner that is used as an organic solvent in industry today. It is widely used in paint, drugs, cosmetics, shoe and automotive industries, and in production of explosive substances and adhesives. Toluene shows its effect through transmission into blood, tissues, and tissue fluids. It is used in dyes, ink, thinner, stuccos and undercoats, adhesives, lac dyes, and other solventrequiring compounds (4,5). Toluene affects many organ systems and tissues in humans. Occupational exposure to toluene usually occurs via inhalation. Cutaneous exposure also occurs. Workers in shoe or press shops who are exposed to toluene for a long time are at risk of chronic toxicity (5,6).

Although it is usually neglected, obtaining a detailed occupational history is very important in terms of the diagnosis and treatment success (5). This study was planned to determine the distribution of allergens and allergic symptoms according to occupation groups in those who were exposed to toluene and presented with allergic rhinitis symptoms as well as to contribute preventive measures by taking environmental factors into consideration.

#### Materials and methods

Patients with the prediagnosis of AR (allergic rhinitis) who had been followed-up with an allergy test in Keçiören State Hospital Otorhinolaryngology Clinic between January 2008 and December 2010 were included in the study. Of the 2005 patients who were administered an allergy test with the prediagnosis of AR, the files of 138 patients who were exposed to toluene were analyzed retrospectively. All the patients were divided into 3 groups according to their

jobs. Those who were painters and plasterers in the construction sector were classified as Group 1, those working in furniture production and printing houses were classified as Group 2, and workers in automotive repair and dyes as well as gas station attendants were classified as Group 3.

Diagnosis of AR was made based on the physical examination findings, nasal endoscopic examination findings, and the skin prick test results. Sneezing, runny nose, nasal obstruction and nasal itching, presence of serous secretion in the nasal cavity, pale nasal mucosa, edema, and pale or purplish concha were interpreted in favor of AR. Patients were analyzed in terms of skin findings and presence of erythema, itching, urticaria, and eruption, and these data were recorded. Cough, dyspnea, and wheezing were investigated as pulmonary symptoms. Itching, redness, and edema were investigated as ocular symptoms.

Alyostal ST-IR (Stallegenes S.A. France) standard allergen extracts were used for the skin prick test. For the test, antihistamines had to be withdrawn 10 days in advance, H, receptor blockers had to be withdrawn 24 h in advance, and antidepressant drugs withdrawn 20 days in advance. Allergen extracts that were obtained in standard doses in quick test applicators with 8 distinct edges were applied onto the skin after the ventral surface of the forearm was wiped with alcohol. The results were evaluated 15 min later. Histamine-HCl was used as positive control and isotonic NaCl was used as negative control. The validity criteria for the test were accepted as >3mm for positive control and <3 mm for negative control. A skin reaction against the allergen with an induration of >3 mm in diameter was accepted as a positive reaction (7).

The most common 30 allergen extracts and positive and negative controls were applied using a total of 4 applicators onto the skin of the forearm for the skin prick test. Two house dust mites, 3 fungal spores, 1 insect, 3 animal epithelia, 15 pollens, and 6 food allergens were used.

The skin prick test was not applied in patients who had been treated with the diagnosis of asthma, nor in those who had suspected asthma and those on beta-blocker agents.

#### Results

The mean age of the patients was  $35 \pm 10$  years (range 17-60 years). Demographic features of the patient groups and prick test results are presented in Table 1.

When the groups were compared in terms of complaints that started at the age of 16 or later, it was found as 76.5% in the positive group and 91.2% in the negative group. The difference was statistically significant (P = 0.039).

Table 2 displays allergens with significant differences among those with positive skin prick test responses according to occupation groups. No differences were found between occupations for other allergens.

Distributions of symptoms and allergens of 57 patients (41.3%) with negative skin prick test and 81

patients (58.7%) with positive skin prick test were analyzed according to occupation groups.

Nasal symptoms of the groups are presented in Table 3, and dermatological, ocular, and pulmonary symptoms are displayed in Figures 1-3. There was no significant difference between the groups in terms of symptoms and nasal examination findings at baseline, except for the symptom of runny nose (P > 0.05).

### Discussion

AR is classified as either perennial (lasting all year long) or seasonal according to the presence of symptoms developing depending on the duration of former allergen exposure (8). While perennial AR develops with house dust mite, fungi, insects, and animal hair, seasonal AR arises with various outdoor

Table 1. The demographic features of the groups.

	Negative	Positive	P value
Age	$37.7 \pm 10.3$	$33.2\pm9.7$	0.006
Age of symptom onset	$30.5\pm10.6$	$25.4\pm10.9$	0.012
Duration of symptoms	$7.2 \pm 8$	$7.9 \pm 8$	0.65
Group 1 (n = 81) n / %	26 / 32.1%	55 / 67.9%	0.028
Group 2 (n = 35) n / %	18 / 51.4%	17 / 48.6%	
Group 3 (n = 22) n / %	13 / 59.1%	9 / 40.9%	

Table 2. Distribution of allergens according to occupation groups.

	Group 1 (n = 81)	Group 2 (n = 35)	Group 3 (n = 22)	P value
D. pteronyssinus	13.6%	11.4%	45.5%	0.001
Tree mix	12.5%	20%	36.4%	0.035
Grass mix	19.8%	31.4%	50%	0.016
Cat	0	7.4%	9.5%	0.047
Alternaria	2.9%	0	14.3%	0.037
Aspergillus	4.3%	0	19%	0.014
Cladosporium	10.1%	0	23.8%	0.026
Willow	2.7%	3.3%	18.2%	0.017
Pine	2.9%	3.7%	19%	0.02
Nettle	13.3%	23.3%	36.4%	0.049
Strawberry	1.4%	0	14.3%	0.009

	Prick test	Group 1 Negative (n = 26) Positive (n = 55)	Group 2 Negative (n = 18) Positive (n = 17)	Group 3 Negative (n = 13) Positive (n = 9)	P value
Runny nose	Negative	69.2%	72.3%	30.8%	0.035
	Positive	80%	82.4%	66.7%	0.61
Nasal obstruction	Negative	76.9%	72.2%	76.9%	0.92
	Positive	89.1%	76.5%	100%	0.18
Sneezing	Negative	61.5%	77.8%	61.5%	0.48
	Positive	65.5%	58.8%	66.7%	0.87
Itchy nose	Negative	76.9%	88.9%	84.6%	0.57
	Positive	83.6%	76.5%	77.8%	0.76
Postnasal drip	Negative	69.2%	77.8%	66.7%	0.75
	Positive	78.2%	64.7%	55.6%	0.25
Headache	Negative	76.9%	77.8%	84.6%	0.84
	Positive	70.9%	88.2%	66.7%	0.31
Smell disorder	Negative	53.8%	55.6%	53.8%	0.9
	Positive	65.5%	35.3%	66.7%	0.07
Dyspnea	Negative	69.2%	44.4%	23.1%	0.02
	Positive	38.2%	35.3%	33.3%	0.94

Table 3. The distribution of nasal symptoms according to the occupation groups.



Figure 1. Frequency (%) of pulmonary symptoms according to prick test results.



Figure 2. Frequency (%) of dermatologic symptoms according to prick test results.

allergens like pollen (9). Allergy is a systemic disease, manifesting with nasal, ocular, dermatological, and pulmonary symptoms. Thus, allergic patients should be evaluated through a multidisciplinary approach (10). Allergen exposure is reported to affect the duration of symptoms in studies investigating the relationship between allergens and occupations (11). In our study, pollen positivity was detected at a higher rate compared to indoor allergens leading to



Figure 3. Frequency (%) of ocular symptoms according to prick test results.

perennial allergic rhinitis. Furthermore, presence of all symptoms all year long inconsistent with allergen distribution is a significant finding that supports occupational exposure.

Although toluene exposure occurs mainly via inhalation, it may also occur via the gastrointestinal system, and the cutaneous and mucosal route. Occupational exposure occurs especially via inhalation (4,12). Toluene exposure is mainly seen in workers in the dye industry, shoe production shops, petrochemical industry, printing, adhesive production, and pharmaceutical industry (4,13,14). Toluene exposure is much more frequent in this occupation group compared to the general population (5). Toluene is absorbed easily and quickly from the lungs. The reported absorption rates vary between 40% and 60% (4,15-18). Toluene has been shown to be absorbed through skin exposure to liquid toluene (19). Absorption of orally ingested toluene is much lower than that of toluene taken via inhalation (5). In our study the finding that complaints beginning after 16 years of age in 91.2% of the group with negative skin prick test is different from the positive group was consistent with the age of starting to work in those working in those sectors.

There is a linear relationship between the amount of toluene in arterial blood and the amount of alveolar air. Thus, the amount of toluene in arterial blood increases as the amount of toluene in alveolar air increases. The concentration of toluene in alveolar air and arterial and venous blood decreases quickly just after termination of toluene exposure and later the rate of decrease gradually decreases (20,21). According to the results of our study, the least skin prick test response was obtained in workers of the automotive sector. The rate of symptoms was found to be high and the allergic symptoms were thought to arise in the negative group with mucosal injury due to higher exposure rates in this sector. The fact that the allergen rate was higher in this group may be explained by the injured mucosa being more sensitized.

Although the smell of toluene provides sufficient warning for dangerous concentrations of toluene, exposure to toluene for 15 min at a concentration of 8 ppm, which is the sensory threshold value, leads to olfactory insufficiency (4). Karabulut et al. reported the rate of smell disorders as 47% in males who presented with allergic rhinitis symptoms (10). In our study, smell disorder was found to be higher in both groups and this was considered to be related to olfactory injury.

Severe toluene exposure may cause fluid deposition in the lungs and respiratory arrest. Chemical pneumonitis may develop as a result of pulmonary aspiration in the course of liquid toluene ingestion or vomiting after ingestion (4). In our study, the fact that the frequency of dyspnea was significantly higher especially in the first and second groups of the negative prick test group compared to the positive group suggests that toluene shows clinical manifestations by mimicking allergic symptoms.

Repeated and long term cutaneous exposure of toluene may cause erythema and urticaria (4). In our study, the symptoms of erythema and urticaria were higher in the negative group compared to the positive group, and this was found to be consistent with cutaneous findings of toluene exposure.

Toluene exposure-related ocular inflammation is usually mild. Burning, conjunctivitis, and keratitis may develop when toluene comes into contact with the eye by accidental splashing (4,22,23). According to our results, the high frequency of ocular symptoms in both groups was found to be consistent with the data in the literature.

In conclusion, although allergen distribution in occupation groups subjected to toluene exposure is lower compared to data in the literature, the high allergic symptom rates may be explained by chronic occupational toluene exposure-related mucosal injury. Occupation should be questioned in patients

# References

- Schäper C, Gustavus B, Koch B, Ewert R, Hanf G, Kunkel G et al. Effects of fexofenadine on inflammatory mediators in nasal lavage fluid in intermittent allergic rhinitis. J Investig Allergol Clin Immunol 2009; 19: 459-464.
- Bauchau V, Durham SR. Epidemiological characterization of the intermittent and persistent types of allergic rhinitis. Allergy 2005; 60: 350-3.
- Nicolaou N, Siddique N, Custovic A. Allergic disease in urban and rural populations: increasing prevalence with increasing urbanization. Allergy 2005; 60: 1357-60.
- Agency for Toxic Substances and Disease Registry (ATSDR). Toluene CAS 108-88-3; UN: 1294. Available from: www.atsdr. cdc.gov/MHMI/mmg56.pdf
- Karabulut I, Balkanci ZD, Pehlivanoglu B, Erdem A, Fadillioglu E. Effect of toluene on erythrocyte membrane stability under in vivo and in vitro conditions with assessment of oxidant/ antioxidant status. Toxicol Ind Health 2009; 25: 545-50.
- Saygun M, Cakmak A, Ekici A, Pinar T, Bulcun E, Ulu N et al. Five annual observations of respiratory findings in gun factory workers exposed to solvents. J Occup Environ Med 2007; 49: 909-12.
- Polosa R, Al-Delaimy WK, Russo C, Piccillo G, Sarva M. Greater risk of incident asthma cases in adults with allergic rhinitis and effect of allergen immunotherapy: a retrospective cohort study. Respir Res 2005; 28: 153.
- 8. International Rhinitis Working Management Group. International Consensus Report on the diagnosis and management of rhinitis. Allergy 1994; 49 Suppl 9: 5-34.
- 9. Lund V. Allergic Rhinitis-Making the correct diagnosis. Clin Exp Allergy 1998; 28: 25-8.
- Karabulut H, Karadağ AS, Acar B, Demir M, Babademez MA, Karaşen RM. Ankara Keçiören bölgesinde deri prick testi sonuçlarının meterolojik ve demografik özelliklere göre değerlendirilmesi. KBB-Forum 2009; 8: 46-54.
- Bıçakçı A, Tatlıdil S, Canıtez Y, Malyer H, Sapan N. Mustafakemalpaşa ilçesi (Bursa) atmosferindeki alerjen Alternaria Sp. ve Cladosporium Sp. sporları. Akciğer Arşivi 2001; 2: 69-72.
- Akgür S, Öztürk P, Kurtulmuş Y, Karali H, Ertürk S. Medicolegal aspects of blood urine toluene and urinary orthocresol concentrations in toluene exposure. Turk J Med Sci 2001; 31: 415-419.

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- McGregor D. The genetic toxicology of toluene. Mutat Research 1994; 317: 213-228.
- Tassaneeyakul W, Birkett DJ. Human Cytocrome P450 isoform specificity in the regioselective metabolism of toluene and o-, m- and p-xylene. J Pharm Exp Therp 1996; 276: 101-108.
- Csanady A, Filser JG. The relevance of physical activity for the kinetics of inhaled gaseous substances. Arch Toxicol 2001; 74: 663-672.
- Pierce CH, Dills R, Silvey GW, Kalman DA. Partition coefficients between human blood or adipose tissue and air for aromatic solvents. Scand J Work Environ Health 1996; 22: 112-118.
- 17. Nomiyama K, Nomiyama H. Respiratory elimination of organic solvents in man. Benzene, toluene, n-hexane, trichloroethylene, acetone, ethyl acetate and ethyl alcohol. Int Arch Arbeitsmed 1974; 32: 85-91.
- Paustenbach D, Alarie Y, Kule T, Schachter N, Smith R, Swenberg J et al. A recommended occupational exposure limit for formaldehyde based on irritation. Journal of Toxicology and Environmental Health 1997; 50: 217-63.
- 19. Dutkiewicz T, Tyras H. The quantitative estimation of toluene skin absorption in man. Int Arch Arbeitsmed 1968; 24: 253-7.
- 20. Sato A, Nakajima T, Fujiwara Y, Hirosawa K. Pharmacokinetics of benzene and toluene. International Archives of Occupational and Environmental Health 1974; 33: 169-82.
- 21. Veulemans H, Masschelein R. Experimental human exposure to toluene. International Archives of Occupational and Environmental Health 1978; 42: 91-103.
- 22. Andersen I, Lundqvist GR, Molhave L, Pedersen OF, Proctor DF, Vaeth M et al. Human response to controlled levels of toluene in six-hour exposures. Scand J Work Environ Health 1983; 9: 405-18.
- 23. Baelum J, Andersen IB, Lundqvist GR, Molhave L, Pedersen OF, Vaeth M et al. Response of solvent-exposed printers and unexposed controls to six-hour toluene exposure. Scand J Work Environ Health 1985; 11: 271-80.