

## High toluene exposure risk increases risk of olfactory dysfunction in furniture workers

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### ABSTRACT

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#### BACKGROUND

Few studies have investigated the impact on olfactory functioning of occupational exposure to toluene, an industrial solvent used in paints and cleaning fluids. The estimated olfactory dysfunction prevalence is 0.5–5%. Patients frequently do not complain about olfactory dysfunction. However, occupational exposure to chemicals may affect workers' health and safety, because of their continuous inhalation. This study aimed to examine the relationship between toluene exposure and olfactory dysfunction in furniture workers.

#### METHODS

This was a cross-sectional study involving 65 workers. Data collection was by observation and interview on demographic characteristics, history of habits, and symptoms of chronic rhinitis. Risk of exposure scores were evaluated from potential hazard, exposure level, duration of employment, type of work, use of masks, ventilation of work space, and education and training. Olfactory function was tested using Sniffin' Sticks, and determination of environmental toluene level was by personal sampling. The odds ratio was used to test correlations between variables.

#### RESULTS

Only 44 subjects could be analyzed, 37 (84.1%) of whom had olfactory dysfunction. Workers with high toluene exposure had a significantly 12.5-fold risk of olfactory dysfunction in comparison with those with low exposure (OR=12.5; CI 95% 1.35 – 115.79).

#### CONCLUSIONS

Toluene exposure increases risk of olfactory dysfunction in furniture workers. Olfactory function testing should be considered for initial screening or periodic testing of furniture workers. Low toluene levels with a high proportion of olfactory dysfunction indicate that olfactory dysfunction is an early negative impact of chemical inhalation.

**Keywords:** Olfactory dysfunction, toluene, sniffin sticks, furniture workers

## ***Risiko pajanan toluen meningkatkan gangguan penghidu pada pekerja mebel***

### **ABSTRAK**

#### **LATAR BELAKANG**

Terdapat sedikit studi yang meneliti dampak pajanan toluen di tempat kerja terhadap fungsi penghidu. Toluene merupakan bahan pelarut cat dan bahan pembersih. Prevalensi gangguan penghidu akibat pajanan bahan kimia pada pekerjaan diperkirakan antara 0.5 – 5%. Gangguan penghidu sering tidak dikeluhkan oleh penderitanya, tetapi dapat mempengaruhi kesehatan dan keselamatan. Penelitian ini bertujuan untuk menentukan adanya hubungan antara besarnya risiko pajanan toluen dengan kejadian gangguan penghidu pada pekerja mebel.

#### **METODE**

Penelitian ini menggunakan desain potong lintang mengikut sertakan 65 orang. Pengumpulan data menggunakan observasi dan wawancara yang meliputi karakteristik demografi, riwayat kebiasaan dan gejala rinitis kronik. Skor besar risiko pajanan dinilai berdasarkan tingkat bahaya potensial, tingkat pajanan, masa kerja, jenis pekerjaan, penggunaan masker, ventilasi ruang kerja, edukasi dan pelatihan. Pemeriksaan fungsi penghidu dengan menggunakan Sniffin' Sticks dan kadar toluen lingkungan diukur dengan menggunakan sampel perorangan. Uji rasio odds digunakan untuk menguji hubungan antara berbagai variabel.

#### **HASIL**

Hanya 44 subjek yang dapat dianalisis, dengan 37 (84,1%) yang mengalami gangguan penghidu. Kelompok pereja yang mengalami risiko pajanan toluene yang tinggi meningkatkan risiko terjadinya gangguan penghidu sebesar 12,5 kali secara bermakna dibandingkan kelompok dengan risiko pajanan yang rendah (RO=12,5; 95% Interval kepercayaan 1,35 – 115,79).

#### **KESIMPULAN**

Pajanan toluen meningkatkan risiko gangguan penghidu pada pekerja mebel. Pemeriksaan fungsi penghidu perlu dipertimbangkan sebagai salah satu skrining awal atau pemeriksaan berkala bagi pekerja di industri mebel. Kadar toluen yang rendah dengan proporsi gangguan penghidu yang besar, menandakan bahwa gangguan fungsi penghidu merupakan dampak negatif dini dari pajanan inhalasi bahan kimia.

**Kata kunci:** Gangguan penghidu, toluen, sniffin sticks, pekerja mebel

## **INTRODUCTION**

Airborne chemicals and volatile molecules enter the nose and can interact with chemoreceptors in the nasal cavity, especially trigeminal and olfactory receptors. Exposure to pollutant or toxic substances is known to induce adverse health effects but few studies have been devoted to the impact on olfactory functioning. Actually, effects of toluene inhalation on human health have been extensively described.<sup>(1,2)</sup>

Toluene is used as an additive in gasoline mixtures to increase octane ratings, in benzene production, and as a solvent in paints, coatings, inks, adhesives, and cleaners. Additionally, toluene is used in the production of nylon, plastics, and polyurethanes. Workers in many occupations, including painting and paint manufacturing, lumber and furniture fabrication, machining operations, equipment cleaning and degreasing, and floor and carpet laying, are exposed over time to significant levels of

solvents, such as acetone, methyl ethyl ketone, and toluene.<sup>(3)</sup>

The Olfaction in Catalonia (OLFACAT) survey was carried out in the general population of Catalonia in Spain and showed that the prevalence of smell dysfunction was 19.4% for detection (0.3% anosmia, 19.1% hyposmia), 43.5% for recognition (0.2% anosmia, 43.3% hyposmia) and 48.8% for identification (0.8% anosmia, 48% hyposmia).<sup>(4)</sup>

The exact prevalence of chemically-induced occupational olfactory dysfunction is unknown, but one proposed estimate is 0.5–5% of all olfactory dysfunctions, including use of pharmaceutical drugs. The real relevance of this problem is possibly overlooked, since occupational exposure may account for a significant part of so-called idiopathic olfactory dysfunction, i.e. 10–25% of all olfactory problems within the general population.<sup>(5)</sup>

Olfactory dysfunction may be caused by various factors, such as mechanical, infectious, traumatic, iatrogenic, metabolic, neurologic, exposure to toxic substances such as organic solvents, metals, and alcohol.<sup>(6)</sup> In contrast to other sensory dysfunctions, olfactory dysfunction is frequently undetected and not complained of by the patient. From the standpoint of safety, olfactory dysfunction may reduce a person's alertness to the hazards of fire, chemical vapors, and spoiled food.<sup>(7,8)</sup>

In a study conducted to detect olfactory dysfunction, where the subjects were exposed to toluene inhalation, there was an increase in olfactory sensitivity after toluene inhalation.<sup>(9)</sup> In contrast, a study involving workers in a plastics factory who were exposed to organic solvents, particularly toluene, found a significant reduction in olfactory threshold scores before and after working hours, with a hyposmia prevalence of 4%.<sup>(7)</sup> An animal study involving rats exposed to 1000 ppm toluene for 5 hours per day, 5 days per week, for 4 weeks, found in the fourth week a reduction in olfactory epithelial thickness, that returned to normal 2 weeks after cessation of the exposure.<sup>(10)</sup>

To date, several olfactory function testing methods of higher sensitivity have been developed and subjected to cultural validation, such as the University of Pennsylvania Smell Identification Test (UPSIT), Brief Smell Identification Test, Japanese Odor Stick Identification Test (OSIT), Scandinavian Odor Identification Test (SOIT), and Sniffin Sticks.<sup>(11)</sup> The present study aimed to determine any association between risk of toluene exposure in furniture workers and olfactory dysfunction (including olfactory threshold, discrimination, and individuality). The risk of toluene exposure in this study was determined semiquantitatively, to obtain estimates of toluene uptake by the workers.<sup>(12)</sup>

## METHODS

### Design of the study

This study was of cross-sectional design and was conducted in a number of furniture workshops in East Jakarta from April to May 2013.

### Subjects of the study

The subjects who participated in the study were furniture workers who had been employed for more than 3 months and were less than 55 years old. The exclusion criteria based on history and anterior rhinoscopy were as follows: workers who had acute or chronic rhinosinusitis, deviation of the anterior superior septum, or a tumor mass or polyps in the nasal cavity, history of functional endoscopic sinus surgery (FESS), currently using steroid nasal sprays, history of head injury, and history of diabetes mellitus.

The sample size was calculated from the cross-sectional study formula with a chemically induced hyposmia prevalence of 5%<sup>(5)</sup> and  $\alpha=0.05$ , giving a minimal sample size of 62 subjects. It was decided to recruit the 65 subjects by total sampling of furniture workers in a factory complex.<sup>(13)</sup>

### Data collection

Each study subject was interviewed using a questionnaire comprising items on age, education, marital status, smoking habit, alcohol consumption, symptoms of chronic rhinitis, and history of atopy.

### Determination of risk of exposure

To determine risk of exposure scores, seven components were evaluated: i) potential hazard level, ii) exposure level, iii) duration of employment, iv) type of work, v) use of masks, vi) ventilation of work space, and vii) education and training. Potential hazard level: the score for toluene exposure had been predetermined from hazard rating tables, giving a score of 3.<sup>(14)</sup> Exposure level: the score was calculated by comparing the mean weekly exposure level (E) with the permissible exposure limit (PEL) for toluene of 50 ppm or 18 mg/m<sup>3</sup>.<sup>(18)</sup> The value for E was obtained by multiplying duration of exposure (D) with the exposure frequency (F), and the measured toluene level (M) and dividing the product by total working hours per week (W). The exposure level scores ranged from 1-5.<sup>(12)</sup>

$$E = \frac{F \times D \times M}{W}$$

Duration of employment: the score was determined from the duration of employment in the furniture production sector, with the following scores: score = 1 if employed for less than or equal to 1 year; score = 2 if employed for 1-5 years, score = 3 if employed from 5 to 10 years, and score = 4 if employed for more than 10 years. Type of work: the score was determined from the task or department in the furniture workshop, as follows: working in the cutting department, score = 1, working in the assembly department, score = 2, and working in the finishing department, score = 3. Use of masks: the scores were given according to continuity of using masks per week of work. If always using masks when working, the score was 1, if occasionally using masks, the score was 2

and if never used masks the score was 3. Ventilation of work space: the scores were given based on the evaluation of adequacy or inadequacy of work space ventilation, by comparing ventilated areas with floor areas. If ventilated area >15%, the score was 1, if <15% the score was 2, and if completely without ventilation, the score was 3. Education and training: the scores were given on the basis of having ever or never received official education and training on management of chemicals and use of personal protective devices. If ever received, the score given was 1, and if never received, the score given was 2.

Scores for the seven components were totalled to give an exposure risk score. The range of scores was 9-23. The workers were considered to be at high risk if the score was 15 -23 and at low risk if the score was less than or equal to 14.

### Olfactory function testing

The selected subjects underwent olfactory function testing by the investigators using Sniffin' Sticks under the supervision of an ENT specialist. The Sniffin' Sticks test kit is a validated and commonly used tool for assessment of olfactory function in subjects with normal sense of smell and in individuals with loss of smell. The kit consists of 32 or 16 pens, 14 cm in length and 1.3 cm in diameter, that can be filled with an odorant to a total volume of 4 ml and then capped, the odorant being perceptible at the tip of the pen.<sup>(15)</sup>

Determination of odor threshold (T), was performed by preparing a 4% solutions of pure butanol or phenyl ethyl alcohol as odorant, diluted in deionized water in a ratio of 1:2. From this odorant solution, 16 dilutions were prepared in a geometric series. Three pens were placed in random order, with 2 pens containing the solvent only and 1 pen containing the odorant at a given dilution. When testing, the cap was taken off the pen, and the tip of the pen was placed approximately 2 cm from the nostrils of the subject for around 3 seconds. The task of the

subject was to identify the pen containing the odorant. The test was done using a single-staircase, 3-alternative forced-choice procedure. If the odorant was identified on two consecutive tests, this triggered a reversal of the staircase. Testing was then performed to a total of 7 reversals. The olfactory threshold value was estimated as the mean of the last 4 staircase reversal points, with scores of 1 to 16.<sup>(14,16)</sup>

Determination of odor discrimination (D) was performed using 3 pens, with 2 pens containing the same odorant and 1 pen containing a different odorant. The testing used the technique of 3-alternative forced-choice, in which the subject had to identify the one pen that had a different odor. A true identification was given 1 point. The total score ranged from 0 to 16 for a set of 16 pens containing odorants.<sup>(14,16)</sup> In the testing for odor threshold and odor discrimination, the subject was blindfolded to prevent visual identification of the pens.<sup>(15)</sup>

The odor identification (I) test used 16 odorants with the multiple forced-choice design method. The subject was asked to identify odors by choosing from a list of 4 descriptors. The score for this test also ranged from 0-16. The odors used were of citrus fruit, peppermint, turpentine, cloves, leather, banana, garlic, rose, fish, lemon, coffee, anise, cinnamon, licorice, apple, and pineapple.<sup>(14,16)</sup>

The values of the three scores were summed and categorized as positive (+) for olfactory dysfunction, if the total of threshold (T), discrimination (D) and identification (I) (TDI) < 29.53 and negative (-) if TDI > 29.53.<sup>(15)</sup>

#### **Measurement of toluene level in the work environment**

This was carried out by personal diffusive sampling of toluene vapour in breathing zone air. In this method the monitor device is placed in the area of respiration of an individual, to measure the total exposure of the worker from inhalation.<sup>(17)</sup> The measurement was carried out according to the procedures of the Industrial Hygiene and Occupational Health Agency,

Jakarta Special Metropolitan Area (Balai Hiperkes DKI Jakarta), with toluene detection limits of 0.001 – 0.01 mg per sample, allowing the results to be expressed as parts per million (ppm). The measurement was done by an expert from the Industrial Hygiene and Occupational Health Agency, Jakarta Special Metropolitan Area (Balai Hiperkes DKI Jakarta).

#### **Measurement of air temperature and relative humidity of the work environment**

This was carried out by means of a wet-bulb globe thermometer at points in the workplace considered to be representative of the temperature and relative humidity of the work environment. The measurement was done by an expert from the Industrial Hygiene and Occupational Health Agency, Jakarta Special Metropolitan Area (Balai Hiperkes DKI Jakarta)

#### **Data analysis**

The odds ratio test was used to test for correlations between independent variables and olfactory dysfunction.

#### **Ethical clearance**

This study obtained ethical clearance in February 2013 from the Health Research Ethics Committee, Faculty of Medicine, University of Indonesia.

## **RESULTS**

Of the 65 workers, for only 44 were the data complete and analyzed, because for 21 workers no personal toluene exposure measurements could be done. All subjects were male, the majority totaling 21 (47.7%) were 18-30 years old and 19 (43.2%) subjects had finished primary school. A total of 40 workers (90.9%) were smokers, 23 (53.5%) had symptoms of chronic rhinitis and 22 (50.0%) admitted to a history of atopy (Table 1).

Measurement of toluene levels by personal sampling yielded a mean toluene level of  $0.94 \pm 1.47$  ppm and a total of 31 (70.5%) had toluene

Table 1. Distribution of demographic characteristics and olfactory function of the study subjects (n=44)

Demographic characteristic	n	%
Age (years)		
18 –30	21	47.7
31 –40	17	38.6
>40	6	13.7
Educational level		
Primary school	19	43.2
Junior high school	19	43.2
Senior high school	6	13.6
Marital status		
Unmarried	12	27.3
Married	32	72.7
Habits		
Smoking		
Non-smoker	4	9.1
Smoker	40	90.9
Alcohol consumption		
Non-drinker	36	81.8
Drinker	8	18.2
Symptoms of chronic rhinitis		
Negative	21	47.7
Positive	23	52.3
History of atopy		
Negative	22	50.0
Positive	22	50.0
Olfactory dysfunction		
Negative	7	15.9
Positive	32	84.3
Descriptors of olfactory dysfunction		
Threshold	32	75.0
Discrimination	11	25.0
Identification	28	63.6
Risk of toluene exposure		
Low	26	59.1
High	18	40.9
Toluene level		
Low	31	70.5
High	13	29.5

levels below the mean. Based on the risk of exposure scores that were obtained, the subjects were subsequently assigned to 2 categories, i.e. those with a high risk of exposure and those with a low risk of exposure. High values for risk of toluene exposure were obtained in 26 (59.1%) subjects, whereas 18 (40.9%) subjects belonged to the group of low risk of toluene exposure. The results of olfactory function testing by means of Sniffin' Sticks showed that 37 (84.1%) subjects had olfactory dysfunction (TDI score < 29.53). The descriptors of the olfactory dysfunction comprised an odor threshold of 75.0%, odor discrimination of 25.0% and odor identification of 63.6% (Table 1).

Results of bivariate analysis showed that the group at high risk of toluene exposure had a 12.5-fold increased risk of olfactory dysfunction (OR=12.5; 95% confidence interval 1.35-115.79). The toluene level in the work environment was not significantly correlated with olfactory dysfunction (OR=0.494; 95% confidence interval 0.094-2.608) (Table 2).

## DISCUSSION

Very few studies have tried to determine the exposure of furniture workers to toluene, probably because of the relatively small population. Our study results showed that the proportion of olfactory dysfunction was 84.1%, which was far higher than the prevalences of 0.5–5% for olfactory dysfunction from chemical exposure in the workplace according to Gobba.<sup>(5)</sup> However, our results were similar to those of

Table 2. Correlation of risk of toluene exposure and toluene level with olfactory dysfunction

Risk factor	Olfactory dysfunction		OR	95% CI
	Positive (n=37)	Negative (n=7)		
Risk of toluene exposure				
High	25 (96.2%)	1 (3.8%)	12.51	1.35 – 115.79
Low	12 (66.7%)	6 (33.3%)		
Toluene level				
High	10 (76.9%)	3 (23.1%)	0.49	0.09-2.61
Low	27 (87.1%)	4 (12.9%)		

the study by Cheng et al.<sup>(7)</sup> who found prevalences for mild and moderate hyposmia in plastic workers of 60.0% and 4.0%, respectively. With regard to descriptors of these olfactory dysfunctions, our study showed a threshold of 75.0%, discrimination of 25.0% and identification of 63.6%. These results differed from the OLFACAT study results, with values of 19.4% for detection (0.3% anosmia, 19.1% hyposmia), 43.5% for recognition (0.2% anosmia, 43.3% hyposmia) and 48.8% for identification (0.8% anosmia, 48% hyposmia).<sup>(4)</sup> However, the instrument used in the OLFACAT study also differed from that used in our study. The OLFACAT study used scratch papers as odor instruments and each study subject was asked to scratch and sniff each odor and then answer three questions, i.e. on odor detection (did you smell any scent? yes, no); odor recognition/memory (have you ever smelt this scent? yes, no); forced-choice odor identification (which name defines the scent you have smelt?).

The percentages of subjective complaints of olfactory dysfunction in the present study were not representative of the proportion of olfactory dysfunction. In the present study, the percentage of subjects complaining of olfactory dysfunction was only 10.8%. These results underline the statement that occupational olfactory dysfunction is subclinical and can be determined only by objective testing using devices for evaluation of olfactory function.<sup>(5)</sup>

Risk of exposure scores in subjects with olfactory dysfunction were higher than those in subjects without olfactory dysfunction, with near-significant differences. The risk scores were obtained from assessment of exposure level (total working hours per week), duration of each exposure, frequency of exposure per week, measured toluene levels, duration of employment, type of work, control measures such as use of masks, ventilation of the work space, and education and training. Among the components of exposure level, although no significant differences were found, exposure frequency exceeded those in subjects without olfactory dysfunction, whereas duration of

employment was shorter. In the present study involving informal workers, it was rather difficult to determine duration of employment objectively, since the workers were employed on a demand basis. In times of great demand, they worked continuously for several months without taking free days off. On the other hand, in times of no demand, they were unable to work for several weeks or months. In addition, the workers frequently moved to other workshops needing their services, possibly with less conducive work environments. Therefore it was difficult to determine duration of employment, since equal durations of employment may not necessarily represent identical total working hours and working days. Therefore to determine the cumulative dose of exposure in such workers, a more accurate way is to determine total working hours, frequency and duration of exposure per week.<sup>(18)</sup>

Our study results showed that subjects belonging to the group at high risk of toluene exposure had a higher risk for olfactory dysfunction, in comparison with the group at low risk of toluene exposure. Improvements in paint materials have caused a substantial reduction of emissions,<sup>(19)</sup> but these are still potentially harmful. Particulate matter and gas emitted from toluene is small enough to reach the lower respiratory system<sup>(20)</sup> and the brain, via the olfactory nerves.<sup>(21)</sup> Especially in the case of benzene and toluene, long-term exposure has negative effects on both the cardiovascular and the respiratory systems.

Our study results showed that among those at high risk of toluene exposure 59.09% subjects were in the category of high risk for olfactory dysfunction, since the bivariate test results showed a 12.51-fold higher risk of olfactory dysfunction in workers at high risk of toluene exposure.

The toluene levels measured in the present study were relatively low and far below the toluene PEL value of 50 ppm.<sup>(22)</sup> Although no significant differences were found, the impact of toluene on olfactory dysfunction at high levels of exposure cannot be ruled out. Toluene is also

known as toluol, phenylmethane, methylbenzol, methylbenzene, monomethyl benzene, and methacide. It is commonly used as a solvent in paints, coatings, inks, adhesives, and cleaners.

Our study points out that olfactory dysfunction is an early negative impact of exposure by inhalation of chemicals and other irritants, which has also been demonstrated by Magagnotti et al.<sup>(24)</sup> Therefore, olfactory function testing should be considered for initial screening or periodic testing of workers in the furniture or other industries that use irritant substances. In addition, a revision of the safe levels of toluene in chronic exposure should be considered, particularly with regard to olfactory functions. Although olfactory dysfunction is not life-threatening by itself, it may have serious consequences, since inability to detect some olfactory warning signals (such as spoiled food, gas leaks, etc.) can have a significant impact on nutritional status and other aspects related to the quality of life.

Among the limitations of the study we would like to point out that we were not able to evaluate occupational risks related to a particular type of activity, primarily due to the rather small number of subjects in each restoration department. Another limitation of this study was the inability to control for other risk factors, such as smoking habit, since more than 90% of subjects were smokers. The study by Katotomichelakis et al.<sup>(25)</sup> found decreased olfactory function, marked by lower scores for threshold, discrimination, and identification, than in the control group and proportional to the number of cigarettes smoked and duration of smoking.

Another risk factor that could not be controlled for was the presence of wood dust as another irritant in the work place. In the present study no measurement of wood dust was performed, but wood dust also cannot be placed in the exclusion criteria, since all workers in the furniture department are certain to be exposed to wood dust. With the unaided eye it could be seen that the floors in all the workshops that were studied always were covered with moderate to high amounts of wood dust. Similarly, the air in

the work environment was mildly to moderately dusty. Wood dust by itself can cause rhinitis, so as to induce mucosal edema that can decrease olfactory function.<sup>(26)</sup> However, the subjects in this study were those who on anterior rhinoscopy had no visible mucosal pathologies such that rhinitis from irritation by wood dust can be eliminated.

The minimal complaints accompanying severe olfactory dysfunction deserve consideration, because in persons with olfactory dysfunction, the nose has reduced protective functions against toxic substances, which eventually impact on their health. Subsequent studies investigating the effects of toluene exposure on olfactory dysfunction should include determination of the toluene levels in the body in a larger sample, nasal examination by endoscopy, and control for other risk factors such as smoking. The relevance of these findings for the future clinical course of occupational or work-exacerbated rhinitis, as well as the underlying mechanisms, should be elucidated through further studies.

## CONCLUSION

A high risk of toluene exposure increases the risk of olfactory dysfunction in furniture workers. Olfactory impairment seems to be highly dependent on chemicals, therefore olfactory function testing should be considered for initial screening or periodic testing for workers in the furniture industry.

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