Arh hig rada toksikol 1994;45:11-18

ORIGINAL SCIENTIFIC PAPER
UDC 613.63:616.233:666.366

AIRWAY HYPERREACTIVITY IN THE ELECTROCERAMIC INDUSTRY

I. ĆOSIĆ,* M. PAVLOVIĆ AND S. MILKOVIĆ-KRAUS

Institute for Medical Research and Occupational Health, Zagreb, Croatia

Received November 30, 1993

Seventy-four female shift workers employed in the oxide ceramics industry were examined: a group of 38 workers from the press workshop and a group of 36 controls from the mounting workshop from the same factory. The two groups did not differ by age, years of employment, smoking habit or height. Persons with atopic constitution and serious respiratory disease were excluded from the study. Interstitial lung disease was eliminated by X-ray examinations. All subjects underwent a clinical examination and completed a questionnaire. Measurements of ventilatory lung functions demonstrated no difference between the groups; lung function values were normal. Non-specific airway reactivity was expressed as PC_{50} Rt i.e. 50% increase in resistance in relation to the value measured after inhalation of the physiological solution. A significant difference was found for PC_{50} Rt between the exposed and control workers during ($P<0.001$) and outside working hours ($P<0.01$). Significantly different PC_{50} Rt values were also established within the group of exposed workers as well as within that of control workers during and outside working hours ($P<0.014$ and $P<0.0018$ respectively). The majority of hyperreactive persons were workers from the press workshop (n=17) when measurements were performed during working hours. For early detection of respiratory diseases in workers employed in the oxide ceramics industry preemployment examinations and regular check-ups aiming to determine non-specific airway reactivity are suggested as necessary.

Key terms
airway hyperreactivity, clinical examination, occupational exposure, oxide ceramics, ventilatory lung function, working environment

The manufacture of clay products can be traced back through the history of mankind. Technological progress has enabled the use of such products in atomic and aeronautic industries, biomedicine and machine engineering. Such a product is the spark plug, a product of high technology, consisting of a ceramic insulator and fuse. The development of the spark plug insulator dates from the discovery of the Otto motor.

* Visiting postgraduate student.

The spark plug insulator is produced from oxide ceramics – a high density material, resistant to high temperatures. It is produced by a dry method and has the characteristics of hard synthetic porcelain. The basic raw material is a type of clay α alumina. A thinner is added to the α alumina (flintstone, oxide titanium, barium, magnesium, manganese, chromium), plastifier (bentonite), defloculants, ammonia salts, additives for lowering the melting point (calcium carbonate, manganese oxide, magnesium hydroxide), polyvalent alcohols, wax, paraffins, paint and glaze (1). Insulators are manufactured in phases: grinding, mixing, drying, shaping, sintering and mounting of the insulators and fuse.

In spite of the modern technological process, which is partly an enclosed system, the pollution of the working environment originates in specific microclimatic conditions in the plant, with the exception of the assembling and packing departments.

During the manufacture of oxide ceramics the worker's respiratory system can become affected. For this reason health control, both before employment and periodically during employment, is obligatory, in accordance with WHO recommendations (2). Medical examinations are intended for persons working in exposure to respirable dusts, free silica, hard metals, dusts of organic origin, allergenic substances, and airway irritants.

Non-specific airway reactivity (NAR) is a pluri-component phenomenon comprising numerous factors (3). Firstly, there are endogenous factors, particularly the inherited tendency to airway hyperreactivity. Then, there are exogenous factors pertaining to the environment (smoking, respiratory infections) (4, 5). Inhalation of allergenic substances and occupational irritants can also influence airway reactivity (6, 7).

In healthy populations altered NAR is a known temporary phenomenon that occurs in exposure to specific substances. Consequently, the borderline between normal and impaired reactivity is not sharply defined (8).

During the manufacture of spark plug insulators, particularly in the course of preparation of raw material casts, excessive values of free SiO_2 were determined in the working environment. This, along with the other components in the manufacture, may have caused an irritative cough and altered NAR (9).

The purpose of this study was to examine the phenomenon of an irritative cough, observed over the previous two years, both during and outside working hours, in workers employed in the press workshop. Workers from the mounting workshop were chosen to serve as controls. Periodic check-ups in accordance with WHO recommendations were included in the study, in addition to non-specific airway challenge.

SUBJECTS AND METHOD

The subjects in the study were 74 female workers: 38 from the press workshop and 36 controls from the mounting workshop. They had not previously been employed in any other work organization. All subjects were smokers. The groups did not differ by age, duration of work service in the factory, smoking habit and

height (Table 1). Analysis of health status over the previous five years in both groups did not indicate atopic constitutions, skin disease or serious respiratory disease (pleurisy, tuberculosis, pneumonia). Chest X-rays did not reveal interstitial lung disease. In the previous six weeks the workers had not suffered from any respiratory disease or a disease which could have induced non-specific bronchial reactivity.

Table 1 *Anthropometric characteristics of compared groups of workers*

	N	Age		Total work service		Height		Smoking index	
		$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD
Press workshop	38	32.5	5.6	12.6	4.8	160	4.7	81	21.1
Mounting workshop	36	34.4	5.1	14.1	3.1	160	6.3	87.1	23.2

All workers underwent a physical examination and were administered a questionnaire, with emphasis on upper respiratory airway infections (10). The occurrence of chronic, irritative cough in the previous two-year period was verified in all workers employed in the press workshop, where a large number of workers were found to have respiratory infections and reported having dyspnoea during exertion (Table 2).

Table 2 *Upper respiratory airway disease frequency and PC_{50} Rt in examined workers*

Disease	Press workshop		Mounting workshop		T-test
	n	%	n	%	
Rhinopharyngitis	11	28.9	5	13.8	NS
Polysinusitis	12	31.7	8	22.2	NS
Respiratory infection	23	60.5	12	33.3	P<0.05
Dyspnoea during exertion	7	18.4	1	2.7	P<0.05

Measurements of ventilatory functions (FVC, FEV_1, MEF_{25}, MEF_{50}) followed by NAR testing were carried out during the work process. Ventilatory functions were measured during the first two hours of work in October 1989 using a Pneumoscreen I, Jaeger, Germany. The values measured were compared to a nomogram (11). In both groups of workers ventilatory parameters were within normal ranges and no difference was found between the examined groups (Table 3).

Non-specific reactivity of airways was determined by the method of Tjwa and co-workers and Takashima and co-workers, with checked reproducibility of the methods (12–14). An Astograph-TCK-6100H, Chest Corporation, USA was used, consisting of an automated inhalation unit with 12 nebulizers, for measuring lung resistance by the oscillation method. Histamine diphosphate (Sigma, USA)

was used as a provocation agent, in doses of 0.5–16.0 mg/ml. The inert agent was non-buffered saline. PC_{50} Rt denotes the provocation concentration during increase in lung resistance greater than 50% of that measured after saline inhalation. Chosen as a status of reactivity PC_{50} Rt was calculated by logarithmic interpolation from dose-response. Usual cautionary measures were respected (15).

Table 3 *Ventilatory functions in the exposed and control groups of workers*

Ventilatory functions (%)	Press workshop workers (n=38)		Mounting workshop workers (n=36)	
	$\bar{X}$	SD	$\bar{X}$	SD
FVC	94.8	11.1	94.2	15..0
FEV_1	93.8	14.0	91.9	16.2
MEF_{25}	130.6	56.6	128.8	40.4
MEF_{50}	93.6	25.2	90.7	25.2
MEF_{75}	77.0	27.1	74.1	24.4

In all subjects NAR testing with histamine diphosphate was carried out on two occasions: during working hours, regardless of shift, and after a three-week annual leave of absence the following year, within two hours of the work shift. The latter was considered to be non-exposure reactivity.

In the press workshop microclimatic conditions were disturbed by increased temperature, dry air and low level of humidity (14, 16). Statistical analysis was performed by parametric and non-parametric analyses of the results for testing small dependent and small independent samples, and by Spearman's test for correlation ranges (17).

RESULTS

The NAR values are presented in tables and graphs, in cumulative dose units of histamine diphosphate (Tables 4 and 5, Figure). Table 4 shows the PC_{50} Rt reactivity in the examined groups.

PC_{50} Rt values were obtained at significantly lower levels of the applied provocation agent in workers in the press workshop during working hours than after a leave of absence. Likewise, PC_{50} Rt values recorded in the press workshop were the result of significantly lower levels of the provocation agent than those registered among the mounting shop workers (Figure). A cumulative histamine dose <8 mg/ml was registered in as many as 17 workers in the press workshop and in 14 workers after a leave of absence, and in only two mounting workshop workers.

Table 4 *PC_{50} Rt during and outside working hours in workers from the press and mounting workshops*

	n	During work PC_{50} Rt*		Outside work PC_{50} Rt*		Statistical significance
		$\bar{X}$	SD	$\bar{X}$	SD	
Press workshop	38	8.83	5.75	10.72	6.13	P<0.01490
Mounting workshop	36	12.32	4.89	14.27	4.04	P<0.00185
Statistical significance		P<0.001		P<0.01		

* Cumulative dose of airway provocation agent (histamine diphosphate) at which PC_{50} Rt was obtained

Table 5 *PC_{50} Rt during working hours in workers from the press and mounting workshops*

	Press workshop PC_{50} Rt*				Mounting workshop PC_{50} Rt*				T-test
	$\bar{X}$	SD	N	%	$\bar{X}$	SD	N	%	
Rhinopharyngitis	9.8	4.3	11	28.4	14.8	6.3	5	13.8	NS
Polysinusitis	8.8	5.2	12	37.7	12.5	2.1	8	22.2	NS
Respiratory infection	9.5	3.5	23	60.5	14.8	5.3	12	37.3	P<0.01
Dyspnoea during exertion	13.5	4.2	7	18.4	9.8		1	2.7	NS

* Cumulative dose of airway provocation agent (histamine diphosphate) at which PC_{50} Rt was obtained

Table 5 shows the number of workers with regard to obtained PC_{50} Rt values matched by data from the questionnaire on dyspnoea, sinusitis, respiratory infections and rhinosinusitis over the previous two years. PC_{50} Rt obtained at a lower level of provocation agent was found in workers with previous respiratory infections in the press workshop.

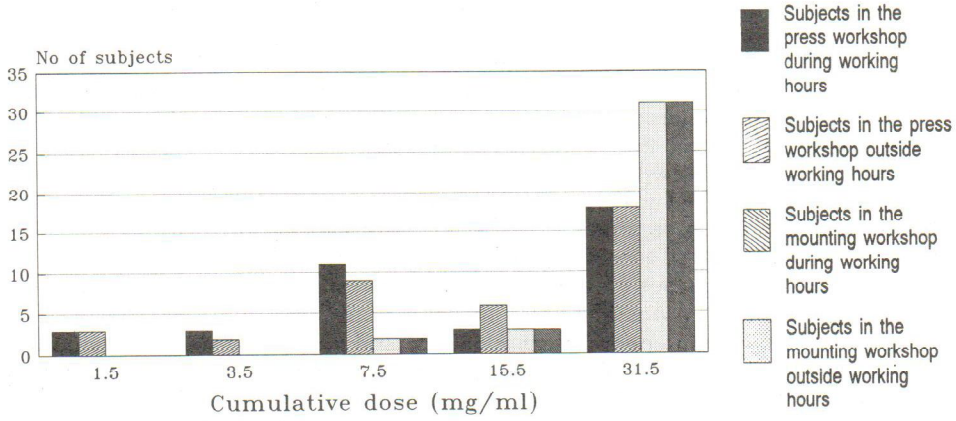

Figure *Cumulative dose of histamine diphosphate for obtaining PC_{50} Rt in examined groups of workers*

A multiple correlation matrix was drawn up for all subjects for the predictors: FEV_1, MEF_{25} and MEF_{50}, dose of histamine diphosphate, years of employment, smoking index and PC_{50} Rt values. No correlation was found between PC_{50} Rt and/or cumulative dose of histamine diphosphate, and age, work service and smoking index.

DISCUSSION

Industrialization and high technology have confronted man with new diseases. It is therefore surprising that we have failed to find any reports in available literature on the oxide ceramics industry, oxide ceramics being an essential component in many modern technologies. On the other hand certain components in the manufacture of oxide ceramics have been thoroughly analysed during investigations of diseases of the respiratory system, although their possible synergistic and/or additive effect is still unknown (18-23). *Piršić* examined NAR in workers in the ceramics industry, but failed to find any difference between the exposed and control workers (24).

Oxide ceramics contains numerous components that can affect the respiratory system. It could be speculated that dispersed free silica dioxide, verified in excessive amounts (6.8-49.34 mg/m^3) in the ambient air of the press workshop, could not be the only cause of the irritative cough and/or altered NAR. Inert chemical pollutants can interact with toxic pollutants and microbial toxins. Their additive and/or synergistic effect indicates an uncertain relationship between the toxic and the allergic effects (25-27). However, the crystal structure of α alumina could be responsible for such an effect, i.e. »l'epine chimique« (28). Inhalation of floating particles (from the raw material of the cast) may cause a chain of interactions, such as epithelial inflammation, damage to smooth muscles and effect of polygenetic factors. No definite opinions, however, have been presented with regard to the etiopathogenesis of non-specific reactivity (29).

Our investigation, apart from indicating the occurrence of altered NAR in workers employed in the manufacture of oxide ceramics, also emphasizes the need for TLV measurements of its various components, other than free SiO_2, which was analysed in this study. The need for improving personal protective devices as well as the working environment is also apparent.

Further research into the mineral structure of certain components in the manufacture of oxide ceramics is called for, with special reference to the components that are added to obtain high quality products.

The results point out the need for further investigation of NAR in the oxide ceramics industry as a possible early indicator of respiratory impairment, and as a useful indicator during periodic examinations and preemployment examinations of workers for specific workplaces and working conditions. The phenomenon that a healthy population may also have altered NAR (8, 20, 30) indicates the need for including NAR testing in examinations of workers employed in the oxide ceramics industry.

Acknowledgement This study was carried out within the framework of Project No. 3-01-130 with the Croatian Ministry of Science and Technology, Zagreb, Croatia.

REFERENCES

1. *Phibbs BP, Sundin RE, Mitchell RS.* Silicosis in Wyoming betonite workers. Am Rev Respir Dis 1971;103:1-7.
2. *World Health Organization (WHO).* Early detection of occupational diseases. Geneva: WHO, 1966:9-69.
3. *Nadel JA, Nolte D, Cockcroft DW, Fabril, Lowhagen B.* Bronchial hyperreactivity, the key to asthma. Fisons Pharmaceuticals 1984;12:8-11.
4. *Powels R, Van der Straelen MO, Bazin H.* Genetic factors in nonspecific bronchial reactivity in rats. Eur J Respir Dis 1985;66:98-104.
5. *Pauwels R, Peeman R, Van der Straeten MO.* Airway inflammation and nonallergic bronchial responsiveness. Eur J Respir Dis 1986;68(suppl 144):137-62.
6. *Pepys J, Hutchcroft BJ.* Bronchial provocation tests in etiologic diagnosis and analysis of asthma. Am Rev Respir Dis 1975;112:529-557.
7. *Godnić-Cvar J.* Normoreaktivnost i respiratornim iritansima inducirana hiperreaktivnost bronha. Pluć Bol 1990;42:30-2.
8. *Cerveri I, Bruschi C, Zoia MC. et al.* Distribution of bronchial nonspecific reactivity of the general population. Chest 1988;93:26-30.
9. *Burge PS.* New developments in occupational asthma. Br Med Bull 1991;48:221-30.
10. *Medical Research Council (MRC).* Definition, classification of chronic bronchitis for clinical and epidemiological purposes. Lancet 1965;1:776.
11. *Quanier RM, Clausen JL, Epler GR, Handkinson JL, Permut S, Plummer AL.* Pulmonary function testing. Bull Eur Physiopathol Resp 1983;19(suppl 5):45-51
12. *Takishima T, Hida W, Suziki S, Sasaki T.* Direct graphical recordings of the cumulative dose-response curves of the airway to methacholine in normal bronchitic and asthmatic subjects. Tohoku J Exp Med 1981;135:117-37.
13. *Tjwa MKT, Smeets JJ, Jansen LPJ, Maesen FPV.* Measurement of the non-specific threshold stimulus for the bronchial tree by continuous monitoring of respiratory resistance using the oscillation method. Respiration 1985;48:1-11.
14. *Ćosić I.* Hiperreaktivnost dišnih puteva u radnica elektrokeramičke struke. (Magistarski rad). Zagreb: Medicinski fakultet Sveučilišta u Zagrebu, 1991.
15. *Cropp GJA, Bernstein I, Boushey RG. et al.* Guidelines for bronchial inhalation challenges with pharmacologic and antigenic agents. News Spring: ATS, 1980:11-9.
16. *Ćosić I.* Ispitivanje ventilacijskih funkcija pluća u radnika izloženih respirabilnim prašinama. XIV kongres zdravstvenih radnika BiH, Kupari 1990. Personal communication.
17. *Petz B.* Osnovne statističke metode. Zagreb: Izdavački zavod JAZU, 1990.
18. *Hale LW, Gough J, King EJ, Nagelschmidt G.* Pneumoconiosis of kaolin workers. Br J Ind Med 1956;13:251-9.
19. *Warraki S, Herant Y.* Pneumoconiosis in china-clay workers. Br J Ind Med 1963;20:226-30.
20. *Idžaralić H, Simeunov Lj, Rustenbegović F, Tanasković B.* Prevalencija kroničnog bronhitisa kod radnika u nekim pogonima preduzeća Energoinvest u Sarajevu. Tuberkuloza 1965; 17:349-56.
21. *Morgan WKC.* Kaolin and the lung. Am Rev Respir Dis 1983;127:141-2.

22. *Simonsson BG, Sjoberg A, Rolf C, Haeger-Aronsen B.* Acute and longterm airway hyperreactivity in aluminium salt exposed workers with nocturnal asthma. Eur J Respir Dis 1985;66:105-18.
23. *Morgan WKC, Danner A, Higins TT, Pearson MG, Rauwelins WJR.* The effects of kaolin on the lung. Am Rev Respir Dis 1988;138:813-20.
24. *Piršić B.* Profesionalna oboljenja disajnih puteva u industriji keramičkih pločica. Pluć bol. 1987;39:163-74.
25. *Beritić T, Beritić-Stahuljak D, Štilinović L.* Profesionalna astma. II. Anorganski profesionalni alergeni i anorganski stimulatori bronhokonstrikcije. Arh hig rada toksikol 1981;32:47-8.
26. *Milković-Kraus S, Bogadi A.* Pneumoconiosis caused by hard metal dust. Arh hig rada toksikol 1987;38:135-40.
27. *Hanke W, Sepulveda MJ, Watson A, Janković J.* Respiratory morbidity in wollastonite workers. Br J Ind Med 1984;41:474-9.
28. *Sheppard D.* Mechanisms of bronchoconstriction from nonimunologic environmental stimuli. Chest 1986;90:584-7.
29. *Rosenstock L, Cullen Mr.* Clinical occupational medicine. Airway irritation syndromes, Saunders WD Company, Harcourt Braće Jovanović Inc 1986: p. 24-25.
30. *Pavlović M.* Nespecifična bronhijalna reaktivnost u kroničnih bronhitičara. Pluć bol 1990;42:24-6.

Sažetak

HIPERREAKTIVNOST BRONHIJA U ELEKTROKERAMIČKOJ INDUSTRIJI

Ispitano je 74 radnica zaposlenih u tvornici oksidne keramike (34 radnice zaposlene u prešaonici i 36 kontrolnih radnica iz montažne hale). Skupine se nisu razlikovale po dobi, trajanju radnog staža, visini i indeksu pušenja. Niti jedna od radnica nije imala znakove atopičke konstitucije, a na rendgenskoj snimci pluća nisu uočene promjene plućnog intersticija. Obje skupine ispitanica podvrgnute su kliničkom pregledu i ispitane su na osnovi standardiziranog upitnika. Izmjerene su i ventilacijske funkcije pluća na uređaju Pneumoscreen I, Jaeger, Njemačka. U obje skupine vrijednosti FVC, FEV_1, MEF_{25}, MEF_{50}, i MEF_{75} bile su u granicama normalnih. Ispitivanje nespecifične reaktivnosti dišnih putova provedeno je histamin difosfatom na uređaju Astograph, Chest Corporation, SAD. Za izraz nespecifične reaktivnosti korišten je PC_{50} Rt tj. porast rezistencije za 50% u odnosu na izmjerenu vrijednost nakon udisanja fiziološke otopine. Nađena je statistički značajna razlika za PC_{50} Rt s obzirom na kumulativnu dozu provokativnog agensa među radnicama prešaonice i montaže izmjeren tijekom ali i izvan radnog vremena ($P<0,001$;$P<0.01$). Nađena je statistički značajna razlika za PC_{50} Rt radnica u prešaonici za vrijeme i izvan radnog vremena ($P<0,014$) ali i radnica u montaži ($P<0,0018$). U skupini radnica prešaonice tijekom radnog vremena utvrđeno je 17 osoba s PC_{50} Rt dobivenim s manje od 8 mg/ml histamin disfosfata. U radu se naglašava potreba za sustavnim praćenjem nespecifične reaktivnosti dišnih putova u keramičkoj industriji.

Ključne riječi:
klinički pregled, profesionalna izloženost, hiperreaktivnost dišnih putova, oksidna keramika

Requests for reprints:

Dr M. Pavlović
Institute for Medical Research
and Occupational Health
2 Ksaverska St., POB 291
41001 Zagreb, Croatia