

Short communication

Formaldehyde and phenol exposure during an anatomy dissection course: a possible source of IgE-mediated sensitization?

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The sensitizing potency of formaldehyde and phenol exposure during 4 weeks of an anatomy dissection course was assessed in 45 medical students. Specific IgE against formaldehyde by RAST and by ELISA and specific IgE against phenol by ELISA were assessed before and after the course. At the start of the course, symptoms, type I allergy, respiratory diseases, and smoking habits were noted. At the end of the course, only symptoms experienced during the dissection lessons were assessed. Indoor formaldehyde levels were measured continuously. The mean indoor formaldehyde level was 0.124 ± 0.05 ppm, with a minimum of 0.059 ppm and a maximum of 0.219 ppm. Specific IgE against formaldehyde or phenol was found in none of the subjects at the beginning of the course, and no student showed specific IgE against formaldehyde or phenol after the course. Assessment of primarily irritant symptoms during the lessons revealed itch and paraesthesia of hands in 33/45 students ($P < 0.00005$), headache in 15/45 students, burning eyes in 13/45 students ($P < 0.02$), dizziness in 8/45 students ($P < 0.008$), sneezing in 4/45 students, epistaxis in 2/45 students, and shortness of breath in 1/45 students. According to our data, 1-month exposure to formaldehyde and phenol during an anatomy dissection course does not induce specific IgE against formaldehyde or phenol.

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Formaldehyde is a known indoor air pollutant causing irritant reactions such as burning eyes and irritation of mucous membranes (1, 2), but rarely causes IgE-mediated sensitization.

Recently, IgE-mediated sensitization to gaseous formaldehyde has been reported in 8-year-old schoolchildren who were exposed to only slightly elevated indoor formaldehyde levels (3). Furthermore, formation of specific IgE against formaldehyde has been reported to cause anaphylactic reactions to formaldehyde-containing tooth-filling materials (4).

As medical students are exposed to both formaldehyde and phenol during their anatomy dissection course, this situation was chosen as a model to

investigate the sensitizing potency of formaldehyde and phenol.

Material and methods

Students

Forty-five medical students (22 women and 23 men, mean age 20.9 years, range 18–33 years) attending their first dissection course at the Institute of Anatomy, University of Vienna, Austria, were investigated. The students dissected arms and legs preserved in 0.7% formaldehyde and 3.8% phenol, but not whole cadavers. A total of 120 students, including our 45 volunteers, worked in one room

($\approx 170 \text{ m}^2$, $\approx 600 \text{ m}^3$). On the first day, type I allergy, respiratory diseases, dermatitis of hands, incidence of headache, nosebleeds, rhinitis, burning eyes, and cough during the last 3 months, as well as smoking habits, were noted by a standardized questionnaire.

The dissection course took place in May 1995. It lasted for 4 weeks with daily 3-h sessions from 3:00 pm to 6:00 pm, Monday–Friday. On the last day, symptoms and complaints experienced during the lessons were assessed by the same standardized questionnaire used at the start of the study, and hand dermatitis was checked. An increase or an aggravation of symptoms experienced only during the dissection lessons was scored positive. In addition, colds and fever during the course were noted. Students served as their own controls.

Assessment of total IgE and specific IgE by RAST and ELISA

Blood samples were drawn on the first and on the last day. Total IgE (PRIST, Pharmacia, Uppsala, Sweden) and specific IgE against formaldehyde (RAST, Biomedica, Freiburg, Germany) were assessed. In addition, specific IgE against formaldehyde and phenol were assessed with a self-made enzyme-linked immunosorbent assay (ELISA) kit.

In 18 controls (nine women, nine men, mean age 39.0 years, range 24–61 years) not occupationally exposed to formaldehyde or phenol, specific IgE against formaldehyde and phenol was assessed by ELISA.

ELISA

The ELISA technique used was adapted from previously published papers (5, 6). Preparation of formaldehyde human serum albumin (FA-HSA) and phenol human serum albumin (PH-HSA) was done as described by Patterson et al. (5). ELISA experiments were carried out by coating microtiter plates with 100 μl FA-HSA or PH-HSA at a concentration of 10 $\mu\text{g}/\text{well}$ and quenching with 0.5% gelatin. Binding of specific IgE was detected by mouse antihuman IgE conjugated with horseradish peroxidase. HSA at a concentration of 100 $\mu\text{g}/\text{ml}$ was used as control for nonspecific binding.

Indoor air formaldehyde

Indoor formaldehyde was continuously measured at two locations in the dissection room when students were present. Assessment was done spectroscopically by the “acetylaceton method” (German Industry Standard – DIN 52368) (3). As the study was done in May, windows were open

most of the time, and the ventilation was continuously working. Lacking suitable testing equipment, we did not assess indoor phenol concentrations.

Statistical analysis

The sign test and the McNemar exact test performed with the StatXact-Turbo[®] computer program were used.

Results

After 4 weeks of exposure to a mean of 0.124 ± 0.05 ppm formaldehyde, none of the 45 students developed specific IgE against formaldehyde. Students were exposed to formaldehyde during 17 days for a total of 51 h. Minimum indoor formaldehyde was 0.059 ppm, reaching a maximum of 0.219 ppm (Fig. 1).

Formaldehyde RAST, total IgE, and specific IgE against formaldehyde and phenol by ELISA of students and controls are listed in Table 1. However, RAST and ELISA were against HSA conjugates, which may not be the relevant antigens *in vivo*. In a positive formaldehyde control, RAST class 2.7 scored 1.150 (1 : 50 diluted) in the ELISA.

Symptoms before the start of the course are shown in Table 2. No sex-related distribution of symptoms was observed except for headache and burning eyes. Fifteen of 45 students (seven women, eight men) had a history of a type I allergy. Twelve of 45 students (seven men, five women) smoked.

Symptoms experienced during the lessons are shown in Table 2. No correlation between sex, smoking, or type I allergy and incidence of symptoms was found. However, the female student experiencing shortness of breath was a smoker and had a history of type I allergy.

Discussion

Our investigations showed that 1-month exposure to formaldehyde and phenol during anatomy dissection does not induce specific IgE against formaldehyde or phenol in students. Specific IgE against formaldehyde has not been detected in pathologists up to now (7), and assessment of specific IgE against formaldehyde or phenol has not been done before in students or medical staff.

Recently, specific IgE against formaldehyde induced by moderate exposure to gaseous formaldehyde was found in 8-year-old schoolchildren (3). Although IgE-mediated sensitization against formaldehyde is considered rare and still is a matter of controversy (8), formaldehyde-containing tooth-fillings have been repeatedly reported to provoke an IgE response (4). Therefore, formation of

Mean indoor formaldehyde $\pm$ SD	0.124 $\pm$ 0.05 ppm	range 0.059–0.219 ppm
Mean indoor temperature $\pm$ SD	23.6 $\pm$ 2.4°C	range 18.8–28.8°C
Mean indoor air humidity $\pm$ SD	33.6 $\pm$ 11.7%	range 13.0–58.0%

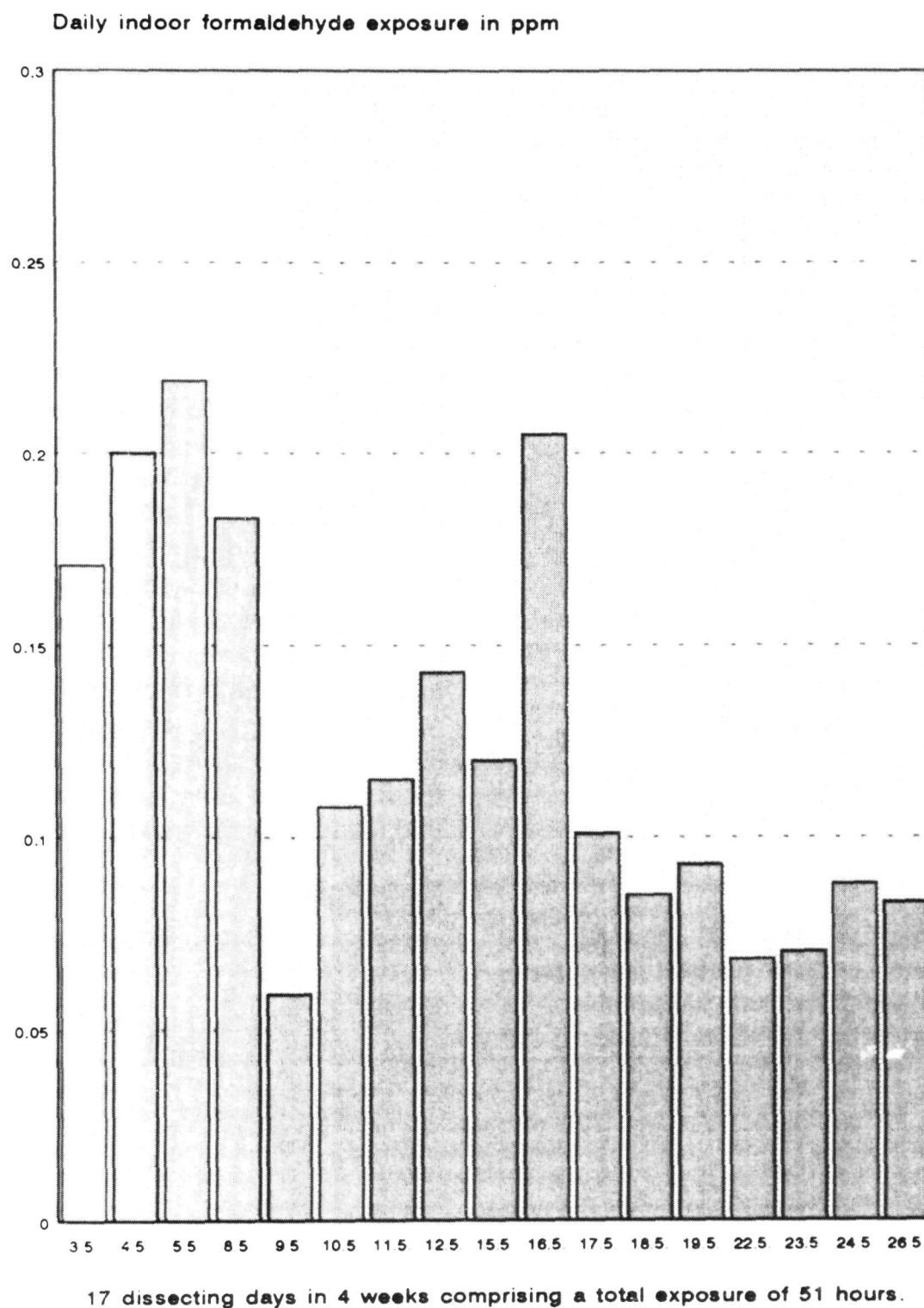


Fig. 1. Daily variations in indoor formaldehyde in dissection room.

specific IgE against formaldehyde appears to occur more often than estimated.

The mean indoor formaldehyde level in the dissection room was 0.124 ± 0.05 ppm, representing by far the lowest formaldehyde level ever found in a dissection room. Other sources have shown levels of 0.500 ppm (9) and 0.730 ppm (10). On only 2 days did formaldehyde exposure exceed 0.200 ppm, with a maximum exposure of 0.219 ppm. Peak formaldehyde levels coincided with dissection of

the skin and subcutaneous fat tissue. The low mean formaldehyde level may be attributed to proper ventilation and open windows, which provided excellent air exchange. Local formaldehyde concentrations close to cadaver parts are probably higher (10, 11).

Although the formaldehyde exposure of 0.124 ± 0.05 ppm was unexpectedly low, irritant symptoms attributable to volatile formaldehyde and phenol, such as headache, burning eyes, and

Table 1. Specific IgE to formaldehyde and phenol in 45 students before and after 4 weeks of exposure to formaldehyde and phenol

	Start	After 4 weeks	Increase/ <i>P</i> value
FA RAST class mean ± SD	1.03 ± 0.11	1.03 ± 0.08	7/45 NS*
Range	1.0–1.5	1.0–1.3	
FA RAST 1.0–1.9	45	45	
FA RAST ≥ 2.0	0	0	
FA ELISA mean ± SD	0.0258 ± 0.0408	0.0176 ± 0.0348	12/45 NS*
Range	0.000–0.175	0.000–0.166	
FA ELISA 0.0–0.200	45	45	
FA ELISA > 0.200	0	0	
FA controls mean ± SD	0.0064 ± 0.0193		
Range	0.000–0.078		
FA controls 0.0–0.200	20		
FA controls > 0.200	0		
FA positive control (<i>n</i> = 1)	1.150		
PH ELISA mean ± SD	0.0337 ± 0.0426	0.0091 ± 0.0228	4/45 NS*
Range	0.000–0.197	0.000–0.106	
PH ELISA 0.0–0.200	45	45	
PH ELISA > 0.200	0	0	
PH controls mean ± SD	0.0219 ± 0.0455		
Range	0.000–0.185		
PH controls 0.0–0.200	20		
PH controls > 0.200	0		
Total IgE mean ± SD	83 ± 100 kU/l	77 ± 86 kU/l	6/45 NS*
Range	5–470	5–400	

FA: formaldehyde; PH: phenol; SD: standard deviation; *sign test.

dizziness, were found. However, dizziness may also be caused by stress and concentration. Direct contact with perfusion fluid caused paraesthesia of hands in 33/45 students (73%). Paraesthesia occurred about 30 min after starting dissection and lasted for about 30 min to 6 h after cessation of

dissection. Paraesthesia and itch of fingertips and hands has not before been reported in students, pathologists, or workers occupationally exposed to formaldehyde or phenol (12). Hand dermatitis was not induced in our students, except in one student whose chronic dermatitis slightly worsened during dissection. Most of our students did not wear gloves; however, two students wearing gloves also reported paraesthesia of fingertips. Only two cases of paraesthesia possibly caused by formaldehyde-containing, tooth/root-filling materials have been reported (13).

Although our students were exposed to remarkably lower indoor formaldehyde levels (9, 10, 14), our findings are mostly in accordance with studies on the health impact of formaldehyde exposure. Respiratory symptoms were not observed except in one nonasthmatic student who had a single attack of shortness of breath (10). However, the particular effects of formaldehyde and phenol could not be separated in our study.

In conclusion, symptoms experienced by students such as itch and paraesthesia of hands, headache, burning eyes, and shortness of breath were primarily irritant effects of formaldehyde and phenol. According to our data, 1-month exposure to formaldehyde and phenol during an anatomy dissection course obviously does not induce specific IgE against formaldehyde or phenol.

References

1. Samet JM, Marbury MC, Spengler JD. Health effects and sources of indoor air pollution. II. *Am Rev Respir Dis* 1988;137:221-42.

2. Bardana EJ, Montanaro A. Formaldehyde: an analysis of its respiratory, cutaneous and immunologic effects. *Ann Allergy* 1991;66:441-52.

3. Wantke F, Demmer CM, Tappler P, Götz M, Jarisch R.

Table 2. Symptoms in 45 students experienced during anatomy dissection course or symptoms aggravated during course

Symptoms	Before dissection course	During dissection course	<i>P</i> value*
By direct contact with perfusion fluid			
Itch of skin or paraesthesia	0 0 F/0 M	33 17 F/16 M	<i>P</i> < 0.00005
Dermatitis of hands	1 0 F/1 M	1 0 F/1 M	NS
By gaseous formaldehyde and phenol			
Headache	9 7 F/2 M	15 8 F/7 M	NS
Burning eyes	6 5 F/1 M	13 7 F/6 M	<i>P</i> < 0.02
Dizziness	0 0 F/0 M	8 4 F/4 M	<i>P</i> < 0.008
Sneezing	11 4 F/7 M	4 2 F/2 M	NS
Nosebleeds	11 5 F/6 M	2 0 F/2 M	NS
Cough	2 1 F/1 M	0 0 F/0 M	NS
Shortness of breath	0 0 F/0 M	1 1 F/0 M	NS
Bronchial asthma	0 0 F/0 M	0 0 F/0 M	NS
Common cold	0 0 F/0 M	13 3 F/10 M	

*McNemar exact test. F = female subject; M = male subject.

- Exposure to gaseous formaldehyde induces IgE mediated sensitization against formaldehyde in schoolchildren. *Clin Exp Allergy* 1996;32:276-80.
4. Wantke F, Hemmer W, Haglmüller T, Götz M, Jarisch R. Anaphylaxis after dental treatment with a formaldehyde-containing tooth-filling material. *Allergy* 1995;50:274-6.
 5. Patterson R, Harris KE, Grammer LC. Canine antibodies against formaldehyde-dog serum albumin conjugates: induction, measurement and specificity. *J Lab Clin Med* 1985;106:93-100.
 6. Voller A, Bidwell DE, Bartlett A. Enzyme immunoassays in diagnostic medicine. Theory and practice. *Bull World Health Organ* 1976;53:55-65.
 7. Salkie ML. The prevalence of atopy and hypersensitivity to formaldehyde in pathologists. *Arch Pathol Lab Med* 1991;115:614-16.
 8. Dykewicz MS, Patterson R, Cugell DW, Harris KE, Fang Wu A. Serum IgE and IgG to formaldehyde-human serum albumin: lack of relation to gaseous formaldehyde exposure and symptoms. *J Allergy Clin Immunol* 1991;87:48-55.
 9. Chia SE, Ong CN, Foo SC, Lee HP. Medical students' exposure to formaldehyde in a gross anatomy dissection laboratory. *J Am Coll Health* 1992;41:115-19.
 10. Kriebel D, Sama SR, Cocanour B. Reversible pulmonary responses to formaldehyde. A study of clinical anatomy students. *Am Rev Respir Dis* 1993;148:1509-15.
 11. Akbar Khanzadeh F, Vaquerano MU, Akbar Khanzadeh M, Bisesi MS. Formaldehyde exposure, acute pulmonary response and exposure control options in a gross anatomy laboratory. *Am J Ind Med* 1994;26:61-75.
 12. Spiller HA, Quadrani Kushner DA, Cleveland P. A five year evaluation of acute exposure to phenol disinfectant (26%). *J Toxicol Clin Toxicol* 1993;31:307-13.
 13. Allard KU. Paraesthesia – a consequence of a controversial root-filling material? A case report. *Int Endol J* 1986;19:205-8.
 14. Holness DL, Nethercott JR. Health status of funeral workers exposed to formaldehyde. *Arch Environ Health* 1989;44:222-8.

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