

Short communication

Exposure to formaldehyde and phenol during an anatomy dissecting course: sensitizing potency of formaldehyde in medical students

Background: The sensitizing potency of formaldehyde and phenol during anatomy dissecting was investigated. The objective was to determine whether exposure induces specific IgE or IgG against formaldehyde-albumin or phenol-albumin.

Methods: In 27 medical students, specific IgE against formaldehyde-albumin by RAST plus ELISA and specific IgE against phenol-albumin by ELISA were assessed. In addition, specific IgG against formaldehyde-albumin was assessed in 23 students. Symptoms before and during dissecting were assessed, and indoor formaldehyde and phenol were measured.

Results: Mean indoor formaldehyde was $0.265 \pm 0.07 \text{ mg/m}^3$, and mean indoor phenol was $4.65 \pm 2.96 \text{ mg/m}^3$. Specific IgE/IgG against formaldehyde-albumin was not found at the beginning. Four students developed specific IgE against formaldehyde-albumin (RAST classes of ≥ 2.0), and all four also had specific IgE in the ELISA, but IgG against formaldehyde-albumin was not found. Specific IgE against phenol-albumin was not seen. Itch and paresthesia of the hands ($P < 0.0001$), dizziness ($P < 0.008$), burning eyes ($P < 0.01$), headache, sneezing, epistaxis, gingival bleeding, oral or pharyngeal itch, and shortness of breath were experienced.

Conclusions: Formaldehyde exposure during dissecting may induce specific IgE, but not IgG, against formaldehyde-albumin. Sensitization did not correlate with symptoms.

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Exposure to formaldehyde and phenol by volatile particles, as well as skin contact, is extensive during dissecting (1). However, IgE-mediated sensitization against formaldehyde-albumin or phenol-albumin associated with dissecting has not been reported so far.

In a previous study, 45 medical students attending their first dissecting course were investigated (2), but no sensitization to formaldehyde-albumin or phenol-albumin was found. In the present study, the same students were investigated during their second dissecting course lasting for 10 weeks.

The aim of the study was to investigate the sensitizing potency of formaldehyde and phenol by means of IgE or IgG antibodies after a second exposure, as well as possible health risks for medical students during dissecting.

Material and methods

Students and assessment of symptoms

Twenty-seven medical students (12 female and 15 male, mean age 21.2 years) who already had been dissecting for 4 weeks were investigated. Whole cadavers preserved in an aqueous perfusion fluid (0.7% formaldehyde, 4.0% phenol) were dissected.

On the first day, type 1 allergy, respiratory diseases, hand dermatitis, medication, incidence of headache, nosebleeds, rhinitis, burning eyes, and cough during the last 3 months, as well as the wearing of contact lenses and smoking habits, were recorded by questionnaire. In addition, all students received daily symptom cards to note headache, burning eyes, and paresthesia of the hands, as well as the wearing of gloves, during the dissecting course. Peak expiratory flow was assessed

daily before and after the course with a Wright Mini Peak Flow Meter®.

In the middle and at the end of the course, symptoms and complaints were assessed by questionnaire, and evidence of hand dermatitis was sought in each student. In addition, any common colds and fever during the course were recorded. An increase in symptoms or an aggravation of symptoms experienced only during dissecting was scored as positive.

Assessment of total IgE, specific IgE by RAST and ELISA, and IgG by ELISA

Blood samples were drawn on the first day, in the middle of the course, and on the last day of the course. Specific IgE against formaldehyde-albumin (RAST, Biomedica, Freiburg, Germany) and total IgE (PRIST, Pharmacia, Uppsala, Sweden) were assessed. In addition, specific IgE and IgG against formaldehyde-albumin and specific IgE against phenol-albumin were assessed with a self-made ELISA kit, as described previously (2, 3).

IgG against formaldehyde-albumin was assessed in 23 students (10 female and 13 male) including all IgE-positive students, at the beginning of the first dissecting course (2) and at the end of the second course. Besides, IgG against formaldehyde-albumin was measured in three patients (two female and one male) with known specific IgE against formaldehyde-albumin who had been treated with formaldehyde containing tooth-filling materials, and who had experienced adverse reactions. Furthermore, specific IgE against latex was assessed in students suffering from itch when wearing gloves.

Controls for IgE and IgG

Eighteen formaldehyde-RAST-negative probands (nine female, nine male, mean age 39.0 years) not occupationally exposed to formaldehyde or phenol served as controls. Specific IgE against formaldehyde-albumin and phenol-albumin was assessed by ELISA.

As IgG assessment was done at the end of the study with the IgE levels against formaldehyde-albumin already known, mean levels of IgG at the beginning of the first course were taken as the normal range. We regarded students as unexposed persons at the start of the study.

The cutoff level for positivity was defined as the mean value plus four standard deviations (4).

Indoor-air formaldehyde and indoor-air phenol

Indoor formaldehyde and phenol were continuously measured, as described before (2). Phenol was adsorbed by silica gel-filled tubes and assessed by gas chromatography with a mass spectrometer.

Statistical analysis

The sign test was used for changes in RAST and ELISA, and the McNemar exact test performed on the StatXact-Turbo® computer program was used.

Results

Specific IgE against formaldehyde-albumin or phenol-albumin

At the beginning, none of the students had specific IgE against formaldehyde-albumin according to RAST or ELISA results. After 10 weeks of exposure, 4/27 students (two female, two male) developed RAST classes of ≥ 2.0 (2.1, 2.1, 2.2, and 3.8), and 4/4 formaldehyde-albumin RAST-positive students also had specific IgE according to ELISA (0.110, 0.424, 0.793, and 1.119 optical density [OD]). One positive man was a smoker. ELISA assessment of specific IgE against phenol-albumin was negative. Mean total IgE remained unchanged during the study (Table 1). In 18 IgE-RAST negative controls, specific IgE against formaldehyde-albumin or phenol-albumin measured by ELISA gave 0.006 ± 0.019 OD and 0.022 ± 0.046 OD, respectively. The cutoff levels for positivity were ≥ 0.082 OD for formaldehyde and ≥ 0.206 OD for phenol.

Specific IgG against formaldehyde-albumin

After a total of 14 weeks (4 plus 10 weeks) of exposure to formaldehyde, 0/23 students developed specific IgG against formaldehyde-albumin (start: 1.8 ± 5.0 OD; end: 2.4 ± 7.8 OD), although 4/23 had specific IgE against formaldehyde-albumin. The cutoff level for a positive result was ≥ 22 OD. In contrast, in three patients developing specific IgE against formaldehyde-albumin (RAST classes 3.0, 2.7, and 2.0) after treatment with formaldehyde-containing tooth-filling materials, 3/3 also had specific IgG against formaldehyde-albumin (950, 109, and 106 OD).

Table 1. Specific IgE against formaldehyde-albumin and phenol-albumin, as well as total IgE, in 27 students before, after 5 weeks, and after 10 weeks of exposure to formaldehyde and phenol. In addition, IgG against formaldehyde-albumin in 23 students at beginning of first course (2) and at end of second course after 14 weeks of exposure

	Start	After 5 weeks	P value	After 10 weeks	P value
FA-IgE-RAST ≥ 2.0	0/27	0/27	NS*	4/27	NS*
FA-IgE-ELISA ≥ 0.082 OD	0/27	0/27	NS*	4/27	NS*
FA-IgG-ELISA ≥ 22 OD	0/23**	Not done		0/23	NS*
PH-IgE-ELISA ≥ 0.206 OD	0/27	0/27	NS*	0/27	NS*
Total IgE mean $\pm$ SD	33 ± 28 kU/l	36 ± 24 kU/l	NS*	30 ± 26 kU/l	NS*

FA: formaldehyde; PH: phenol.

* Sign test.

** Start of first dissecting course.

Symptoms before the course, type 1 allergy, use of contact lenses, and smoking habits

Symptoms and complaints are listed in Table 2. Exactly 12/27 students (four female, eight male) had a history of type 1 allergy; 11/12 (three female, eight male) were sensitized to a perennial allergen. Exactly 4/27 students (three male, one female) smoked, and seven students (four male, three female) wore contact lenses regularly.

Symptoms after 5 and 10 weeks of exposure

Symptoms and complaints are listed in Table 2. No sex-related distribution of symptoms could be observed except for dizziness, which occurred only in men in the last observation period. No correlation was found between smoking or type 1 allergy and incidence of symptoms and complaints. In the first 5 weeks, six students wore gloves, and 4/6 had paresthesia of the fingertips and hands. In the last 5 weeks, eight students wore gloves, and 7/8 had paresthesia of the fingertips and hands, three of them only when wearing gloves. Their latex RAST was negative. Symptoms in the four formaldehyde-albumin-sensitized students did not differ from the unsensitized students.

Peak expiratory flow screening

In 10/27 students (not significant; sign test), a decrease of peak expiratory flow of ≥ 10 l/min was found.

Indoor-air formaldehyde and phenol

Students were exposed to a mean indoor formaldehyde level of 0.265 ± 0.07 mg/m³ (range 0.133–0.410 mg/m³) and a mean indoor phenol level of 4.65 ± 2.96 mg/m³ (range 0.09–11.8 mg/m³) for 43 days.

Table 2. Symptoms in students before, after 5 weeks, and after 10 weeks of anatomy dissecting course

Symptoms	Before	After 5 weeks	After 10 weeks
By direct contact with perfusion fluid			
Paresthesia of fingers	0	20 $P < 0.00001^*$	22 $P < 0.00001^*$
Scaling of skin on hands	0	0 NS*	3 NS*
Hand dermatitis	1	1 NS*	1 NS*
By volatile compounds of perfusion fluid			
Burning eyes	3	13 $P < 0.01^*$	9 $P < 0.03^*$
Headache	5	11 NS*	13 $P < 0.05^*$
Dizziness	0	8 $P < 0.008^*$	6 $P < 0.03^*$
Shortness of breath	0	5 NS*	1 NS*
Cough	2	4 NS*	2 NS*
Nosebleed	5	3 NS*	5 NS*
Sneezing	2**	1 NS*	1 NS*
Gingival bleeding	0	0 NS*	2 NS*
Oral and pharyngeal itch	0	0 NS*	1 NS*
Bronchial asthma	0	0 NS*	0 NS*
Common cold	0	14 $P < 0.0001^*$	12 $P < 0.0005^*$

* McNemar exact test (incidence of symptoms in October compared to November and incidence of symptoms in October compared to December).

** Only perennial rhinitis was documented, as seasonal allergic rhinitis is not relevant from October to December.

Discussion

Our investigations showed that a 10-week exposure to inhaled formaldehyde and phenol during anatomy dissecting seemed to induce an IgE-mediated sensitization to formaldehyde-albumin in 4/27 students, but not to phenol-albumin. On the other hand, we could not detect IgG-mediated sensitization after exposure to gaseous formaldehyde. In three patients suffering from adverse reactions to formaldehyde-containing tooth-filling materials who showed specific IgE against formaldehyde-albumin, we could detect IgG antibodies against formaldehyde-albumin. These findings need further investigation but suggest that the route and extent of exposure to formaldehyde may be crucial for the kind of sensitization.

However, there may be limitations to our findings. RAST and ELISA were directed against human-serum-albumin conjugates, which probably are the relevant antigens *in vivo* (4). Unfortunately, RAST-inhibition experiments, although repeated three times, gave inconclusive results. Finally, a positive control for IgE against phenol-albumin was not available, but, to our knowledge, specific IgE against phenol-albumin has not been described so far.

Specific IgE (5), but also IgG, IgA, and IgM (6), antibodies against formaldehyde-albumin have been detected. Exposure to volatile formaldehyde may sensitize (7) but does not seem to cause immunologically mediated symptoms. This phenomenon, already seen in previous studies (6, 8, 9), appears to be characteristic of inhalative exposure but cannot be conclusively explained yet. Only formaldehyde released from tooth fillings or from hemodialysis gear into the blood may induce specific IgE and even cause anaphylactic reactions (10, 11). However, the role of IgG antibodies against formaldehyde-albumin in these patients, as found in our investigation, remains unclear.

Indoor air formaldehyde showed the lowest formaldehyde level ever assessed in a dissecting room except in our first investigation (2). Dissection of skin and subcutaneous fat tissue induced a sharp increase in indoor formaldehyde and phenol, and the highest levels were seen when the abdomen and the thorax were opened (12). The peak incidence of headache and burning eyes coincided with the first increase in formaldehyde and phenol, within the first 2 weeks, indicating that students became accustomed and less sensitive to the effects of formaldehyde and phenol. Direct contact with perfusion fluid caused paresthesia of the hands, which started about 30 min after dissecting and lasted up to 6 h afterward. Even wearing gloves did not protect against embalming fluid, as formaldehyde and phenol may penetrate latex gloves within 30 min. Dermatitis did not develop (13), but scaling of the skin was found in three students.

The irritant effects of formaldehyde on the respiratory tract have been noted in numerous publications (1, 6, 12), but we could not find a significant decrease in peak expiratory flow (12). Only one nonasthmatic student had a single attack of shortness of breath.

In conclusion, the symptoms experienced by students were primarily the irritant effects of formaldehyde and phenol. A 4-week followed by a 10-week exposure to formaldehyde during dissecting did not induce IgG-

mediated sensitization. Although we could detect specific IgE against formaldehyde-albumin, these antibodies do not seem to have clinical relevance.

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