ORIGINAL ARTICLE

Immunoglobulin E level in response to Formaldehyde Exposure in Anatomy Laboratoryat King Saud University Riyadh

IQRA VOHRA[1], MOHAMMAD S VOHRA[2], MOHAMMED E ALQAHTANI[2], *MOHAMMED H ALAHMARI[2], ABDULLAH S MIRZA[2], ABDULLAH S ALZAHRANI[2], NAIF A ALAJJI[2], KHALID S ALKRAIDA[2], ZAHID A KAIMKHANI[2]*

ABSTRACT

Aim: To examine the level of total and specific IgE to FA in response to the higher FA level.
Methods: A gross anatomy lab was evaluated for FA concentration during the 4th 10th & 14th weeks. Personal samples were taken from instructors and students using a sampling device pinned on individual's collar for 2 to 3 hours. Analysis was carried out using high performance liquid chromatography. Blood samples from all participants were analyzed by radio allergosorbent test (RAST) using Pharmacia ImmunoCAP 250 analyzer.
Result: The average indoor FA concentration was 0.68, 0.85, and 0.73, ppm in the 4th, 10th and 14th weeks. The average personal exposure level for students was 0.75, 1.20, and 1.10 ppm and 1.27, 1.44 and 1.33 ppm for instructors. Total blood IgE and IgE specific to FA of all students and instructors did not increase significantly.
Conclusion: Increased concentration and personal exposure to FA did not stimulate the production of IgE specific to FA. Thus allergic symptoms are not directly related to IgE but likely to be related with irritants.
Keyword: Formaldehyde**,** dissection lab, IgE

INTRODUCTION

FA (also known as formalin) is used as a preservative for human cadavers during anatomy dissection laboratories.Regulatory authorities around the globe including World Health Organization (WHO)proposed that the indoor concentration of formaldehyde must be less than 0.08 ppm[1]. The acceptable level of FA set by the American Conference of Governmental Industrial Hygienists (ACGIH) is 0.3 ppm[7].The exposure of FA is always greater in the participants of anatomy lab than non-participants[2,3,&12-14]

Recently, people are more apprehensive about the effect of FA andit has long been questioned whether the exposure to formaldehyde in indoor environments may be a risk factor for developing allergic specific IgE-mediated inflammatory responses. Little evidences are present to support this hypothesis at present. FA is declared as a known human carcinogenic agent[2,5].

Prolong exposure of FA is also considered a carcinogenic in human[9,10]. FA is also considered a persuasive contact sensitizer that can produce contact dermatitis and respiratory symptoms, by irritant mechanisms[4]. Symptoms like irritation of throat, nose and eyes have also been reported[8]. FA is a hepten and Formaldehyde-protein complex may be considered as immunogenic[6].

In 2009, one of our study reported that mean concentration of FA in anatomy lab during week 4th,10th and 11th were 0.68, 0.85 and 0.73 ppm respectively[11]. These levels ofFA concentration in our laboratory during the session exceeded the guidelines of WHO (0.08ppm)[1,10] and ACGIH (0.3 ppm)[7]. *Achatzet al*[15] reported an IgE antibody mediated allergic response following to exposure to allergens. In children an IgE mediated sensitization to gaseous form of FA has been observed by *Wantke,et.al*[16], whereas in atopics, long term exposure is likely to stimulate the typical IgE mediated response[17]. Many researchers[18,19,20] reported that there is no production of IgE specific to FA. This study has designed to establish further evidence about IgE-mediated sensitization related to the high level of FA during teaching sessions in anatomy lab.

MATERIALS & METHOD

Anatomy Lab: The size of the anatomy lab used in this study is 30m x 15m x4m in dimensionwith total volume of 1800m[3]**.** The lab is provided with 3 doors and 6 fixed windows. The main door (DR1) opens in main lobby whereas, other 2 doors (DR2 and DR3) open in small corridor (Fig. 1). The DR2 and DR3

[1]*Alfarabi College of Dentistry & Nursing Riyadh*
[2]*Dept of Anatomy, College of Medicine, King Saud University*
Correspondence to Mohammad Saeed Vohra Professor of Anatomy & Stem Cell Unit, College of Medicine, King Saud University, P O Box 2925 (28), Riyadh-11461. Contact +966-1-4699329 (Off), +966-508845648 (Cell), Email: vohra@ksu.edu.sa; vohra66@hotmail.comHome page: fac.ksu.edu.sa/vohra

usedonly during practical examinations sessions. The lab has 24 ceiling outlet vents connected to central air conditioning system and 4 exhausts (Fig.1) for general ventilation. There isno natural and cross-ventilation in the lab.A total of fourteen cadavers used during the teaching session of this study. A group of 15 students under the supervision of instructor dissected one cadaver. The cadavers and pro-sections are preserved in a solution containing glycerin, 10% FA and tape water. After dissections session the cadavers are covered in a wet sheet of cotton.

FA Concentration in Anatomy Lab: A sampling device manufactured bySigma Aldrich MO, USA, was used to collect air sample [21-23] from 3 different locations; the center (CE) , besides the doors (DR1 – DR3 and all 4 corners (CR1-CR4) (Fig-1). The sampling devices were fixed at the mean height of the breathing zones of the participants and were also attached to the collar of participants for about 2-3 hours for personal exposure sample. The collected samples were analyzed by using high performance liquid chromatography (HPLC).

Blood sampling For IgE: Ten ml of blood samples were taken fromall students (n=10)presenting with clinical signsand symptoms similar to those of allergic reactions during the 4^{th}, 10^{th}& 14^{th}weeks. The samples were analyzed in accordance with the recommendations outlined of the manufacturer's guidelines using radioallergosorbent test (RAST) to determine the presence of IgE level after exposure to FA. All the samples were collected at the start &at the end of the 4^{th}, 10^{th}& 14^{th} weeklab sessions.

Measurement of Specific IgE: In order to measure the level of specific IgE, the response of the blood samples were transformed to kU/L by using calibration curve. Only the valuethat is more than 0.35 kU/Lwas considered significant.

Table 1 shows the interpretation of RAST score based on quantitative assessment of the IgE in kU/L.

Furthermore 4 samples were collectedfrom four instructors as they spent more time in the lab andwere exposed to FA for a longer duration than that of students. Four samples from students to measure the specific IgE to FA. These instructors and students were selected because they had complained of sensitivities to FA. For control4 samples were collected from the laboratory assistants who did not participated in dissection sessions.

RESULTS

FA Exposure Level in Anatomy Lab: The mean concentration of FA during the 4^{th}, 10^{th} and 14^{th} week of dissection was 0.68,0.85 and 0.73 ppm.The sample fromdifferent locations (Fig.1) i.e.central (CE),corners (CR1-CR4) and doors (DR1-DR3) showed a significant variations in the levels of FA concentrations. During the dissection of body cavities, a higherFA concentration was noted.

The mean personal exposure level of students during 4^{th},10^{th} and 14^{th} week was 0.75, 1.20 and 1.10 ppm whereas; the mean personal exposure level of instructors was 1.27, 1.44 and 1.33 ppm (Fig-2).

IgE Level of Students & Instructors: Total blood IgE levels of all 10 studentsand instructors did not increase significantly(Table 1) during the dissection session at 4^{th} 10^{th} and 14^{th} week. Also, a clear relationship between FA exposure levels and total blood IgE levels was not observed (Table 1). In samples from all instructor and first 4 students the specific IgE to FA was negative (less than 0.35kU/L). Similarly the 4 control sample did not show any change in total IgE levels (Table 1).

Table 1: Each box shows average reading of two samples of total blood IgEin kU/L

Student	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Week 4	65	234	56	76	219	65	237	37	52	296
Week 10	73	219	71	65	254	59	241	38	71	275
Week 14	58	244	65	88	233	70	249	28	66	243
Instructors	**1**	**2**	**3**	**4**	**CONTROL**	**1**	**2**	**3**	**4**	
Week 4	89	30	93	32	**Week 4**	251	91	34	87	
Week 10	91	44	87	38	**Week 10**	230	89	41	79	
Week 14	103	37	99	44	**Week 14**	243	88	36	86	

Fig. 1:Lay out of the anatomy lab

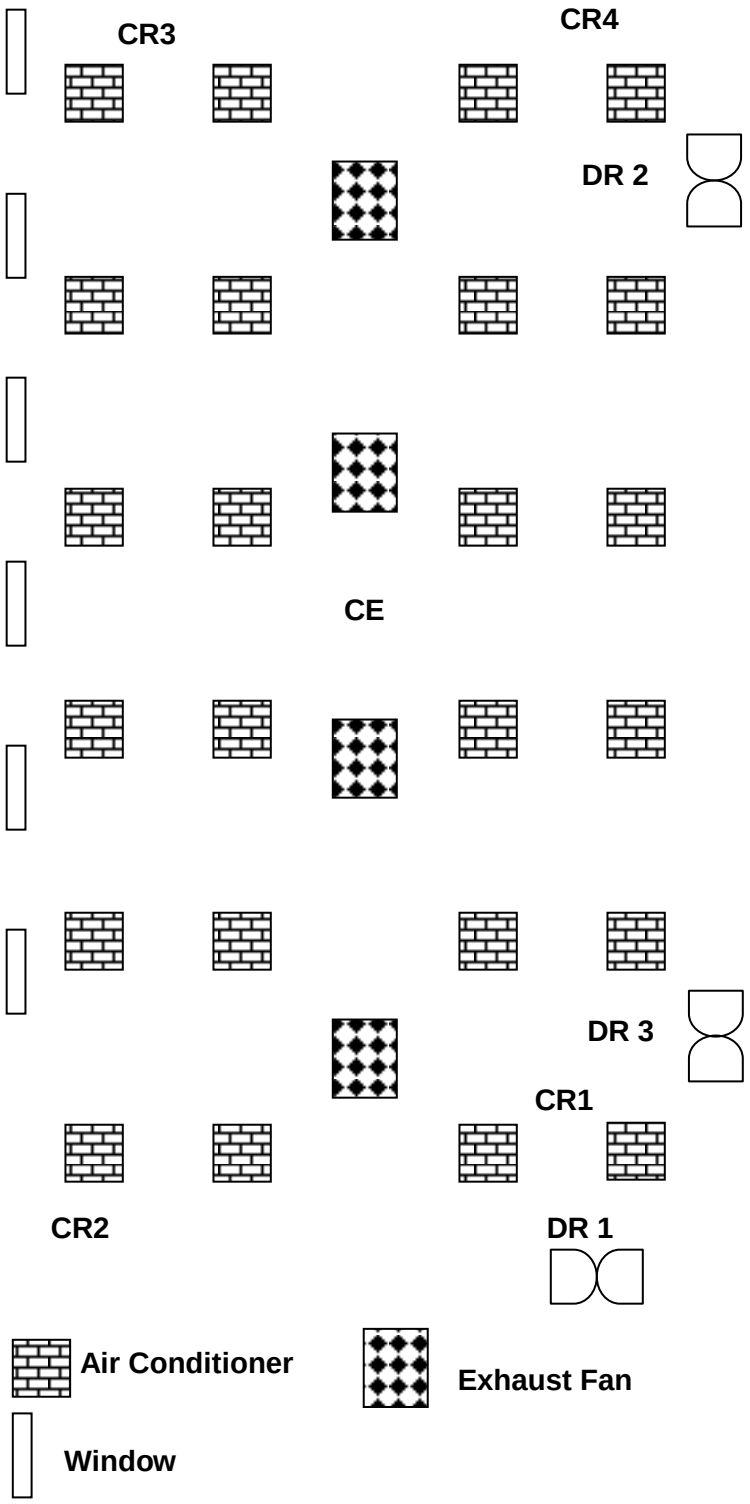
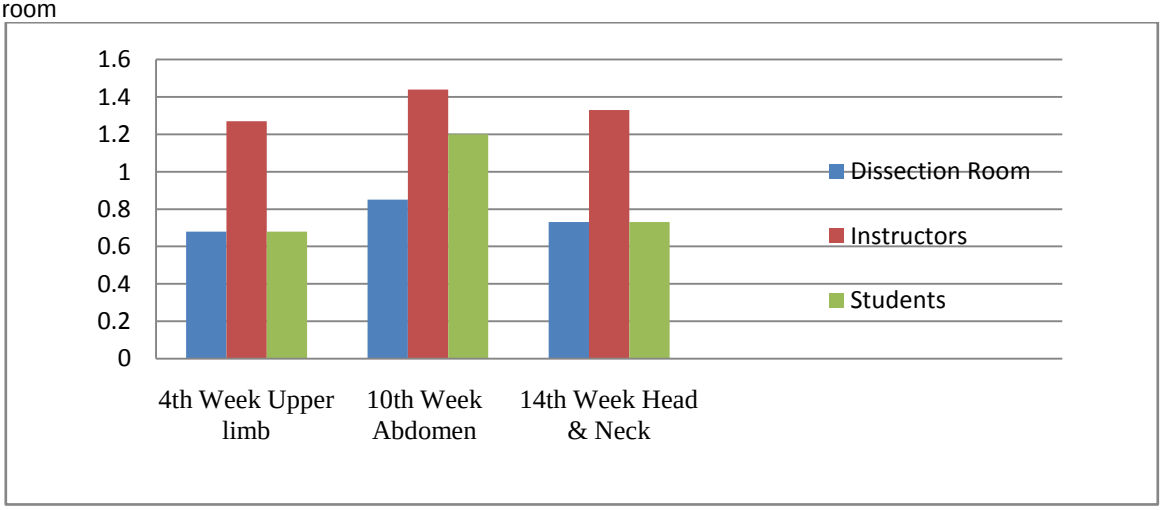


Fig 2: Showing the average concentration andthe exposure level of formalinof the instructors and students in the dissection room



DISCUSSION

FA is volatile organic compounds and recognized as a harmful chemical which produces symptoms of allergic diseases. The cadaveric dissection session is an essential component of anatomy practical inmedical and dental colleges. Therefore the students and instructors participating in the anatomy labs are exposed more to FA than the nonparticipants[3,12 13, 14]. At many occasionsthe participants in our lab reported symptomssimilar to those of allergic reactions. Higher indoor FA concentration during the lab session may provoke the production of IgE which is responsible for producing the allergic symptoms. This study is designed to establish relationship between thehigher concentration of FAand IgEproductioninour lab. Following every dissection session some students developed symptoms similar to allergic reactions with no previous history. These symptoms were linked with the higher & prolong exposure to FA. Our lab exceeded not only the guideline of 0.08 of WHO[1] but also the ACGIH permissible limit of 0.3 ppm[7]. Previous reports documented that indoor FA concentration and personal exposure levels in anatomy labs exceed the permissible limits[24].Keeping these facts in mind it is anticipated that exposure to FA may evoke total blood IgE and specific IgE to FA during the lab session. Our results do not show any significant changes the blood IgE in the participants.Exposurelevels of FA for instructors were higher than students(Fig 2) possibly because the instructors devote more hours in the lab due to occupational reasons. Specific IgE to FA has hardly been found in general workers[25] and participants of pathology lab.[26]. *Bousquet et.al*[27]reported that FA might lead to IgE-mediated sensitization and specific IgE antibodies against FA. Children suffering from respiratory diseases are more susceptible to produce respiratory symptoms when they are exposed to higher FA exposure level[28].Asthma is also related to higher concentrations of FA[29] in children. Therefore, it is possible that higher and prolong exposure to FA may increase allergic disease in children. Contrary to this *Doisat*[30] do not consider FA as a major allergens causing childhood asthma. FA is a hepten and Formaldehyde-protein complex may be considered as immunogenic6. In fact hapten is a small molecule that elicits an immune response only when attached to a large carrier. In the present study specific IgE to FA was found negative (below 0.35 kU/L) in all instructors, students and control group participants. The total blood IgE levels of participant did not show any significant difference with that of control. Findings of this studyshows that exposure to high level of FA do not evoke an IgE-mediated reaction. Indeed no significant difference was observed in production of IgE even during the 10th week when the FA exposure level & indoor concentration was highest (Fig 2) during the dissection of body cavities. Higher indoor FA concentration as well as the higher personal exposure level in our lab did evoke IgE production suggesting that in vivo relationship between FA and IgE induced clinical symptoms remains a dilemma. It is recommended that the students enrolled in anatomy courses must disclose their allergic history.

REFERENCES

1. World Health Organization (Regional Office for Europe) 2001; WHO air quality guidelines — Sec- ond Edition, WHO, Copenhagen
2. Ohmichi K, Komiyama M, Matsuno Y, Takanashi Y,

Miyamoto H, Kadota T, et al. Formaldehyde exposure in a gross anatomy laboratory — personal exposure level is higher than indoor concentration. Environ SciPollut Res Int 2006;13(2):120–4.
3. Muhammad S. Vohra International Journal of Occupational Medicine and Environmental Health 2011;24(1):108 – 113 DOI 10.2478/s13382-011-0004-4
4. Gibson, J. E. (1983) Formaldehyde toxicity, Hemisphere, Washington DC.
5. International Agency for Research on Cancer (IARC) Monographs on the Evalua- tion of Carcinogenic risk of Chemicals to Humans, Wood dust and Formaldehyde 1995; Vol.62, International Agency for Research on Cancer, Lyon.
6. Maibach H Formaldehyde: Effects on animal and human skin. In: Gibson J (Ed). Formaldehyde Toxicity. New York: Hemisphere Publishing, 1983; pp 166-74.
7. American Conference of Governmental Industrial Hygienists (ACGIH). Notice of intended change — formaldehyde. ApplOccup Environ Hyg 1992;7:852–74.
8. Paustenbach D, Alarie Y, Kulle T, Schachter N, Smith R, Swenberg J, et al. A recommended occupational exposure limit for formaldehyde based on irritation. J Toxicol Environ Health 1997;50 (3):217–63.
9. International Agency for Research on Cancer (IARC). IARC Monograph on the Evaluation of Carcinogenic risks to Humans. Formaldehyde, 2-Butoxyethanol and 1-tert-Butoxypropan-2006.2-vol.Lyon: IARC;
10. WHO. Air Quantity Guidelines for Europe. 2nd ed. Chapter 5.8. Formaldehyde. Copenhagen: WHO; 2000. p. 87–91 [cited 2010 Feb 1]. Available from URL: http://www.euro. who.int/_data/assets/pdf_file/0005/74732/E71922.pdf.
11. Muhammad Saeed Vohra International Journal of Occupational Medicine and Environmental Health 2011;24(1):108– 113 DOI 10.2478/s13382-011-0004-4
12. Skisak CM. Formaldehyde vapor exposures in anatomy laboratories. Am Ind Hyg Assoc J 1983; 44: 948–50.
13. Ohmichi K, Komiyama M, Matsuno Y, Takanashi Y, Miyamoto H, Kadota T, et al. Formaldehyde exposure in a gross anatomy laboratory personal exposure level is higher than indoor concentration. Environ SciPollut Res Int 2006;13(2):120–4. 7. Tanaka K, Nishiyama K, Yaginuma H, Sasaki A, Maeda T,
14. Kaneko SY, et al. Formaldehyde exposure levels and exposure control measures during an anatomy dissecting course. KaibogakuZasshi 2003; 78 (2):43–51)
15. Achatz, G., Achatz-Straussberger, G., Lamers, R. and Crameri, RRegulation of the IgE Response at the Molecular Level: Impact on the De- velopment on Systemic Anti IgE Therapeutic Strat- egies. *Chem. Immunol. Allergy*,2006; 91, 204-217
16. Wantke, F., Demmer, C. M., Tappler, P., Gotz, M. and Jarisch, R. Exposure to gaseous formal- dehyde induces IgE-mediated sensitization to form- aldehyde in school-children.*Clin. Exp. Allergy*,1996;26, 276-280
17. Wilhelmsson, B. and Holmstrom, M. Positive Formaldehyde-RAST after prolonged formaldehyde exposure by inhalation. *Lancet*,1987; 8551, 164
18. Kramps, J. A., Pltenburg. L. T. C., Kerklaan, P. R. (M., Spieksma, F. T. H. M.., Valentijn, R. M. and Dijkman, J. H. Measurement of specific IgE antibodies in individuals exposed to formaldehyde. *Clin. Exp. Allergy*,1989; 19, 509-514
19. Dykewicz, M. S., Patterson, R., Cugell, D. W., Harris, K. E. and FangWu, 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
20. Liden, S., Scheynius, A., Fischer, T., Johansson, S. G. O., Ruhnek-Forsbeck, M. and Stejskal, V. Absence of specific IgE antibodies in allergic con- tact sensitivity to formaldehyde. *Allergy*,1983; 48, 525- 529
21. Uchiyama S, Hasegawa S. *A reactive and sensitive diffusion sampler for the determination of aldehydes and ketones in ambient air*. Atomosph Environ 1999;33(13):1999–2005.
22. EPA. *Determination of Formaldehyde in Ambient Air Using Adsorbent Cartridge Followed by High-Performance Liquid Chromatography (HPLC), Method TO-11A*. EPA/625/R- 96/010b; Washington, DC: Center for Environmental Research Information Office of Research and Development, 1999 [cited 2010 Feb 1]. Available from URL: http://www.epa.gov/ttn/amtic/files/ambient/airtox/to-11ar.pdf.
23. 10. NIOSH. *Formaldehyde: method 2016*. In: NIOSH. *Manual of analytical method*. 4th ed. [cited 2005 May 15]. Available from URL: http://www.cdc.gov/niosh/nmam/pdfs/2016.pdf.
24. Perkins JL, Kimbrough JD. *Formaldehyde exposure in a gross anatomy laboratory*. J Occup Med 1985; 27(11): 813–5.
25. Grammer, L. C., Harris, K. E., Shaughnessy, M. A., Sparks, P., Ayars, G. H., Altman, L. C. and Patterson, R. 1990 Clinical and immunologic evaluation of 37 workers exposed to gaseous formaldehyde. *J.*
26. Salkie, M. L. The prevalence of atopy and hypersensitivity to latex in medical laboratory tech- nologists. *Arch. Pathol. Lab. Med.*,1993;117, 897-899.
27. Bousquet, J., Maurice, F., Rivory, J. P., SkassaBrociek, W., Florence, P., Chouzenox, R., Mion, C. and Michel, F. B. Allergy in long term he- modialysis. II. Allergic and atopic patterns of a popu- lation of patients undergoing long-termhemodialysis. *J. Allergy Clin. Immunol.*,1988;81, 605-610.
28. Garrett, M. H., Hooper, M. A., Hooper, B. M., Rayment, P. R. and Abramson, M. J. In- creased risk of allergy in children due to formalde- hyde exposure in home. *Allergy*,1999; 54, 330-337.
29. Smedje, G., Norback, D. and Edling, C. Asthma among secondary schoolchildren in relation to the school environment.*Clin. Exp. Allergy*,1997;27, 1270-1278.
30. Doi S, Suzuki S, Morishita M, Yamada M, Kanda Y, Torii S, Sakamoto T. TheprevalenceofIg Esensitization to formaldehyde in asthmatic children. Allergy. 2003; Jul;58(7):668-71.