EVALUATION OF FORMALDEHYDE EXPOSURE DURING A GROSS ANATOMY DISSECTION COURSE

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ABSTRACT
Formaldehyde has been widely used as a disinfectant and preservative in medical fields. Medical students during their dissection course are exposed to formaldehyde, whose exposure is recently considered to be one of the causes of multiple chemical sensitivity. At first, we evaluated formaldehyde exposures that occurred in the gross anatomy laboratory with a general ventilation system. Formaldehyde in air was sampled by an active 2,4-dinitrophenylhydrazine (DNPH)-silica gel cartridge, extracted with acetonitrile and analyzed with a high performance liquid chromatography (HPLC). The geometric mean formaldehyde concentration was 20-93 ppb in the anatomy laboratory before starting the anatomy dissecting. After beginning the dissecting, the highest geometric mean concentrations were 1011-1380 ppb, for more than WHO guideline. It means we should reduce formaldehyde exposure when medical students and lecturers are exposed during gross anatomy dissection courses. Then we improved the ventilation by a local ventilation system using the existing ventilation assigned to the laboratory and develop local ventilation apparatus for each dissection table. After these improvements, the geometric mean concentrations could be kept about 100 ppb. Significant decreases were also observed during the exposed period for symptoms of "unusual thirst", "burning eyes", "itchy eyes", "bad feeling", "fatigue", etc. in comparison with symptoms before improvement of the ventilation system.

KEYWORDS
Formaldehyde, Anatomy dissection, Local ventilation, Concentration, Symptoms

INTRODUCTION
Formaldehyde is a flammable, colorless and readily polymerized gas at ambient temperature, and is one of the major pollutants in indoor air. It is present in the environment as a result of natural processes and from man-made sources, including motor vehicle exhaust, residues, emissions, or wastes produced during the manufacture of formaldehyde, and cigarette smoke (World Health Organization Regional Office for Europe 2000). Formaldehyde also has been widely used during disinfection procedures or embalming of bodies in medical fields. Medical students during their dissection course are exposed to formaldehyde.

The use of volatile substances including formaldehyde in the building causes a particular health hazard commonly referred to as sick-house syndrome and multiple chemical sensitivity (MCS). MCS is
characterized by various somatic symptoms which cannot be explained organically and by sensitivity to extremely low concentrations of chemicals including formaldehyde (Kunugita 2003). In 1997, the former Ministry of Health and Welfare proposed that the concentration of formaldehyde should be less than 80 ppb; a value in line with that of the WHO indoor air quality guideline (WHO Regional Office for Europe 2000, Japan Ministry of Health and Welfare 1997). Furthermore, in 2002, the Ministry of Health, Labour and Welfare issued guidelines for the reduction of formaldehyde concentrations in workplaces, requiring that the employer should make effort to maintain indoor concentrations of formaldehyde below 80 ppb for general workplaces and 250 ppb for specific workplaces where formaldehyde is handled (Japan Ministry of Health, Labour and Welfare 2002).

For the solution of exposure problem to formaldehyde in gross anatomy laboratories, Japan Ministry of Education, Culture, Sports, Science and Technology took action to improve plans for the dissection course in medical and dental school to reduce formaldehyde concentration (2001).

Moreover, the International Agency for Research on Cancer (IARC) re-evaluated the carcinogenicity of formaldehyde based on recent research in humans in 2004. IARC concluded that formaldehyde is carcinogenic to humans (Group 1) (IARC 2006), therefore, urgent and concrete measures to reduce exposure to formaldehyde during anatomy dissecting courses should be taken.

METHODS

Construction of a gross anatomy laboratory and improvement of the air quality

This study was conducted in a gross anatomy laboratory in a medical school. The laboratory space is 19.5 m x 24 m, and 3 m in height (1,400 m$^3$). There are 25 dissection tables (Fig. 1). The air in the laboratory was suctioned by general ventilation system with three outlet openings leading to a main duct that transports the air to the rooftop of the building where it was discharged into the atmosphere. The ventilation rate had been designed as 14,800 m$^3$/h and the capacity of ventilation was 10.6 air changes per hour when the equipment was installed in 1989. However, the ventilation rate reduced to 8,000 m$^3$/h (5.7 air changes/h) in 2001 because of the poor maintenance.

We started to improve the general ventilation system by changing the filters, and the ventilation rate was increased to 12,000 m$^3$/h (8.6 air changes/h) in 2002.

We decided to adopt a local ventilation system using the existing ventilation assigned to the laboratory and develop novel local ventilation apparatus for each dissection table in 2005. We designed a local ventilation apparatus (Grid type of hood: a downward suction) that can be attached to ordinary dissection tables and connected to the ventilation duct as shown in Fig. 2 (Yamato et al. 2005).

Measurement of a concentration of formaldehyde

Formaldehyde in air was actively sampled by a 2,4-dinitrophenylhydrazone (DNPH)-silica gel cartridge (Sep-Pak XpOSure Aldehyde Sampler, Nihon Waters K.K., Tokyo, Japan). The aldehydes absorbed on the silica gel had been extracted with the 3ml acetonitrile and analyzed with a high performance liquid chromatography (HPLC, Shimadzu LC-10 AD, Kyoto, Japan). Air samples were taken and measured at 12 points (measurement A for environmental assessment) and 2 or 3 points (measurement B to evaluate a personal exposure) in the laboratory. In each year, we measured the concentration four times. First sampling was done before starting the anatomy dissecting. Other three sampling was done at the beginning, middle, and ending sessions in a long period to observe human body structures.
Fig. 1. Design for air sampling in the gross anatomy laboratory.

Fig. 2. Dissection tables with the newly developed local ventilation apparatus. Dotted arrows show the flow of air.
Table 1. Summary of formaldehyde concentration (ppb) at an anatomy laboratory before and after improvement of the ventilation system

<table>
<thead>
<tr>
<th>Measurement</th>
<th>2001</th>
<th>2002</th>
<th>2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (Environmental measurement)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st 10/4(Thu)</td>
<td>95</td>
<td>104</td>
<td>116</td>
</tr>
<tr>
<td>2nd 10/5(Fri)</td>
<td>501</td>
<td>552</td>
<td>443</td>
</tr>
<tr>
<td>3rd 11/12(Mon)</td>
<td>1261</td>
<td>1158</td>
<td>1273</td>
</tr>
<tr>
<td>4th 12/14(Fri)</td>
<td>1266</td>
<td>872</td>
<td>813</td>
</tr>
<tr>
<td>B (Personal measurement)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st 10/17(Mon)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2nd 11/1(Wed)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3rd 11/30(Wed)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4th 12/18(Fri)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

| Arithmetic mean | 94 | 605 | 1386 | 986 | 22 | 669 | 795 | 1024 | 66 | 43 | 60 | 35 |
| SD | 14 | 103 | 138 | 163 | 8 | 156 | 209 | 162 | 9 | 2 | 9 | 13 |
| Geometric mean | 93 | 596 | 1380 | 974 | 20 | 654 | 766 | 1011 | 66 | 43 | 59 | 33 |
| Geometric SD | 1.2 | 1.2 | 1.1 | 1.2 | 1.4 | 1.2 | 1.3 | 1.2 | 1.2 | 1.1 | 1.2 | 1.4 |

Measurement A and B are measurement methods to assess working environment. "A" examines a concentration of harmful matter to humans in working place. The value for measurement "B" was defined as the maximum value shown in bold. SD: standard deviation.

We first measured the concentration before improvement of ventilation system in 2001. In 2002, the general ventilation system was improved. Finally, we installed the novel local ventilation apparatus for each dissection table in 2005.
Questionnaires
To observe health effects by exposure to formaldehyde in the gross anatomy laboratory, we assessed their self-reported physical symptoms using questionnaires before (in 2001) and after (in 2005) improvement of the ventilation system by a local ventilation system. Each question has 7 degree from “poor (-3)” to “well (+3)”, and “zero (0)” is normal condition. We compared the symptoms of students between the period of exposure to formaldehyde in the gross anatomy laboratory and non-exposure period in each year. Statistical significance between conditions in each year assessed by paired t-Test.

RESULTS
Concentration of formaldehyde
In 2001, the geometric mean formaldehyde concentration was 93 ppb in the anatomy laboratory before starting the anatomy dissecting. The concentration of formaldehyde significantly increased during the laboratory sessions. The highest geometric mean concentrations after beginning the dissecting were 1380 ppb.

After these measurements, the filters in the general ventilation system were changed to new one, and then ventilation rate increased to 12,000 m³/h in 2002. And in this gross anatomy laboratory, the concentration of formaldehyde in embalming solution was decreased from 20% to 10%. In 2002, however, the average formaldehyde concentration in the laboratory was found to be 1011 ppb at the highest concentration. The formaldehyde concentration exceeded both of the guideline values for indoor concentration; 80ppb for general indoor environment by WHO and Japan Ministry of Health, Labour and Welfare, and 250 ppb for specific workplaces by Japan Ministry of Health, Labour and Welfare. It was necessary to reduce formaldehyde exposure when medical students and lecturers are exposed during gross anatomy dissection courses.

Finally, in 2005, we installed the novel local ventilation system for each dissection table (Yamato et al. 2005). We could significantly reduce the formaldehyde concentration, that could be kept under 100 ppb during the whole dissection courses (Table 1).

We have already reported a part of these results obtained in 2001 and 2002 (Kunugita et al. 2004).

Physical symptoms
In 2001, significant differences were observed during the exposed period for symptoms of "unusual thirst", "burning eyes", "itchy eyes", "bad feeling", "fatigue", etc in comparison with the non-exposed period. In 2005 after installation of local ventilation system, the symptoms of students were significantly reduced compared to before improvement of ventilation system (Fig. 3).

DISCUSSIONS
In this report, we showed the very high concentration of formaldehyde in gross anatomy laboratory with general ventilation system. Students complained many physical symptoms in the laboratory. Many other reports showed the similarly high concentration of formaldehyde in gross anatomy laboratories (Ohmichi et al. 2006, Kim et al. 1999).

Biological exposure monitoring by hemoglobin associated with formaldehyde
We have already reported the biological monitoring of student exposed to formaldehyde in 2001(Matsui et al. 2006). Once aldehyde invade blood vessel, these bind chemically to hemoglobin in red blood cell.
Nasal stuffiness
Dry nose
Unusual thirst
Dry mouth
Dry eyes
Burning eyes
Itchy eyes
Headache
Bad feeling
Low energy, fatigue
Inability to concentrate
Depressed feeling
Awakening

Fig. 3. Comparison of the symptoms of students between the period of exposure to formaldehyde in the gross anatomy laboratory (●) and non-exposure period (○). Left and right panels show the results of questionnaires before (in 2001) and after (in 2005) improvement of the ventilation by a local ventilation system, respectively. (* P<0.05, **P<0.01, ***P<0.001, paired t-test)

Fig. 4 Comparison of the formaldehyde hemoglobin adducts in blood between medical students studying anatomy dissection and non-medical students.
Thus, hemoglobin associated with formaldehyde (FA-Hb) is expected to be a good biological exposure index of formaldehyde. FA-Hb can be a long-term biomarker of exposure for a few months, because a red blood cell usually lives for about 120 days. We selected two groups which consisted of medical students (n=25) exposed to formaldehyde at high concentration in the anatomy laboratory, and non-medical students (n=8), who were not exposed to formaldehyde at high concentration. We collected blood samples at the end of practice in 2001. Non porous cation-exchange column is able to separate FA-Hb from kinds of hemoglobin in human. FA-Hb was estimated ratio of area of chromatogram. The amounts of FA-Hb in medical students were significantly greater than those of non-medical students as shown in Fig. 4.

Recently, IARC re-evaluated that formaldehyde is classified as carcinogenic to humans (group 1) in 2004 (IARC 2006). Formaldehyde exposure is also considered to be one of the causes of MCS. We have already shown the low levels of formaldehyde effects on neurological, immunological, and endocrinological systems in vivo (Fujimaki et al. 2004, Hayashi et al. 2004, Sari et al. 2004, Tsukahara et al. 2006). Therefore, these showed that urgent and concrete measures should be taken. Finally, we installed the novel local ventilation system, and could significantly reduce the formaldehyde concentration, that could be kept under 100 ppb during the whole dissection courses.

CONCLUSIONS
To avoid the personal exposure to the formaldehyde, the local exhaust ventilation system should be used, if formaldehyde must be used. Only a few medical schools have installed the local ventilation system in anatomy laboratories still now. Medical schools should take more concrete measures to reduce exposure to formaldehyde.

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REFERENCES
5. Japan Ministry of Education, Culture, Sports, Science and Technology (2001) “The improvement plan for the dissection course in medical and dental school (in Japanese. Title was translated by the authors)”


