# CYTOGENETIC EFFECTS OF FORMALDEHYDE EXPOSURE IN STUDENTS OF MORTUARY SCIENCE

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Formaldehyde exposure has been associated with nasal cancer,[1,2] nasopharyngeal cancer,[3,4,5] buccal and pharyngeal cancer,[6] and with leukemia.[7,8] The International Agency for Research on Cancer (IARC) found limited evidence for the carcinogenicity of formaldehyde in humans.[9] The National Institute for Occupational Safety and Health (NIOSH) considers formaldehyde to be a potential human carcinogen.[10] The U.S. Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) for formaldehyde is 0.75 ppm, calculated as an 8 hour time-weighted-average (TWA).[11]

The effect of low-level exposure to formaldehyde on oral, nasal, and lymphocyte biological markers was studied prospectively in a group of 29 mortician students who were about to take a course in embalming. Students of mortuary science with little or no prior embalming experience were encouraged to enroll in the study. Eight of the subjects had never participated in an embalming prior to the study, six had assisted with from one to four embalmings, and 15 had assisted with five or more embalmings in their lifetimes. The average age of the subjects was 23.6 years. Seven of the 29 subjects were women, and five of the 29 (two of whom were women) were current smokers.

Exposures to formaldehyde were assessed by personal sampling using a passive monitoring device (PF-20 STEL monitor, Air Quality Research, Berkeley California). Prior to using the PF-20 passive monitor, it was evaluated in a laboratory exposure chamber and under field conditions in the embalming area of the mortuary college. In addition to the personal monitoring, short-term (peak) exposure measurements were performed using a continuous reading instrument (Interscan Model 4160 SP, Chatsworth, California).

Subjects were enrolled in the study during the first quarter of school, three weeks prior to their first embalming course. Each subject completed a questionnaire concerning past occupational activity, past embalming experience, smoking, diet, medication, and X-ray exposure. Swabs of the nose and mouth and blood samples were taken. The blood, oral, and nasal sampling was repeated after the first nine weeks in the embalming laboratory, and an interim questionnaire was administered.

All blood and tissue specimens were obtained in the morning, prior to any embalming, and were processed by the cytogenetic laboratory on the same day that they were obtained from the subjects. Assays for micronuclei and sister chromatid exchange (SCE) were done using standard methods. All slides were coded and marked by one of the investigators to blind the reader to the exposure status of any individual. To avoid reader variation caused by analyzing pre- and post-exposure slides at different times, staining of epithelial cell and lymphocyte micronuclei specimens was deferred until both pre- and post-exposure samples had been obtained, and then both sets of slides from each subject were stained together on the same day. Slides from any one individual were then read on the same day by the same reader. A 10% sample of all slides was chosen for quality control analysis. These slides were recoded and then rescored for micronuclei or SCE in the same manner and by the same reader.

Each subject was used as his or her own control in the analysis of change in levels of the various cytogenetic markers. Differences in mean pre- and post-exposure marker values were assessed by using a matched Student's "t" test for values that were normally distributed (SCE) or by the Wilcoxon sign-rank test, a non-parametric test, for values that were not normally distributed (micronuclei).[12] Comparison of the change in cytogenetic markers with cumulative

formaldehyde exposure was done using Spearman's rank correlation coefficient and by linear regression if the regression residuals were normally distributed.

During the 85 day study period, the subjects performed an average of 6.9 embalmings and had average cumulative formaldehyde exposures of 14.8 ppm-hours, with an average air concentration of 1.4 ppm during embalming. Since the average time spent embalming was 125 minutes, formaldehyde exposures calculated as an 8 hour TWA were 0.35 ppm on days when embalmings were done, which was less than the OSHA PEL of 0.75 ppm.

Short-term exposure monitoring during 11 embalmings found peak exposures from 3 to 9 times that of the corresponding TWA. Peak exposures were associated with leaks of embalming fluid occurring during injection into vessels and body cavities, application of embalming gels to hands, feet, or facial parts, and leaks of embalming fluid from tubing and other appliances. Instantaneous peak exposures ranged up to 6.6 ppm and some exposures exceeded the OSHA STEL (short term exposure limit) of 3 ppm for a 15 minute period. Male and female subjects performed similar numbers and types of embalmings and had similar average cumulative exposures and TWA exposures. Air sampling measurements indicated little or no exposure to substances in the laboratory other than formaldehyde.

Epithelial cells from the buccal area of the mouth showed a 12-fold increase in micronucleus frequency during the study period, from 0.046 $\pm$0.17 pre-exposure to 0.60 $\pm$1.27/1000 cells at the end of the course ($p < .05$). Nasal epithelial micronuclei increased 22%, from 0.41 $\pm$0.52 to 0.50 $\pm$0.67/1,000 cells ($p = 0.26$). In blood cells, the frequency of micronucleated lymphocytes increased 28%, from 4.95 $\pm$1.72 to 6.36 $\pm$2.03/1000 cells ($p < .05$) while sister chromatid exchanges decreased 7.5% ($p < .05$). A dose-response relationship was observed between cumulative exposure to formaldehyde and increases in buccal micronuclei in the 22 male subjects but not in the seven female subjects.

We conclude that low-level exposure to formaldehyde is associated with cytogenetic changes in epithelial cells of the mouth and in blood lymphocytes. In vivo cytogenetic changes in humans due to

formaldehyde exposure are of great interest because it is a suspect human carcinogen. The findings of changes in oral and nasal epithelial cells and peripheral blood cells do not indicate a direct mechanism for carcinogenesis but do indicate that DNA alteration has occurred. The changes seen in peripheral lymphocytes indicate that cytogenetic effects can be seen in tissues distant from the area of initial contact. The association of these cytogenetic effects with formaldehyde exposure indicate that they may be useful as markers of biologically effective dose.[13]

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