

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/281963822>

# Formaldehyde exposure and its effects during pregnancy: Recommendations for laboratory attendance based on available data

Article in *Clinical Anatomy* · September 2015

DOI: 10.1002/ca.22623

CITATIONS

5

READS

2,610

7 authors, including:



**Amin Demerdash**  
Geisinger Health System

15 PUBLICATIONS 35 CITATIONS

SEE PROFILE



**Kaissar Yammine**  
Lebanese American University

62 PUBLICATIONS 417 CITATIONS

SEE PROFILE



**Koichi Watanabe**  
Kurume University

85 PUBLICATIONS 330 CITATIONS

SEE PROFILE



**Marios Loukas**  
St. George's University

911 PUBLICATIONS 7,816 CITATIONS

SEE PROFILE

Some of the authors of this publication are also working on these related projects:



Evidence-based Medical Education Research [View project](#)



A comparative review of mandibular orthognathic surgery with a focus on vertical sagittal ramus osteotomy [View project](#)

## **Formaldehyde Exposure and its Effects during Pregnancy: Recommendations for Laboratory Attendance Based on Available Data**

Matthew J. Haffner<sup>1</sup>, Peter Oakes<sup>2</sup>, Amin Demerdash<sup>2</sup>, Kaissar Cesar Yammine<sup>3</sup>, Koichi Watanabe<sup>2</sup>, Marios Loukas<sup>1</sup>, R. Shane Tubbs<sup>4</sup>

1 Department of Anatomical Sciences, St. George's University, Grenada

2 Pediatric Neurosurgery, Children's of Alabama, Birmingham, AL

3 Foot and Hand Clinic, Center for Evidence-Based Sport and Orthopedic Research, Emirates Hospital, Dubai, UAE

4 Seattle Science Foundation, Seattle, WA

Key words: formalin, embalming, formaldehyde, dissection, cadavers, medical students, pregnancy, women, pregnant, laboratory, anatomy

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as an 'Accepted Article', doi: 10.1002/ca.22623

## Abstract

Formalin is commonly used in fixation of cadaveric specimens. Exposure to formaldehyde, a component of formalin and a known carcinogen, during gross anatomy laboratory dissection is a continuing concern for pregnant students and instructors. Since there is little literature on this specific topic, the current review was compiled in the hope of offering recommendations to pregnant students and instructors who are engaged in human anatomical dissection where formalin is used. Relevant articles were obtained through searches of PubMed and Google Scholar for the terms “formaldehyde”, “pregnant”, “formalin”, and “exposure.” A literature search was conducted for chemical information and articles about exposure as issued by government regulatory agencies and chemical companies that produce formaldehyde. This led to the compilation of 29 articles each of which included references to previous, relevant, human research. The reviewed literature contains data strongly suggesting that pregnancy can be affected by formaldehyde exposure. Therefore, on the basis our analysis, female students who might be pregnant should avoid formaldehyde exposure, including that in a gross anatomy laboratory. Instructors should find other means of ensuring anatomical competence for these students.

## Introduction

Formaldehyde exposure during pregnancy is associated with increased risks of defects ranging from birth malformations to spontaneous abortions (Duong et al., 2011; McMartin et al., 1998). Although thorough human studies cannot be conducted for ethical reasons, animal studies have revealed that formaldehyde exposure is detrimental to the developing fetus (Thrasher et al., 2001). Exposure to formaldehyde during gross anatomy dissection is an area of concern for pregnant students and instructors as the common fixation solution, formalin, contains formaldehyde. The route of exposure to formaldehyde within the dissection laboratory is from the preserved specimens via the air within the laboratory (Keil et al., 2001). While it is easy to protect against physical contact with formaldehyde by wearing gloves, the route of exposure for pregnant students and instructors that causes most concern is via airborne formaldehyde. Some techniques for neutralizing the formaldehyde used in gross anatomy laboratories have been advocated, such as using monoethanolamine (Coskey and Gest, 2015).

Animal models have shown that formaldehyde has detrimental effects upon fetal development when high blood levels are reached. High serum formaldehyde leads to a harsher environment for fetal development by lowering the maternal pH and  $pO_2$  while increasing the  $pCO_2$  (Thrasher et al., 2001). Not only does formaldehyde cause a shift in maternal blood chemistry, but also dissolved formaldehyde is more readily taken up by fetal tissue, specifically by the fetal brain and liver (Thrasher et al., 2001). The incorporated formaldehyde is also

eliminated much more slowly from fetal than maternal tissue (Thrasher et al., 2001). This means that fetal tissues (specifically the developing fetal brain and liver) more readily take up dissolved formaldehyde and are exposed to it for longer. Taking this information into account, it is easy to see that a moderate increase in formaldehyde exposure increases the detrimental effect upon the developing fetus, potentially leading to fetal malformations and spontaneous abortions. In addition, if the murine mother is iron deficient, formaldehyde exposure poses a threat exceeding the additive effects of formaldehyde and iron deficiency alone (Thrasher et al., 2001). Some of the effects commonly reported within the literature are rates of spontaneous abortions, fetal malformations, and birth weight.

### **Formaldehyde Dosage-dependent Effects and Exposure Regulations**

The odor threshold for formaldehyde ranges from 0.5 to 1 ppm. Eye irritation is associated with airborne concentrations ranging from 0.3 to 0.5 ppm. Moderate to severe eye, nose, and throat irritation occurs at 2 to 3 ppm (UNEP, 2002). Exposure to levels of formaldehyde of 20 ppm or above for 13-30 minutes is categorized as an immediate danger to life and health (Thrasher et al., 2001).

Since June 2004, formaldehyde has been classified as a carcinogen according to the International Agency for Research on Cancer (IARC) (Goyer et al., 2006). Formalin, generally composed of 37% formaldehyde dissolved in aqueous methanol, is commonly used as a fixative for biological specimens (Goyer et al., 2006), though more dilute formalin preparations have been reported within gross anatomy laboratories (Keil et al., 2001). The United States Occupational Safety and Health Administration (OSHA) has limited exposure levels to 0.75 ppm (parts per million) for an eight hour time-weighted average exposure and an absolute exposure

limit of 2 ppm for 15 minutes (Goyer et al., 2006). According to the US Center for Disease Control and Prevention (CDC), formaldehyde levels in ambient air increase with increases in temperature and humidity.

### **Formaldehyde within Medical Dissection Laboratories**

In Japan, Hisamitsu et al. (2011) found average formaldehyde concentrations of 0.67 ppm (range 0.51 - 0.97 ppm) in the center of a gross anatomy laboratory, which was 15m x 25m x 3m in size, and an average of 0.44 ppm (range 0.22 - 0.70 ppm) in the corners (Table 1). These levels of airborne formaldehyde were constant throughout the day (Hisamitsu et al., 2011), consistent with previous findings in gross anatomy dissection laboratories (Keil et al., 2001).

Additional studies conducted in gross anatomy dissection laboratories measuring the formaldehyde content of the air indicated an average of 0.95 ppm (Akbar-Khanadeh et al., 1997), which agrees with the range of 0.51 - 1.48 ppm (Keil et al., 2001).

The overall formaldehyde content of a gross anatomy dissection laboratory depends upon a number of factors, namely the number of cadavers, the concentration of formalin used as the fixative, the distribution of specimens within the laboratory, the size and shape of the laboratory, the ventilation flow rate, and vent location within the laboratory (Klein et al., 2013). In addition to the variability among dissection laboratories, the exposure level of formaldehyde varies with distance from the exposure source (e.g. preserved specimens); the levels are dramatically greater during close dissection (in excess of 11 ppm) than during passive viewing of dissected animal specimens (0.42 ppm) (Ryan et al., 2003).

### **Inhaled Formaldehyde**

Once formaldehyde is inhaled, it is deposited and absorbed in tissues within the upper respiratory tract (Heck et al., 1983; Swenberg et al., 1983; Patterson et al., 1986 [as cited in Liteplo et al., 2001]), which in humans includes the nasal passages and the oral cavity as well as the trachea and bronchi (Liteplo et al., 2001). After the formaldehyde is absorbed, it quickly forms inter- and intra-molecular cross-links within proteins and nucleic acids at the site of contact (Swenberg et al., 1983 [as cited in Liteplo et al., 2001]). It is also rapidly metabolized to formate by the widely-distributed enzyme formaldehyde dehydrogenase. Oxidation of the absorbed formaldehyde by formaldehyde dehydrogenase requires glutathione (UNEP, 2002), and when glutathione in the absorbing tissues is depleted, more formaldehyde is bound to DNA within the cells of those tissues (Casanova et al., 1987; Lam et al., 1985 [as cited in UNEP, 2002]). Because of the rapid metabolism of inhaled formaldehyde via the respiratory tract, the levels within the blood do not increase significantly (Heck et al., 1985; Casanova et al., 1988 [as cited in Liteplo et al., 2001]).

Mucociliary clearance is inhibited by exposure to formaldehyde concentrations of 1.944 ppm (Morgan et al., 1986 [as cited in Liteplo et al., 2001]) and glutathione-mediated metabolism is saturated at exposure levels at 4 ppm (Casanova et al., 1987 [as cited in Liteplo et al., 2001]). Histological changes within the nasal epithelium are more closely related to the exposure concentration than the total cumulative exposure (Senberg et al., 1983; Casanova et al., 1994 [as cited in Liteplo et al., 2001]). Additionally, no significant effects upon pulmonary function have been observed in either asthmatic or non-asthmatic populations after three hours of exposure to formaldehyde levels of 0.5 - 3 ppm (Kulle et al., 1987; Sauder et al., 1986, 1987 [as cited in UNEP, 2002]). This is supported by research showing no significant changes in pulmonary function tests when a two-hour exposure group (meeting OSHA requirements for work place

exposure levels, < 0.75 ppm) was compared to a control group (Rahimifard et al., 2013).

However, Rahimifard et al. (2013) did find data suggesting that formaldehyde exposure can cause mild transient bronchoconstriction.

The goal of the present article is to review the current literature concerning the effects of formaldehyde exposure on developing fetal tissue, with the specific aim of ascertaining whether formaldehyde exposure during dissection laboratory work poses a danger to developing fetal tissue within pregnant students and instructors, and if such a risk exists, what steps can be taken to minimize formaldehyde exposure in this environment.

## **Methods**

Relevant articles were obtained through a search for PubMed and Google Scholar for the terms “formaldehyde,” “pregnant,” “formalin,” and “exposure” as of February 2014. In addition, the chemical information literature and articles about exposure as issued by government regulatory agencies (US and Canadian) and chemical companies that produce formaldehyde were searched. This led to the compilation of 29 articles, each including references to previous relevant *human* research.

The criterion for article inclusion was the investigation of predefined outcomes in the article. The predefined outcomes used for article selection were dosage-dependent effects of formaldehyde upon humans in vivo, measured non-fetal IgE levels following formaldehyde exposure, and pregnancy outcomes following formaldehyde exposure. Pregnancy outcomes included in the inclusion criteria were: premature birth, low birth weight, fetal mortality, spontaneous abortion, and birth defects.



Search results were excluded on the basis of type of study as well as line of inquiry, so a number of articles relating to the effects of direct exposure of formaldehyde upon tissue cultures were excluded. Additionally, all duplicate search results were omitted. The included studies provided information about the effects of formaldehyde exposure on both maternal and fetal tissues.

## **Results**

### **Search results**

The large number of articles yielded by our search strategy was limited by the inclusion criteria to a total of 32 papers. The included articles (30 and two articles from electronic searches and the grey literature, respectively) are: Akbar-Khanzadeh et al., 1997; Bendino, 2002; Casanova et al., 1987; Casanova et al., 1988; Casanova et al., 1991; Casanova et al., 1994; Duong et al., 2011; Goyer, 2007; Goyer et al., 2006; Heck et al., 1983; Heck et al., 1985; Hemminki et al., 1982; Hemminki et al., 1985; Hisamitsu et al., 2011; Keil et al., 2001; Klein et al., 2013; Kligerman et al., 1984; Kulle et al., 1987; Lam et al., 1985; Liteplo et al., 2003; Marozienne et al., 2002; McMartin et al., 1998; Morgan et al., 1986; Rahimifard et al., 2013; Ryan et al., 2003; Sauder et al., 1986; Sauder et al., 1987; Swenberg et al., 1983; Thrasher et al., 2001; Zhu et al., 2006; UNEP Chemicals, 2002; US CDC, 2013.

### **Human Study Results:**

Twenty-nine studies reported at least one pre-defined outcome for *human* data: Akbar-Khanzadeh et al., 1997; Bendino, 2002; Casanova et al., 1987; Casanova et al., 1988; Casanova et al., 1994; Duong et al., 2011; Goyer, 2007; Goyer et al., 2006; Heck et al., 1983; Heck et al.,

1985; Hemminki et al., 1982; Hemminki et al., 1985; Hisamitsu et al., 2011; Keil et al., 2001; Klein et al., 2013; Kulle et al., 1987; Lam et al., 1985; Liteplo et al., 2003; Maroziene et al., 2002; McMartin et al., 1998; Morgan et al., 1986; Rahimifard et al., 2013; Ryan et al., 2003; Sauder et al., 1986; Sauder et al., 1987; Swenberg et al., 1983; Zhu et al., 2006; UNEP Chemicals, 2002; US CDC, 2013.

Maroziene et al. (2002) conducted an epidemiological study of human pregnancy outcomes and ambient formaldehyde exposure in Lithuania. The results are presented as adjusted odd ratios with 95% confidence intervals in parentheses (Table 1). The data are analyzed in terms of three groups of ambient formaldehyde exposure (low, medium, and high).

Table 1:

		Adjusted Odds Ratio	
		Premature Birth	Low Birth Weight
Ambient Formaldehyde Levels	Low ( $< 2.00 \mu\text{g}/\text{m}^3$ )	1	1
	Medium ( $2.01 - 3.9 \mu\text{g}/\text{m}^3$ )	1.11 (0.72 – 1.71)	2.15 (0.96 – 4.81)
	High ( $> 3.9 \mu\text{g}/\text{m}^3$ )	1.37 (0.91 – 2.05)	2.09 (1.03 – 4.26)
	Continuous Variable (per $5 \mu\text{g}/\text{m}^3$ increase)	1.07 (0.77 – 1.49)	1.36 (0.75 – 2.74)

A large scale meta-analysis of formaldehyde exposure by Duong et al. (2011) compared the risk ratios of maternal exposure to formaldehyde and for both maternal and paternal formaldehyde exposure. The results from Duong et al. (2011), with all risk ratios given with 95% confidence intervals within parentheses, are presented in Table 2. The effects are broken into spontaneous abortion (miscarriage) and all other adverse outcomes (birth defects, malformations, etc.).

Maroziene et al. (2002) showed that exposure to high ambient levels of formaldehyde carried the highest risk of low birth weight (adjusted OR = 2.09; 95% CI 1.03–4.26). Doung et al. (2011) concluded that maternal exposure to formaldehyde was associated with a higher risk of spontaneous abortion and other adverse outcomes than both maternal and paternal exposure.

Table 2:

Duong et al. (2011) Meta-Analysis Conclusions			Number of Studies	Risk Ratio
Maternal Exposure only	Spontaneous Abortion	Total	7	1.76 (1.29 – 2.41)
		Self-Reported	4	2.04 (1.40 – 2.97)
		Not Self-Reported	3	1.29 (0.74 – 2.25)
	All Outcomes	Total	12	1.54 (1.27 – 1.88)
		Self-Reported	5	1.95 (1.35 – 2.81)
		Not Self-Reported	7	1.40 (1.11 – 1.78)
Maternal and Paternal Exposure	Spontaneous Abortion		8	1.29 (1.04 – 1.59)
	All Outcomes		13	1.34 (1.14 – 1.57)

Three papers studied the effects of formaldehyde exposure and its possible relationship to premature birth (Table 3).

Table 3

Study	Study Subjects	Study Groups	Measure of Premature Birth Outcomes
Shimilina et al. (1975)	Russian Factory Workers		Rate of Premature Water Breaking
		Exposed	37.23 ± 2.41 %

		Unexposed	23.63 ± 1.23 %
Zhu et al. (2006)	Danish Laboratory Workers		Odds Ratio for Premature Birth w/ 95% CI
		Frequent and/or High Exposure	0.7 (0.3 – 1.7)
		Infrequent and/or Low Exposure	1
Marozienne et al. (2002)	Residents of Kaunas, Lithuania	Ambient Formaldehyde Exposure Levels	Adjusted Odds Ratio w/ 95% CI Premature Birth
		Low ( < 2.00 µg/m <sup>3</sup> )	1
		Medium (2.01 – 3.9 µg/m <sup>3</sup> )	1.11 (0.72 – 1.71)
		High ( > 3.9 µg/m <sup>3</sup> )	1.37 (0.91 – 2.05)
		Time of Exposure	Adjusted Odds Ratio w/ 95% CI Premature Birth (Multiple Pollutant Model)
		1st Trimester	0.91 (0.49 – 1.68)
		2nd Trimester	0.38 (0.21 – 0.67)
		3rd Trimester	0.94 (0.57 – 1.53)

Shimilina et al. (1975) concluded that subjects exposed to formaldehyde have a higher rate of premature rupture of membranes than the unexposed cohort. The other two studies showed no statistically significant effect and the trimester of gestation had no particular outcome in regard to premature birth.

In addition to the results from the Duong et al. (2011) meta-analysis, other articles also presented data for spontaneous abortion (miscarriage) and its relationship to formaldehyde exposure (Table 4). Saurel-Cubizolles et al. (1994) showed that the rate of spontaneous abortion was higher among the exposed group (11.10%) than the unexposed group (6.90%). The other studies did not provide enough support for this hypothesis.

Table 4

Study	Exposure Agent Studied	Study Groups	Measure of Spontaneous Abortion Outcomes
Hemminki et al. (1985)	Formaldehyde		Spontaneous Abortion Crude Odds Ratio w/ 95% CI
		Exposed	0.7 (0.28 – 1.73)
		Unexposed	1
Hemminki et al. (1982)	Formaldehyde		Spontaneous Abortion Adjusted Rates
		Exposed	8.40%
		Unexposed	8.30%
Saurel-Cubizolles et al. (1994)	Formaldehyde		Spontaneous Abortion Rates
		Exposed	11.10%
		Unexposed	6.90%
McMartin et al. (1998)	Organic Solvent (not exclusive Formaldehyde data)		Spontaneous Abortion Odds Ratio w/ 95% CI
		Exposed	1.25 (0.99 – 1.58)
		Unexposed	1

Additionally, Duong et al. (2011) included birth defects/malformations in the category of all other birth outcomes (only presented data of non-normal birth outcomes in data). Four other articles include data for birth defects/malformation (Table 5).

Table 5

Study	Exposure Agent Studied	Type	Maternal v. Biparental Exposure	Study Groups	Measure of Birth Malformation	
Hemminki et al. (1985)	Formaldehyde	Case-Control	N/A		Birth Defect/Malformation Crude Odds Ratio w/ 95% CI	Rate of Birth Defects
				Exposed	1.74 (0.40 – 7.60)	8.80%
				Unexposed	1	5.50%
Saurel-Cubizolles et al. (1994)	Formaldehyde	Cohort	N/A		Rate of Birth Defects	
				Exposed	5.20%	
				Unexposed	2.20%	
Zhu et al. (2006)	Formaldehyde	Cohort	N/A		Adjusted Odds Ratio of Major Birth Malformations w/ 95% CI	
				High Exposure	1.5 (0.8 – 2.9)	
				Unexposed	1	
McMartin et al. (1998)	Organic Solvent (not exclusive Formaldehyde data)	Case-Control	N/A	Exposed	1.62 (1.12 – 2.35)	
				Unexposed	1	
		Cohort	N/A	Exposed	1.73 (0.74 – 4.08)	

				Unexposed	1	
					Risk Ratio Birth Defect/Malformation	
Duong et al. (2011)	Formaldehyde	Meta-Analysis	Maternal Exposure only	Exposed	1.54 (1.27 – 1.88)	
				Unexposed	1	
			Maternal and Paternal Exposure	Exposed	1.34 (1.14 – 1.57)	
				Unexposed	1	

Hisamitsu et al. (2011) studied the effects of formaldehyde exposure and the production of both general and formaldehyde-specific IgE antibodies in serum. These data were not included in their article; however, the authors stated, “total serum IgE levels did not significantly change between the first to third testings 12 months apart.” With regard to the formaldehyde-specific IgE antibodies, it was stated that they were “only detected in one case at 1st examination” and that “no correlation existed between severity of symptoms and formaldehyde-specific IgE levels.”

Saurel-Cubizolles et al. (1994) assumed that the rate of birth defects/malformations was higher among exposed (5.20%) than unexposed (2.20%) subjects, while Duong et al. (2011) showed that maternal exposure carries more risk than biparental exposure. There are also varied reports of the average formaldehyde content of ambient air within medical gross anatomy laboratories (Table 6).

Table 6

Study	Location	Room Dimensions	Number of Cadavers Present	Average Formaldehyde Concentration	Range	Subgroups
Hisamitsu et al. (2011)	Japan	15m x 25m x 3m	51	0.67 ppm	0.51 – 0.97 ppm	Center of Room
				0.44 ppm	0.22 – 0.70 ppm	Corners of Room
Ryan et al. (2003)	USA	2820 sq. ft	Not Given	0.42 ppm	0.08 – 1.20 ppm	Passive, Personal
				0.21 ppm	0.07 – 0.43 ppm	Active, Personal
				0.21 ppm	0.15 – 0.22 ppm	Passive, Area
				0.16 ppm	0.06 – 0.38 ppm	Active, Area
Akbar-Khanzadeh et al. (1997)	USA	37.5m x 7.5m x 3.5m	38	0.95 ± 0.31 ppm	0.05 – 1.72 ppm	
Keil et al. (2001)	USA	37.5m x 7.5m x 3.5m	47	0.635 – 1.82 mg/m <sup>3</sup>	0.308 – 3.18 mg/m <sup>3</sup>	
				(0.516 – 1.48 ppm)	(0.25 – 2.59 ppm)	

for formaldehyde, 1 ppm = 1.23 mg/m<sup>3</sup>

There is wide variation among the reported values of formaldehyde concentrations within gross anatomy laboratories; ranging from 0.16 ppm by Ryan et al. (2003) to 1.48 ppm by Keil et al. (2001).

## Discussion



The level of exposure within controlled environments (such as medical anatomy dissection laboratories) can be controlled much more precisely. While parameters innate in the laboratory (such as laboratory size and shape) cannot easily be changed, other factors can be altered much more readily to decrease the formaldehyde content of the air. The amount of formaldehyde used to fix and preserve biological specimens can be decreased and the ventilation flow rate as well as the spread and number of vents can be increased to decrease the amount of formaldehyde within this controlled environment (Keil et al., 2001).

Formaldehyde is found in ambient air but causes negligible effects because the levels are below the physiological threshold of 0.3 ppm (UNEP, 2002). Once local concentrations of airborne formaldehyde exceed the physiological threshold of perception, symptoms of eye irritation are likely to occur, followed by nose and throat irritation as formaldehyde concentrations increase (UNEP, 2002). The use of formalin as a fixative for biological specimens is almost universal within medical universities and is especially prevalent in anatomical dissection laboratories. The concern is whether exposure to formaldehyde during fundamental courses in medical education, such as medical anatomy, poses health risks for any person who is pregnant, and if so what steps can be taken to minimize such risks.

Studies of ambient formaldehyde levels within an urban area showed that the effects of greater average formaldehyde exposure are correlated with a lower average birth weight (Marozienne et al., 2002). This was found for both pre-term and full-term babies.

Numerous studies have shown that increased formaldehyde exposure to pregnant women results in an increased risk of spontaneous abortion (Hemminki et al., 1985; Saurel-Cubizolles et al., 1994; McMartin et al., 1998; Zhu et al., 2006; Duong et al., 2011). Additionally, a large-scale meta-analysis demonstrated that formaldehyde exposure was associated with an increased risk

ratio of 1.29 for spontaneous abortion (Duong et al., 2011). Birth defect rates among French nurses who were exposed occupationally to increased levels of formaldehyde were more than doubled (2.2% to 5.2%) (Saurel-Cubizolles et al., 1994). Formaldehyde exposure is associated with even greater rates of birth malformations when it occurs during the first trimester, with an increase from 5.3% to 8.8% (Duong et al., 2011). However, the data show that formaldehyde exposure, though a risk factor for low birth weight, is not a risk factor for premature birth (Shimilina et al., 1975; Marozieni et al., 2002; Zhu et al., 2006).

The levels of formaldehyde encountered within an average medical anatomy dissection laboratory are commonly reported as between 0.44 and 0.95 ppm; however, levels as high as 1.48 ppm have been reported (Keil et al., 2001; Hisamitsu et al., 2011; Akbar-Khanadeh et al., 1997; Ryan et al., 2003). These are ambient formaldehyde levels within medical anatomy dissection laboratories, but exposure levels have been shown to increase dramatically (from 0.42 ppm to 11+ ppm) with greater proximity to preserved specimens, as during close dissection (Ryan et al., 2003). These data indicate that formaldehyde exposure levels are dependent upon proximity to a source (e.g. a preserved specimen), and that measurement of ambient room formaldehyde levels are not accurate for procedures commonly undertaken during medical dissection, such as close dissection of a preserved specimen. Safe ambient levels of formaldehyde have been established for enclosed environments (e.g. medical dissection laboratories) but no regulations are in place to establish a safe distance from preserved specimens. There is a gradient of formaldehyde exposure levels around any preserved specimen, but the variability within this gradient depends upon a large number of variables in the preservation procedure (fixative dilution, exposure time of specimen to air and fixative, etc.).

## Recommendations

Wear gloves to protect from direct contact - nitrile or other synthetic-based impervious material gloves will protect against formaldehyde exposure whereas latex gloves will not (Bedino, 2002). To protect against the inhalation of formaldehyde, it is recommended that a filter cartridge mask be worn. If this is not possible, a full mask or half mask with a face shield should be worn, a full mask providing 10-fold greater protection than a half-mask (Goyer, 2007). “Neither a surgical mask nor a Class FFP 2 Anti-Odor mask nor a N-95 Particle Mask are designed for protection against formaldehyde” (Goyer, 2007) - so masks for formaldehyde protection are recommended in place of the aforementioned types.

Within a formaldehyde-containing environment such as a gross anatomy laboratory, the best way to minimize exposure is through dilution of formaldehyde within the environment, which is why the US EPA requires six air exchanges per hour with two for outdoor air (Goyer, 2007). Also, keeping gross anatomy dissection laboratories cold and dry lowers the ambient airborne formaldehyde concentration (CDC). Another proposed method for limiting formaldehyde exposure is to use glutaraldehyde, which has a much lower vapor pressure than formaldehyde - resulting in lower amounts of airborne aldehyde - and attains the same fixative quality as formaldehyde but with much smaller amounts (Bendino, 2002).

These guidelines should be followed by students wishing to minimize formaldehyde exposure. However, the literature contains data strongly suggesting that pregnancy can be affected by formaldehyde exposure. Therefore, on the basis of our analysis, female students who might be pregnant should avoid formaldehyde exposure including that in a gross anatomy laboratory. Instructors should find other means of ensuring anatomical competence in these students.

## **Limitations**

The limitations of this review lie in relevant articles that failed to include the terms “formaldehyde,” “formalin,” “pregnant,” “pregnancy,” or “exposure.” Articles that did not include these terms within the initial search results were omitted. Published literature values are for ambient formaldehyde levels, but formaldehyde exposure during close dissection, which is a vital part of medical anatomy dissection laboratory work, has not been measured or reported within the literature.

## **Conclusions**

The results of most studies suggest that avoiding formaldehyde exposure while pregnant will lead to a decrease in the relative risk of low birth weight, birth malformations, and spontaneous abortions. Additionally, the relative risk for adverse effects of formaldehyde exposure is greatest during the first trimester.

While measurements from reports in the literature are scant, it is recommended that formaldehyde exposure be avoided if the student believes she could be pregnant.

## **References:**

Akbar-Khazadeh F, Park CK. 1997. Field precision of formaldehyde sampling and analysis using NIOSH method 3500. *Am IndHygAssoc J* 58: 657-660.

Bendino JH. 2002. Pregnancy and embalming: formaldehyde and other dangers for female embalmers. *Champion: Expanding Encyclopedia of Mortuary Practices* 647:2603-2606.

Casanova M, Heck Hd'A. 1987. Further studies of the metabolic incorporation and covalent binding of inhaled [3H]- and [14C]formaldehyde in Fischer-344 rats: effects of glutathione depletion. *ToxicolApplPharmacol* 89:105-121.

Casanova M, Morgan KT, Steinhagen WH, Everitt JI, Popp JA, Heck HD. 1991. Covalent binding of inhaled formaldehyde to DNA in the respiratory tract of rhesus monkeys: pharmacokinetics, rat-to-monkey interspecies scaling, and extrapolation to man.

*FundApplToxicol* 17: 409-28.

Casanova M, Morgan KT, Gross EA, Moss OR, Heck HA. 1994. DNA-protein cross-links and cell replication at specific sites in the nose of F344 rats exposed subchronically to formaldehyde. *FundApplToxicol* 23: 525-36.

Coskey A, Gest TR. 2015. Effectiveness of various methods of formaldehyde neutralization using monoethanolamine. *ClinAnat* 2015.

Duong A, Steinmaus C, McHale CM, Vaughn CP, Zhang L. 2011. Reproductive and developmental toxicity of formaldehyde: a systematic review. *Mutat Res* 728:118-38.

Goyer N. 2007. Prevention Fact Sheet: Exposure to Formaldehyde in the Workplace: Pathology Lab. Technical data sheet RG3-473: 1-4.

Goyer N, Begin D, Beaudry C, Bouchard M, Carrier G, Lavoue J, Noisel N, Gerin M. 2006. IRST Studies and Research Project: Prevention Guide-Formaldehyde in the Workplace. Guide RG-473:1-51.

Heck Hd' A, Chin TY, Schmitz MC. 1983. Distribution of [C-14] Formaldehyde in rats after inhalation exposure. J.E. Gibson Formaldehyde Toxicity: 26-37.

Heck HD, Casanova-Schmitz M, Dodd PB, Schachter EN, Wiltek TJ, Tosun T. 1985. Formaldehyde (CH<sub>2</sub>O) concentrations in the blood of humans and Fischer-344 rats exposed to CH<sub>2</sub>O under controlled conditions. Am IndHygAssoc J 46:1-3.

Hemminki K, Mutanen P, Saloniemi I, Niemi ML, Vainio H. 1982. Spontaneous abortions in hospital staff engaged in sterilising instruments with chemical agents. Br Med J (Clin Res Ed) 285: 1461-3.

Hemminki K, Kyyrönen P, Lindbohm ML. 1985. Spontaneous abortions and malformations in the offspring of nurses exposed to anaesthetic gases, cytostatic drugs, and other potential hazards in hospitals, based on registered information of outcome. J Epidemiol Community Health 39: 141-7.

Hisamitsu M, Okamoto Y, Chazono H, Yonekura S, Sakurai D, Horiguchi S, Hanazawa T, Terada N, Konno A, Matsuno Y, Tokada E, Mori C. 2011. The influence of environmental exposure to formaldehyde in nasal mucosa of medical students during cadaver dissection. *AllergolInt* 60: 373-9.

Keil CB, Akbar-Khanzadeh F, Konecny KA. 2001. Characterizing formaldehyde emission rates in a gross anatomy laboratory. *ApplOccup Environ Hyg* 16: 962-72.

Klein RC, King C, Castagna P. 2013. Controlling formaldehyde exposures in an academic gross anatomy lab. *J Occup Environ Hygiene*.

Kligerman AD, Phelps MC, Erexson GL. 1984. Cytogenetic analysis of lymphocytes from rats following formaldehyde inhalation. *ToxicolLett* 21: 241-6.

Kulle TJ, Sauder LR, Hebel JR, Green DJ, Chatham MD. 1987. Formaldehyde dose-response in healthy nonsmokers. *JAPCA* 37: 919-24.

Lam CW, Casanova M, Heck HD. 1985. Depletion of nasal mucosal glutathione by acrolein and enhancement of formaldehyde-induced DNA-protein cross-linking by simultaneous exposure to acrolein. *Arch Toxicol* 58: 67-71.

Liteplo RG, Meek ME. 2003. Inhaled formaldehyde: exposure estimation, hazard characterization, and exposure-response analysis. *J Toxicol Environ Health B Crit Rev* 6: 85-114.

Maroziene L, Grazuleviciene R. 2002. Maternal exposure to low-level air pollution and pregnancy outcomes: a population-based study. *Environ Health* 1: 6.

McMartin KI, Chu M, Kopecky E, Einarson TR, Korn G. 1998. Pregnancy outcome following maternal organic solvent exposure: a meta-analysis of epidemiologic studies. *Am J Ind Med* 34: 288-92.

Morgan KT, Patterson DL, Gross EA. 1986. Responses of the nasal mucociliary apparatus of F-344 rats to formaldehyde gas. *ToxicolApplPharmacol* 82: 1-13.

Rahimifard H, Heidari H, Abbasinia M, Noruzi M, Mahdinia M, Arast Y. 2013. Respiratory effects induced by occupational exposure to formaldehyde among health care staff. *Int J Occup Hygiene* 5: 26-30.

Ryan TJ, Burroughs GE, Taylor K, Kovein RJ. 2003. Video exposure assessments demonstrate excessive laboratory formaldehyde exposures. *ApplOccup Environ Hyg* 18: 450-7.

Sauder LR, Chatham MD, Green DJ, Kulle TJ. 1986. Acute pulmonary response to formaldehyde exposure in healthy nonsmokers. *J Occup Med* 28: 420-4.



Sauder LR, Green DJ, Chatham MD, Kulle TJ. 1987. Acute pulmonary response of asthmatics to 3.0 ppm formaldehyde. *ToxicolInd Health* 3: 569-78.

Saurel-Cubizolles MJ, Hays M, Estry-Behar M. 1994. Work in operating rooms and pregnancy outcome among nurses. *Int Arch Occup Environ Health* 66: 235-41.

Swenberg JA, Gross EA, Martin J, Popp JA. 1983. Mechanisms of formaldehyde toxicity. *J.E. Gibson*: 132-142.

Thrasher JD, Kilburn KH. 2001. Embryo toxicity and teratogenicity of formaldehyde. *Arch Environ Health* 56: 300-11.

UNEP Chemicals. 2002. Formaldehyde CAS N: 50-00-0. SIDS Initial Assessment Report for SIAM 14: 1-43.

US Center for Disease Control and Prevention. What you should know about formaldehyde. <http://www.cdc.gov/nceh/drywall/docs/whatyoushouldknowaboutformaldehyde.pdf>

Zhu JL, Knudsen LE, Andersen AM, Hjollund NH, Olsen J. 2006. Laboratory work and pregnancy outcomes: a study within the National Birth Cohort in Denmark. *Occup Environ Med* 63: 53-8.