Abstract
Formaldehyde, which has been a well-established preservative for cadavers in the anatomy laboratory for years, has an odor that many anatomy students find unpleasant. Anatomy faculty and students, embalmers in funeral homes, histopathology laboratory workers, and other biological researchers are continually exposed to the toxic vapors of formaldehyde. The immediate effects of that agent are nausea, headache, and ocular irritation that causes tear overflow and a burning sensation in the throat. Long-term exposure to formaldehyde can cause contact dermatitis, congenital defects, and cancer. This article discusses the adverse effects of continual exposure to formaldehyde and formalin and suggests various measures that can eliminate or minimize that danger to staff and students in gross anatomy laboratories.

Introduction
Formalin, an aqueous solution of formaldehyde, is the chemical most commonly used for embalming. In 1867, the German chemist August Wilhelm von Hofmann identified formaldehyde, which is a colorless, flammable gas that is quite soluble in water. Formaldehyde is colorless at room temperature and has an irritating, pungent smell. It is commercially obtainable as formalin, which contains 37% by weight or 40% by volume of formaldehyde gas in water. In the body, formaldehyde quickly metabolizes to formic acid. The measurement of formate (formic acid minus 1 hydrogen ion) levels indicates the severity of formaldehyde intoxication. Formaldehyde is used extensively in the chemical, adhesive, paint, plastic, construction, textile, paper, and cosmetic industries; in the manufacture of pressed wood products (urea resins in plywood wall paneling, particle board, and fiber board); in fertilizers; in permanent press and other textiles; in paper; and in glue (Bernstein et al., 1984). It is also formed during the burning of organic materials and is found in tobacco smoke (U.S. Environmental Protection Agency [U.S. EPA], 2011). The concentration of formaldehyde in the air is often expressed in terms of parts per million (ppm) (1 ppm = 1.248 mg/m³).

A cadaver is embalmed via the infusion of chemical substances that include formalin (which contains formaldehyde), alcohol, glycerin, carbolic acid, and dye. Those substances have specific roles (e.g., preservation, denaturalization, solidification of tissue protein disinfection, and maintenance of the integrity of the anatomic relation), and they are usually infused via the femoral arteries or the internal carotid arteries (Coleman & Kogan, 1998). Thus anatomists, technicians in biological science laboratories, and anatomy students during their dissection course are continually exposed to formaldehyde. The level of exposure to that agent depends on the duration of time spent in the gross anato-
continual exposure to formaldehyde are described, and methods of reducing the likelihood of that exposure are presented.

Discussion

During gross anatomy dissection, exposure to formaldehyde vapors and contact with formalin can cause adverse effects. Dissection and prosection are, however, essential parts of an education in anatomy. The acute effects of exposure can be caused by inhalation of formaldehyde vapors, which irritate the respiratory tract and eyes and cause lacrimation, burning of the nose and throat, dyspnea, and headache and can result in pulmonary edema and pneumonitis (Kurose, Kodera, Aoyama, & Kawamata, 2004). Some individuals are highly susceptible to the adverse effects caused by formaldehyde, but others have no reaction to the same levels of exposure (Mizuki & Tsuda, 2001). The most common adverse effects of exposure to formaldehyde are described below.

Skin Disorders

Formaldehyde is absorbed through intact skin and can cause severe irritation or allergic dermatitis. Formalin can cause white discoloration of the skin as well as burning, drying, cracking, blistering, and scaling of the skin. These skin disorders can occur after contact with formaldehyde at levels well below those of many formaldehyde workers. Other signs of exposure to formaldehyde include erythema, edema, and hives (Cotran, Kumar, & Collins, 1999). Exposure to liquid formalin or formaldehyde vapor can provoke skin reactions in sensitized individuals, even when airborne concentrations of formaldehyde are below 1 ppm (Charpin, Dutau, & Falzon, 2000). Exposure to formaldehyde gas can cause major allergic symptoms and exacerbate chemical sensitivities (Takahashi et al., 2007). The modification of tissue proteins by formaldehyde causes local toxicity and initiates allergic reactions, and repeated contact with formaldehyde can produce eczematous dermatitis. Dermatitis can also be caused by contact with formaldehyde-treated clothing (Wartew, 1983). Formaldehyde resins are used in the textile industry to make clothing that is wrinkle resistant (e.g., permanent-press clothing), and those resins can release significant amounts of formaldehyde and cause contact dermatitis. Many preservatives used in cosmetics, pharmaceuticals, and industrial biocides also release formaldehyde. Students who have been diagnosed as having atopic dermatitis and allergic rhinitis are susceptible to the effects of formaldehyde exposure and can exhibit mucocutaneous symptoms caused by impaired barrier function and the remodeling of the skin and mucosa (Wantke et al., 2000).

Congenital Malformations

Formaldehyde is a proven teratogen in rats and mice (Hansen, Contreras, & Harris, 2005), in which it crosses the placental barrier and can affect the embryo (Thrasher & Kilburn, 2001). Participation in cadaver dissection is compulsory for students in most medical schools worldwide and for those in most physical therapy, occupational therapy, chiropractic, osteopathic, dental, and veterinary schools. Anatomy students who are pregnant should consult an obstetrician before attending the first gross anatomy laboratory and must take precautions to ensure minimal exposure to formaldehyde. The teratogenic effect of formaldehyde in humans is questionable owing to inconclusive, ambiguous study results (Taskinen et al., 1999), but the risk of congenital anomalies appears to be greater in women who experience symptoms from organic solvent exposure (Khattach et al., 1999).

Ocular Irritation

Formaldehyde is corrosive to the eyes. Formaldehyde solutions that splash into the eye can cause injuries ranging from brief discomfort to corneal clouding and loss of vision and may be trapped behind contact lenses, which usually discolor and solidify when exposed to formalin. Some individuals with daily-wear disposable lenses do not experience problems (Yang, Zhang, Chen, & Wang, 2001). Most laboratories suggest that students not wear contact lenses during a gross anatomy session because even if safety goggles are worn, corrosive vapors can accumulate under contact lenses and cause serious injuries or blindness. Before anatomy coursework begins, instructors and emergency care providers should be notified of any students who will wear contact lenses during gross anatomy laboratory sessions. Contact lenses can be difficult to remove after a chemical splash to the eye. If ocular exposure to corrosive agents occurs during a laboratory session, the injured eye(s) should be held open and immediately irrigated with a gentle stream of large volumes of clean water. This may dislodge contact lenses, and trained staff can later remove lenses that have remained in place (NIOSH, 2005).

Cancer Risk

Laboratory studies suggest that exposure to formaldehyde may cause nasal cancer in rats. In 1987, the U.S. Environmental Protection Agency (U.S. EPA) classified formaldehyde as a possible human carcinogen under conditions of extraordinarily high or prolonged exposure (Luce et al., 1993). Since that time, some studies of industrial workers have suggested that formaldehyde exposure is associated with nasal sinus cancer, nasopharyngeal cancer, and possibly leukemia (Pinkerton, Hein, & Stayner, 2004). In 1995, the International Agency for Research on Cancer concluded that formaldehyde is a likely human carcinogen. In June 2004, after evaluating all accessible data, the International Agency for Research on Cancer reclassified formaldehyde as a recognized human carcinogen (International Agency for Research on Cancer, 2006).

Several National Cancer Institute surveys have revealed that professionals (such as anatomists and embalmers) who are likely to be exposed to formaldehyde are at greater risk for leukemia and brain cancer than are individuals in the general population (Hauptmann, Lubin, Stewart, Hayes, & Blair, 2003). A National Cancer Institute case-control study of funeral home workers exposed to formaldehyde also suggested an association between increasing formaldehyde exposure and mortality from myeloid leukemia (Beane Freeman et al., 2009).

A study by Hauptmann and co-authors compared funeral home workers who died from hematopoietic, lymphatic cancer and brain tumors with funeral home workers who died from other causes between 1960 and 1986. The funeral home workers who had performed the most embalming and those with the highest estimated formaldehyde exposure had the greatest risk of myeloid leukemia. Excessive formaldehyde exposure was not linked to other cancers of the hematopoietic and lymphatic system or to brain cancer (Hauptmann, Lubin, Stewart, Hayes, & Blair, 2004).
Ingestion-Related Gastrointestinal Effects
Formaldehyde ingestion by anatomy students or instructors is unlikely, although formalin (which is poured onto a dissected specimen to prevent drying and tissue destruction) is ubiquitous in the gross anatomy laboratory. Formalin is irritating, corrosive, and toxic. Ingestion of that substance is unusual because of its unpleasant odor and irritant effect, but such exposure has been documented in accidental incidents and suicide attempts (Pandey, Agarwal, Baronia, & Singh, 2000). The ingestion of formaldehyde can cause death even in doses as little as 30 mL of a 37% solution. Alimentary toxicity after ingestion is most severe in the stomach and causes nausea, vomiting, and severe abdominal pain. Gastrointestinal hemorrhage and gastric outlet obstruction are late complications of formaldehyde ingestion (Hawley & Harsch, 1999). Extensive damage to other organs including the liver, kidneys, spleen, pancreas, and brain as well as the central nervous system can occur from the ingestion of formaldehyde (Köppel, Baudisch, Schneider, & Ihe, 1990).

Inhalation-Related Upper Airway Irritation and Bronchial Asthma
Formaldehyde irritates the upper airway. The exposure level of formaldehyde that is instantly hazardous to life and health is 100 ppm. Exposure above 50 ppm can produce severe pulmonary reactions (pulmonary edema, pneumonia, bronchospasm) that can cause death within minutes. Concentrations greater than 5 ppm promptly cause lower respiratory tract irritation characterized by cough, chest tightness, and wheezing (Monticello, Morgan, Everitt, & Popp, 1989).

Whether formaldehyde gas is a pulmonary sensitizer that can cause work-related asthma in a previously healthy individual remains controversial (Martin, Nemitz, Hendley, Fisk, & Wells, 1995). Formaldehyde can cause symptoms of bronchial asthma in humans (Harving, Korsgaard, Dahl, Pedersen, & Molhave, 1986). Upper airway soreness, which is the most common respiratory effect reported by workers exposed to formaldehyde, can develop after exposure to a wide range of concentrations (usually above 1 ppm) of formaldehyde. Previously sensitized persons can develop severe constriction of the bronchi at very low concentrations (e.g., 0.3 ppm) (ATSDR, 2008). Symptoms of upper airway irritation caused by formaldehyde exposure include a dry or sore throat, nasal itching and burning, and nasal congestion. Tolerance to formaldehyde exposure can develop within one to two hours and can enable workers in an environment of steadily increasing formaldehyde concentrations to be oblivious to their increasingly hazardous exposure (Burge, Harries, Lam, O’Brien, & Patchett, 1985).

Recommendations for Minimizing Formaldehyde Exposure
1. Students and instructors should be aware of the potential health hazards of formaldehyde exposure.
2. The gross anatomy laboratory should have a standard ventilation system. According to the American Conference of Governmental Industrial Hygienists (2001), the ventilation rate should exceed 15 room changes per hour.
3. Negative-pressure ventilation and monitoring systems should be installed to further reduce exposure to formaldehyde vapor.
4. Cadaver bags should be opened, and vapors should be allowed to escape.
5. Protective garments and equipment (a laboratory coat, protective goggles, and gloves) should be worn or used to prevent direct skin contact with formaldehyde.
6. Contact lenses should not be worn in the gross anatomy laboratory.
7. The bucket at the end of the cadaver table should be emptied frequently.
8. Excess fluid should be removed from the cadaver bag with a sponge or by tilting the table to drain it.
9. Nitrile gloves or 2 pairs of latex gloves should be worn during cadaver dissection and demonstration. Students who are allergic to latex gloves should wear plastic gloves.
10. Pregnant students should minimize their exposure to formalin. Models and three-dimensional figures can often be used for the study of anatomy, or anatomy courses can be taken after the baby has been born.
11. Pregnant students should explain the likelihood of their exposure to formalin and formaldehyde to their obstetrician. They should be fitted with a mask approved for preventing formaldehyde exposure. They should be advised to dissect and study the cadaver for periods no longer than an hour at a time, and to take 15-minute breaks between dissection sessions.

Conclusion
Regardless of its toxic effects, formaldehyde remains a popular choice of tissue fixative because of its effectiveness, low cost, and consistent results. Because of the toxic effects of that agent, however, identifying a cost-effective, environmentally friendly alternative is essential and far preferable to decreasing hours spent learning or working in the gross anatomy laboratory.

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