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Methylene Chloride Poisoning in a Cabinet Worker

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More than a million workers are at risk for methylene chloride exposure. Aerosol sprays and paint stripping may also cause significant nonoccupational exposures. After methylene chloride inhalation, significant amounts of carbon monoxide are formed *in vivo* as a metabolic by-product. Poisoning predominantly affects the central nervous system and results from both carboxyhemoglobin formation and direct solvent-related narcosis. In this report, we describe a case of methylene chloride intoxication probably complicated by exogenous carbon monoxide exposure. The worker's presentation of intermittent headaches was consistent with both methylene chloride intoxication and carbon monoxide poisoning. The exposures and symptoms were corroborated by elevated carboxyhemoglobin saturations and a workplace inspection that documented significant exposures to both methylene chloride and carbon monoxide. When both carbon monoxide and methylene chloride are inhaled, additional carboxyhemoglobin formation is expected. Preventive efforts should include education, air monitoring, and periodic carboxyhemoglobin determinations. Methylene chloride should never be used in enclosed or poorly ventilated areas because of the well-documented dangers of loss of consciousness and death. *Key words*: carbon monoxide, carboxyhemoglobin, methylene chloride, occupational exposure. *Environ Health Perspect* 107:769–772 (1999). [Online 10 August 1999]
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Case Presentation

A 26-year-old male presented in February 1996 with the complaint of persistent headaches for 1 month. The patient had two evaluations in an emergency department and a subsequent consultation with a headache specialist whose working diagnosis was that the headaches were stress related with possible exacerbation by fumes at the patient's workplace.

The patient had a history of occasional headaches since adolescence; during the past 4 months, his symptoms had increased in intensity and frequency and were no longer relieved by over-the-counter medication. The headaches were retroorbital with radiation to the back of the head and were associated with sensitivity to bright lights and noise and occasionally with nausea. He denied other neurologic symptoms.

He had worked as a carpenter in a laminated product manufacturing company for the previous 6 months. He worked with 10 other cabinet workers in a building approximately 50 ft × 200 ft in size. There was an unenclosed spray booth with some local exhaust ventilation and with gas-powered heating fans hanging from the ceilings. The doors were kept closed during winter months to prevent heat loss.

The patient's job tasks at the time of presentation involved working with lacquer thinner to clean cabinet surfaces and spraying laminating materials over cabinet surfaces. Neither he nor the other workers used any type of personal protective equipment while working with these chemicals. He reported that he and several of his co-workers had recently noticed drying and cracking of the skin on their hands from touching lacquer thinner. Some of the other workers had also complained of headaches, but their headaches were not as severe as his.

The patient brought material safety data sheets for two compounds he often used: a clear, nonflammable spray contact cement that contained 70% methylene chloride ($MeCl_2$), toluene, and methyl ethyl ketone, and a lacquer thinner that contained toluene, isopropyl alcohol, ethyl acetate, isobutyl alcohol, and isobutyl acetate.

The patient's environmental history was noncontributory. The patient was a nonsmoker, reported drinking one beer per week, and denied any illicit drug use. His current medications included amitriptyline (50 mg/day) and diphenhydramine (150 mg every night at bedtime). The patient's significant past medical history revealed depression and a motor vehicle accident with resultant whiplash and back injuries 18 months before presentation. He denied any headaches after the accident. At 8 years of age, the patient had also sustained a basilar skull fracture from a bicycle accident and had some residual hearing loss on the left side. His family history was significant only in that his mother suffers from migraine headaches.

On physical examination, the patient appeared well nourished, well hydrated, and in no apparent distress. Vital signs included a blood pressure of 110/72 and unremarkable pulse, respirations, and temperature. The patient's skin on both hands showed marked dermal thickening and very dry skin with fissures and cracking. A fundoscopic exam was unremarkable. No paranasal sinus tenderness was noted. A neurological exam revealed no deficits, and the rest of the physical examination was unremarkable.

Initial lab data revealed a normal complete blood count, normal liver function tests, and a blood COHb saturation of 2.8% (normal < 3% for nonsmokers).

The patient was instructed to have his primary care physician check his COHb saturation after a work shift, particularly when he was symptomatic, in order to exclude carbon monoxide intoxication from $MeCl_2$ exposure. On the following day, although the doors of the workplace were open, he had a mild headache and his post-shift COHb saturation was 6.4%. The consultants, however, were not notified at this time.

Four days later, the doors of the patient's workplace were closed for the day and he reported poor ventilation. He became extremely symptomatic, including nausea and vomiting, and left work early for his primary care physician's office. He was

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reported to have a COHb saturation of 21% approximately 35 min after leaving his work site. He subsequently received normobaric oxygen therapy at the affiliated emergency department. A follow-up COHb saturation the next day was normal, and the consultants were notified at this time.

Based on the patient's elevated COHb saturations and the presence of the $MeCl_2$-containing product, the Commonwealth of Massachusetts Division of Occupational Hygiene (DOH) and the local health department were contacted immediately. An immediate inspection was conducted by the DOH and local health and fire departments. The major findings were the use of the product containing 70% $MeCl_2$ and area samples with $MeCl_2$ levels of 300–500 ppm and CO levels of 28 ppm. Based on this information, the company immediately substituted a water-based process for the one previously utilizing $MeCl_2$.

A second inspection was conducted 8 days later to evaluate the new process. Repeat air sampling showed unremarkable levels of solvents in both area and personal breathing zone samples and a peak CO measurement of 8 ppm. Additionally, a propane-powered fork lift inside the plant was considered a potential source of carbon monoxide exposure.

Discussion

$MeCl_2$, also known as dichloromethane (DCM), methylene dichloride, and methylene bichloride, is a volatile, clear, and colorless lipophilic solvent (*1,2*). It has a mild, sweet odor with an olfactory threshold of 100–300 ppm (*1*).

Human exposure is mainly due to inhalation. The liver is the primary site of metabolism, where significant amounts are biotransformed to carbon monoxide (CO) (*3*). The primary target organ of $MeCl_2$ toxicity is the central nervous system (*1,4,5*). These effects result from both direct solvent-related narcosis and endogenous production of CO with subsequent carboxyhemoglobin (COHb) formation (*4,6–8*). If CO is inhaled from either the environment or from tobacco smoke, this exogenous CO exposure leads to additional COHb formation in an additive fashion (*9,10*). The most serious manifestations of $MeCl_2$ poisoning are unconsciousness and death, and a number of fatalities have been reported in the literature (*5,8,9,11,12*). Most of these cases were associated with paint or furniture stripping and/or enclosed spaces.

Once $MeCl_2$ is inhaled, the major sites of distribution are the liver, brain, and fat (*1*). Factors affecting the resulting body burden are the ambient $MeCl_2$ concentration, duration of exposure, route of exposure, physical activity, and the amount of body fat (*1,6,9,13*). In addition to the liver, metabolism may also occur in the lungs and kidneys (*1*). Metabolism occurs via two basic routes, a mixed-function oxidase (MFO) pathway and a glutathione transferase (GST) pathway (*2,6*). The MFO pathway is predominant and converts $MeCl_2$ to CO, but is saturable at high exposure levels (*2,6*). Both the direct neurologic effects of $MeCl_2$ and CO toxicity appear to contribute to the adverse effects of $MeCl_2$ exposure (*4,6–8,14*). During acute and intense exposures to $MeCl_2$, which usually occur in poorly ventilated areas, the direct solvent-related narcotic effects may play a greater initial role in central nervous system depression (*5,7,8,11,14*). For example, Rioux and Myers (*4*) reported two workers who were found unconscious in a semienclosed area with high levels of $MeCl_2$ fumes. Despite prior loss of consciousness, their initial presenting COHb saturations were only 5 and 7%.

The metabolic formation of CO and subsequent COHb formation may continue for several hours after the cessation of $MeCl_2$ exposure, as fat and other tissues continue to release accumulated solvent (*4,9,15,16*). Endogenous CO production at a rate greater than the rate of excretion accounts for a gradual increase in the COHb level in blood (*16*). Rioux and Myers (*4*) reported that, despite treatment with hyperbaric oxygen, the COHb levels of both men continued to rise after they were removed from exposure due to their high body burdens of $MeCl_2$.

The dose response demonstrates a linear relationship between $MeCl_2$ exposure (for both duration of exposure and intensity of exposure) and COHb levels (*9,10,16,17*). This is illustrated in Figure 1. In smokers, the dose response is shifted upward by the additional CO inhalation (*10*). At approximately 180 ppm $MeCl_2$, the rate of increase is 0.5% COHb/hr (*16*). Therefore, during nonoverwhelming and longer exposures to $MeCl_2$, carboxyhemoglobinemia resulting from hepatic conversion may be responsible for most of the observed toxicity. Other dihalomethanes, including dibromomethane, diiodomethane, and bromochloromethane, have also been documented to undergo *in vivo* biotransformation to CO (*6*).

This case study describes $MeCl_2$ intoxication resulting from an industrial process. The workers' symptoms of intermittent headaches, nausea, and vomiting and elevated COHb saturations are consistent with both $MeCl_2$ intoxication (*1,5,17*) and CO poisoning (*18,19*). The marked degree of carboxyhemoglobinemia (> 20%) without loss of consciousness and the significant ambient CO concentration in the workplace suggest that our patient's situation was probably complicated by exogenous CO exposure. Sources of exogenous CO in the present case could have been the gas-powered heating fans and/or the propane-powered forklift. The operation of propane-fueled forklifts in unventilated areas is a documented cause of CO poisoning (*20*).

When ambient CO exposure and $MeCl_2$ exposure occur simultaneously, the exogenous CO exposure results in COHb formation in addition to that generated by hepatic transformation of $MeCl_2$ to CO (*1,10*). The conditions found during the inspection of the patient's workplace were probably similar to those that produced the poisoning episode. The inspection documented spot exposures via area samples of 300–500 ppm $MeCl_2$ and 28 ppm CO. Ratney et al. (*16*) reported that 8-hr exposure to $MeCl_2$ at approximately 180 ppm resulted in COHb saturations of 6–12% in nonsmokers. Shusterman et al. (*17*) found COHb saturations of 10–11% and similar presenting symptoms in a worker after 6.5–7.5 hr of exposure to approximately 350 ppm $MeCl_2$. Eight hour exposure at 500 ppm $MeCl_2$ would be expected to produce COHb saturations in excess of 12% (*17*). Exposures to exogenous CO in nonsmokers at 25 and 50 ppm are expected to produce COHb saturations of 3–4% and 6–8%, respectively (*21*). Thus, the combined exposures observed during the inspection of the patient's workplace might have been expected to produce COHb saturations of approximately 16%, which is within the order of magnitude of the 21% reported in our patient.

Our patient's actual exposures could have been even higher if the $MeCl_2$ concentrations had been higher in his breathing zone during

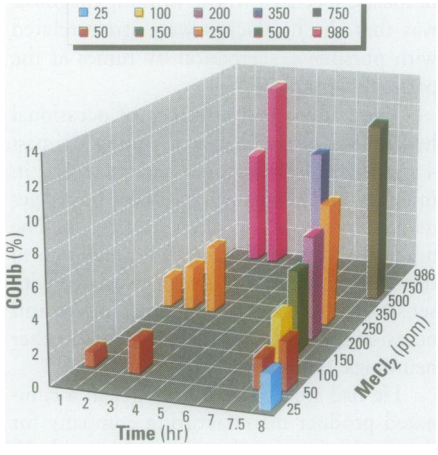

Figure 1. Methylene chloride dose response between carboxyhemoglobin (COHb) formation and both the duration and intensity of exposure to $MeCl_2$. The measured COHb saturation is shown as a function of the exposure duration and the $MeCl_2$ concentration in parts per million. Data from Stewart and Hake (*9*), Soden et al. (*10*), DiVincenzo and Kaplan (*13*), and Shusterman et al. (*17*).

the spray operation (versus areas samples), if ambient $MeCl_2$ and CO concentrations had been higher due to decreased ventilation, and if there had been increased absorption due to physical activity. Absorption can also result from skin contact, but at a lower rate compared to other routes because of rapid evaporation (*1*). Because of our patient's solvent-related dermatitis, facilitated skin absorption could have made a small contribution to exposure in his case (*22*).

Appropriate treatment of $MeCl_2$ intoxication includes removal from exposure, supplemental 100% oxygen, and supportive measures as indicated. As absorbed $MeCl_2$ is depleted, CO excretion continues and COHb saturations will eventually begin to decrease. After exposure has been terminated, however, $MeCl_2$ stores continue to be converted to CO. Therefore, the decay of $MeCl_2$-induced COHb is slower than that of COHb derived from ambient inhaled CO. The elimination half-life of $MeCl_2$-derived COHb is 13 hr when breathing room air (*16*) and has been estimated to fall to approximately 6 hr with the administration of 100% normobaric oxygen (*4*). These values compare with elimination half-lives of COHb derived from exogenous CO inhalation of approximately 4 hr for room air, 60 min for 100% normobaric oxygen, and < 30 min for 100% hyperbaric oxygen at 3 atmospheres (*18*). Therefore, $MeCl_2$-induced carboxyhemoglobinemia may require prolonged treatment (*4*).

Other central nervous system effects of $MeCl_2$ exposure include impaired visual, auditory, and psychomotor performance (*2*). $MeCl_2$ may also be an ocular and respiratory irritant (*17,23,24*). Snyder et al. (*25,26*) reported pulmonary edema in two victims, with subsequent *de novo* asthma developing in one of the two cases; however, the two individuals were also exposed to phosgene. Direct contact with the eyes may result in corneal burns (*5*), dermal exposure may cause erythema and burning (*27*), and skin immersion may produce chemical burns (*5*).

High $MeCl_2$ exposures have anecdotally been linked to ischemic electrocardiographic changes (*14*) and myocardial infarction (*9*). Studies demonstrating decreased exercise times to angina or increased arrhymias in coronary heart disease patients with COHb saturations of 2–6% (*28–31*) have raised concern that $MeCl_2$ exposures producing similar COHbs could also produce cardiac disturbances in susceptible individuals (*32*). However, epidemiologic studies of workers exposed to several hundred parts per million $MeCl_2$ have not documented excess mortality due to ischemic heart disease (*33–35*) or increased cardiac symptoms (*36*).

Human epidemiologic studies have either failed to show evidence for excess cancer deaths in $MeCl_2$-exposed workers or to demonstrate inconsistent associations (*2*). Based on all of the evidence, the International Agency for Research on Cancer (*37*) considers $MeCl_2$ to be possibly carcinogenic to humans, whereas the U.S. Environmental Protection Agency has classified it as a probable human carcinogen (*2*).

$MeCl_2$ exposure is usually occupational in nature. It has a wide variety of applications including cleaning, degreasing, paint and varnish thinning and removal, manufacturing of synthetic fibers and plastics, use as an aerosol propellant, use as a blowing agent for foods and spices, use as a grain fumigant and low-pressure refrigerant, and use in certain paints, inks, adhesives, pharmaceuticals, and photographic films (*1,6*). It has been estimated that more than a million workers are at risk for potential exposure (*1*).

Environmental and household exposures are also primarily due to inhalation (*2*). $MeCl_2$ is found in a number of common household products such as flame retardants, hair sprays, antiperspirants, air fresheners, and spray paints; the most significant exposures probably result from aerosol sprays and from paint, varnish, or furniture stripping (*1*).

Conclusion

Adverse health effects due to $MeCl_2$ can be avoided by substituting safer products or processes for those using $MeCl_2$, such as the alternative process adopted by the manufacturer in this case. When $MeCl_2$ is used, adequate ventilation is essential to keep exposures at low levels. $MeCl_2$ should never be used in enclosed or poorly ventilated areas because of the unacceptable risk of loss of consciousness and death (*4,5,8,11*). It is important to educate those using $MeCl_2$-containing products about safety hazards and monitoring of airborne concentrations. Table 1 summarizes regulatory data for $MeCl_2$ and CO and expected biologic exposures to COHb. Ambient exposure standards may not adequately protect all susceptible individuals such as those with significant underlying coronary heart disease. In addition, these guidelines are not designed to account for additional CO exposures from ambient air and/or concomitant smoking. Therefore, these measures should be supplemented by monitoring exposed workers for COHb. COHb saturations > 3% should be considered elevated in nonsmokers (*39*).

Table 1. Exposure guidelines for methylene chloride and carbon monoxide with corresponding carboxyhemoglobin saturations for nonsmokers.

	Methylene chloride			Carbon monoxide		
	Exposure limit	COHb level		Exposure limit	COHb level	
Agency	(ppm)	(%)	Ref	(ppm)	(%)	Ref
OSHA PEL	25	2.3	11	50	7.0	21
	500[a]	>12	17			
ACGIH TLV	50	3.1	11	25	3.5	21
NIOSH REL	Ca (lowest feasible conc)	—		35	5.0	21

Abbreviations: ACGIH TLV, American Conference of Governmental Industrial Hygienists threshold limit value; Ca, carcinogen; conc, concentration; NIOSH REL, National Institute for Occupational Safety and Health recommended exposure limit; OSHA PEL, Occupational Safety and Health Administration permissible exposure limit; Ref, reference.
[a]OSHA PEL at the time of the inspection; the PEL was reduced in 1998 (*38*).

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