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Death and Injury Caused by Methyl Bromide, An Insecticide Fumigant

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ABSTRACT: Methyl bromide (MeBr) is used as an insecticide fumigant. Four deaths and three recent hospitalizations have resulted from exposures to MeBr in Dade County, FL. Six cases occurred during burglaries of tented houses over a nine-month period. In four lethal exposures, the symptoms of nausea, vomiting, and malaise preceeded fulminant respiratory failure. Two of these also had seizures, delirium, and agitation. Serum or plasma bromide ion levels ranged from 40 to 583 mg/L. Pulmonary edema, hyaline membranes, and hemorrhagic alveolitis were present at autopsy along with varying degrees of cerebral edema. The nonlethal exposures resulted in symptoms of conjunctival irritation, headache, or nausea. Plasma bromide concentrations varied between 17.5 and 321 mg/L. Methyl bromide characteristics, use, morbidity, and mortality in Florida during the past 25 years are reviewed. Remedies for illegal entry are proposed.

KEYWORDS: pathology and biology, methyl bromide, spectroscopic analysis, fumigation, tented dwelling, burglary, inhalation injury, respiratory failure, deaths

Methyl bromide, CH3Br (MeBr), is a colorless gas that has a musty odor at extremely high concentrations. It has a molecular weight of 94.94 and a boiling point of 3.6°C. The latent heat of vaporization is 257 400 cal/kg (61.52 cal/g). As a vapor, MeBr is 3.27 times as heavy as air [*1-3*]. Its main industrial use is methylation of synthetic compounds [*2*]. It has been used as a fire extinguishing agent because of its nonflammability and heavier-than-air properties [*1,2*].

In the 1930s, LeGroupil discovered MeBr to be lethal to insects in all stages of development [*3*]. Its use as an insecticide fumigant for agriculture and residential dwellings is well established in Dade County and other communities [*3-5*].[5] Because it is a simple, nonpatentable compound, the cost of MeBr is much less than that of alternative agents used in home fumigation.[5] Another inexpensive fumigant, acrylonitrile, was abandoned when deaths caused by toxic residues were discovered [*6*].

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A residence is fumigated by covering the structure with a large vapor-tight tent assembled in sections (Fig. 1). This "tented dwelling" is exposed to MeBr volatilized from a pressurized canister using a heating element to facilitate complete vaporization. After 18 to 24 h, the gas is flushed with blowers [3].[5]

Four fatalities caused by this agent have occurred in Dade County, FL during the period 1957 to 1982. The intervals between exposure and death ranged from 2½ to 36 h. Three of the four deaths and three additional hospitalizations followed burglaries of tented houses during a recent nine-month period.

Materials and Methods

Case files include witness accounts from newspaper and police reports, medical records, and consultations with industrial manufacturers as well as commercial users. Autopsy analysis included gross evaluation and hematoxylin and eosin stained microscopic slides, some with luxol-fast-blue counterstain for myelin on brain sections.

Premortem and postmortem determination of bromides in plasma or serum were performed by the gold chloride technique [7]. Postmortem tissues were analyzed for the intact MeBr molecule by mass spectroscopy using a previously described purged trap technique [8-9]. Urine drug screening using the EMIT®-d.a.u. system (Syva, Palo Alto, CA) was performed on Cases 2, 3, and 4.

Lethal Cases

Case 1

A 27-year-old black woman was present in her apartment when a conjoined building was fumigated with MeBr. The gas leaked directly through a wall opening into the floor of her apartment. At 1:00 a.m., she was seen by a visiting physician because of headache, abdominal cramps, vomiting, and weakness. A viral disorder was diagnosed. She died in her bed 2½ h later. A dog in the apartment also died. Eighteen other apartment house dwellers and two police rescuers were treated at a hospital with complaints ranging from dyspnea to flu-like syndrome. One required endotracheal intubation briefly and all recovered.

At autopsy, the lungs had a combined weight of 1000 g and dark purple pleura. Copious amounts of pink, frothy edema fluid exuded from the sectioned lungs and was present in the airway. Microscopically, there were intra-alveolar hemorrhages and variable degrees of residual alveolar air. The kidneys were unremarkable except for a slight degree of cortical swelling and focal congestion. There was no microscopic evidence of tubular necrosis. The 1200-g brain had congested meninges. Nonspecific pyknosis of some neurons were seen microscopically.

The postmortem serum bromide concentration was 40 mg/L.

The dog present in the apartment had similar pulmonary findings at necropsy.

Cases 2 and 3

Two black men, ages 18 and 19 years, illegally entered a tented dwelling 12 h after the onset of fumigation with MeBr. After approximately 1-h exposure within the house, they were found collapsed outside by police.

The 18-year-old victim (Case 2) initially experienced nausea, emesis, and watery diarrhea followed by status epilepticus. Initial chest X-rays were clear, but the arterial partial pressure of oxygen (pO_2) was reduced and continued to decline. Only a few millilitres of isotonic urine was produced despite diuretic therapy. Admission and sequential serum bromide concentrations were 232, 171, and 70 mg/L, the latter after treatment by hemoperfusion. Hypotension then occurred. Although the prothrombin time was elevated late in the course, no other tests

FIG. 1—*A tent is assembled around the residence to create a nearly vapor tight enclosure.*

or findings suggested liver failure. Diffuse interstitial changes were visible on X-ray. Pulmonary respiratory failure ensued and death occurred 18 h following exposure.

The 19-year-old victim (Case 3) experienced lethargy, nausea, emesis, ataxia, delirium, and agitation. He had proteinuria and oliguria initially but responded well to diuretics and fluid. Although the initial chest X-ray was normal, the arterial pO_2 had declined and rales and rhonchi were heard. Antemortem bromide was 108 mg/L and an ophthalmologist observed a cherry-red spot in the macula, thought to be a sign of toxicity. Hypotension developed. Hemoperfusion was unsuccessful and peritoneal dialysis was initiated. Interstitial changes appeared on X-ray. Respiratory failure ensued and death occurred 36 h after exposure.

At autopsy, in Cases 2 and 3, a musty odor was present. The pleural spaces contained 100 to 400 mL of straw-colored fluid. The mucosa of the larynx, trachea, and the conjunctivae were slightly congested. The visceral pleura was dark purple with scattered petechiae. The combined weights of the lungs were 1190 and 2170 g for Cases 2 and 3, respectively. The sectioned surfaces of each lung were red, firm, beefy, airless, and exuded frothy pink fluid. Microscopically, there was intra-alveolar blood, early hyaline membranes, and air trapped within pulmonary edema fluid (Fig. 2). Focal neutrophilic infiltrates were present around distal respiratory bronchioles and within alveoli, predominantly in Case 3. The respiratory mucosa was intact in all cases (Fig. 3).

The kidneys and liver were congested in each case. In Case 3, dilated tubules and histologically evident acute tubular necrosis were present.

The brain weights were 1370 and 1150 g for Cases 2 and 3, respectively, and each had varying degrees of cerebral edema and meningeal congestion. In Case 2, a few focal subarachnoid hemorrhages were also present. In both cases, nonspecific, pyknotic changes in frontal and temporal cortical neurons were present.

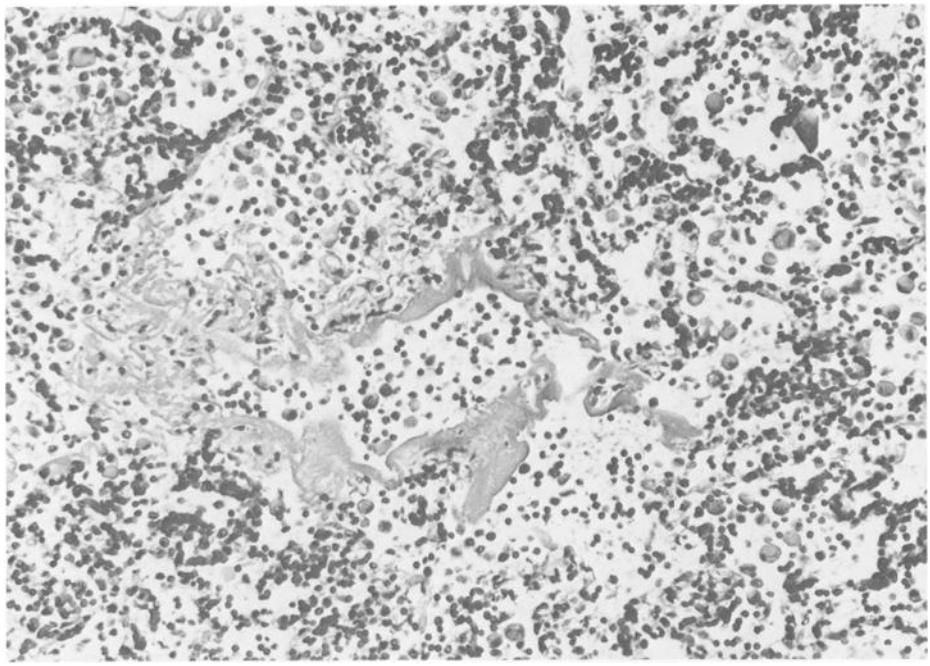

FIG. 2—*Intra-alveolar red cells, macrophages, and hyaline membranes typical of MeBr gas intoxication (from Case 2). Focal neutrophilic infiltrates were additionally present in some cases.*

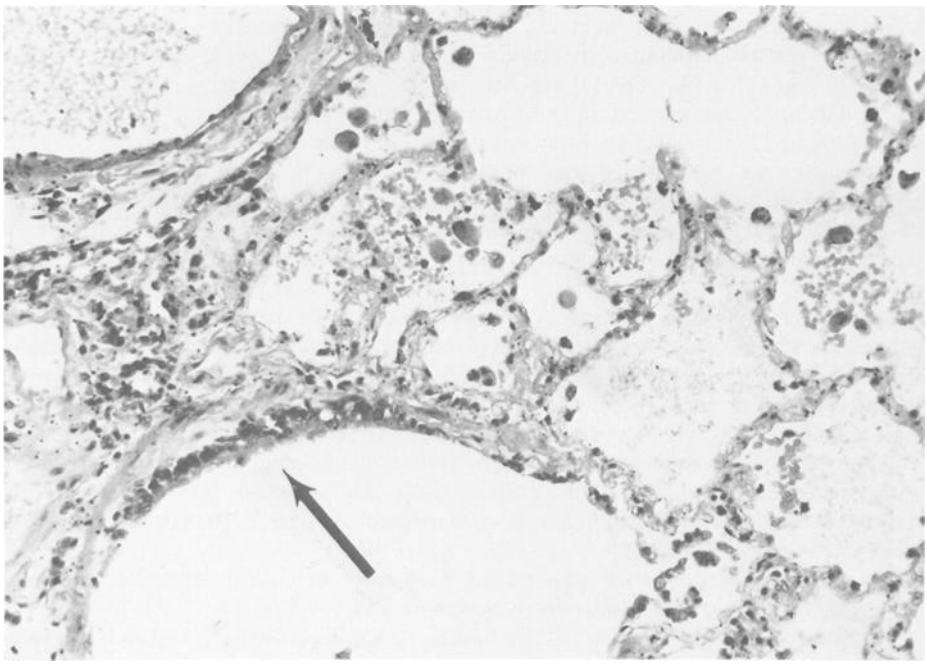

FIG. 3—*Relative sparing of bronchiolar respiratory mucosal lining characteristically found with MeBr inhalation injury* (arrow). *Air trapping is also evident.*

Urine drug screens were negative in both cases.

Mass spectroscopy detected threshold concentrations of MeBr (less than 1 ppm) in the brain in Case 2, but not Case 3. All other tissues were negative.

Case 4

A 25-year-old white male was found collapsed under the edge of a fumigation tent of a house that had been charged with MeBr approximately 12 h earlier. He was initially drowsy and unsteady of gait. Four hours after admission he developed grand mal seizures. Admission and sequential serum bromide concentrations were 518, 628, and 656 mg/L. No renal or hepatic abnormalities were noted either clinically or chemically. The urine drug screen was negative. As with Cases 2 and 3, the initial chest X-rays were negative only to be followed by fulminant respiratory failure with interstitial changes on X-ray. Dilantin®, phenobarbital, mannitol, steroids, and British antilewisite (BAL) were administered. Pulmonary failure and bradycardia resulted in his demise 6-½ h after exposure.

Autopsy findings were almost identical to that of Case 2, and MeBr was detected by mass spectroscopy at threshold concentrations in ocular fluid, but not in brain, fat, or blood.

Nonlethal Cases

Three young men were exposed to MeBr after illegal entries into tented houses where exposures of 5 to 30 min were experienced.

Admission symptoms included conjunctival irritation and headaches or nausea or both. Plasma and serum bromide concentrations varied between 17.9 and 321 mg/L. All recovered without sequellae.

Discussion

Wyers [*11*] described three phases of acute MeBr intoxication:

The premonitory phase occurs ½ to 48 h after exposure and consists of dimness of vision, diplopia, staggering gait, headache, vertigo, vomiting, euphoria or delirium, or syncope.

The stage of cerebral irritation consists of twitching of muscles with or without convulsions, mania, and diaphoresis. Trismus may occur. Fulminant respiratory failure ensues, with or without focal or progressive seizures.

If the patient survives, the recovery phase may include hallucinations, apathy, amnesia, aphasia, ataxia, sensory changes and defects, and tremors or recurrent seizures or both [*4,12*]. This phase, sometimes associated with psychoneurotic symptoms, may also be the presenting syndrome of chronic, low level MeBr intoxication [*4,11,13*].

As with some pulmonary irritants such as phosgene [*14,15*], the initial chest X-ray may be negative even in the presence of decreased pO_2 and positive physical findings. Radiographic interstitial infiltrates and fulminant respiratory failure occur after a variable delay with both MeBr and phosgene intoxication.

Skin sensitivity and cutaneous toxicity, not seen in our cases, have been reported following contact with liquid MeBr in fire fighting [*1,2,16*] and in the industrial chemical industry.

Benatt [*17*] has suggested a specific renal tubular toxicity in humans and a tubular lesion has been observed in animals [*1,18*]. Case 2 and 3 above did have clinical evidence of acute tubular necrosis and microscopic renal tubular changes were present in Case 3.

In some reports, liver failure has been a prominent feature [*4,13,19*] resembling Reye syndrome. Of the four lethal cases studied above, only one had a documented elevation prothrombin time in the absence of other liver abnormalities, and only congestion was seen histologically.

The mechanism of MeBr toxicity that have been proposed include systemic bromism, intracellular effects of bromide, methanolism, and methylation effects [*1,18,20–22*]. The first

three may be discounted because of inconsistencies between concentrations of the proposed damaging metabolite and clinical effects. Bromism does not have respiratory failure as a prominent feature, and bromoderma is absent in the inhalation cases of MeBr. Methanolism, with its prominent visual effects, does not resemble the clinical cases described above. The mechanism of methylation in vivo of sulfhydryl groups of vital enzymes is currently favored [*20,22*]. This is strongly supported by the similarity of methyl chloride and methyl bromide experimental poisonings.

Rathus and Landy [*19*], Wyers [*11*], and Drawneek et al [*23*] have reported great variation in serum or plasma bromide concentrations following different exposures and presentations. In our three lethal and three nonlethal cases following burglary it was not possible to predict survival based on bromide concentration at time of admission, perhaps because of variation in susceptibility, metabolism, or other factors. It is noteworthy that the shortest interval between exposure and death (6½ h) was associated with the highest admission bromide level in this series (518 mg/L). The intact MeBr molecule could not be detected in fat despite its lipid solubility. Its presence in brain and ocular fluid may well suggest decreased metabolism at those sites.

Occupational standards for exposure to MeBr described by Hine [*4*] state that exposure to MeBr concentrations of 1000 ppm is permissible for only 5 min. In Cases 2, 3, and 4, the initial concentration of MeBr just after tenting is calculated to be 3000 ppm confirming the lethal potential of the environment. Had some gas leakage from intact or disrupted tents not occurred before or during the illegal entry, more fatalities among burglars might be expected. Whether or not some burglars use gas masks is an unanswered question.

Chloropicrin is an irritant lacrimal gas used to warn of the presence of MeBr [*3*]. It is mixed with MeBr at 0.25% concentration to meet the minimum state law requirement for residential dwellings.[5] Whether through dissipation or differential absorption of chloropicrin to materials within the house, it is not sufficiently noxious to prevent the entry of unprotected individuals into lethal concentrations of MeBr. Possible remedies including using increased concentrations of chloropicrin, use of some other warning gas, or the posting of guards to prevent intrusions into tented dwellings. It is unclear whether these suggested remedies are workable or economically feasible. State of Florida regulations formerly did require the posting of guards at tented houses [*24*], but these requirements were discontinued in 1974.

Lethal intoxications with MeBr are on the increase in Florida. Prior to 1981, there was only one death other than those reported above, a suicide, caused by MeBr. From November 1957 to October 1981, there were also 27 nonfatal cases of MeBr intoxication reported to the Bureau of Entomology of the State of Florida, as well as reportings of chloropicrin toxicity in the same setting.[5]

As economic influences lead to expanded use, physicians and health authorities should expect increasing frequency of MeBr poisoning in the coming years. Clinical outcome is probably more related to idiosyncracies of patient exposure and susceptibility than to any specific treatment. Prevention is the best means to limit morbidity and mortality.

Reckless intruders have brought into focus a problem in industrial safety just as drunken drivers have helped to define problems in road design. Although our recent cases have involved illegal entry, the potential for curious children to get into tented houses exists. It is recommended that these tented dwellings be guarded while the atmosphere within is still hazardous.

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References

[*1*] Von Oettingen, W. F., in *The Halogenated Aliphatic, Olefinic, Cyclic, Aromatic, and Aliphatic-Aromatic Hydrocarbons Including the Halogenated Insecticides, Their Toxicity and Potential*

Dangers, Public Health Service Publication No. 414, United States Government Printing Office, Washington, DC, 1955, pp. 15-30.

[2] Hunter, D., in *The Diseases of Occupation*, 6th ed., Hodder and Stoughton, London, 1978, pp. 574-579.

[3] *Manual of Fumigation for Insect Control*, 2nd ed., United Nations Food and Agriculture Organization, Italy, 1969, pp. 119-144.

[4] Hine, C. H., "Methyl Bromide Poisoning—A Review of Ten Cases," *Journal of Occupational Medicine*, Vol. 11, No. 1, Jan. 1969, pp. 1-10.

[5] "Illness Associated with Soil Fumigation," *Morbidity and Mortality Weekly Report*, Vol. 23 No. 25, 22 June 1974, pp. 217-218.

[6] Davis, J. H., Davies, J. E., Raffonelli, A., and Reich, G., *The Investigation of Fatal Acrylonitrile Intoxications, in Pesticides and the Environment: A Continuing Controversy*, W. B. Deichman, Ed., Intercontinental, Book Corp., New York, 1973.

[7] Sunshine, I., *Methodology for Analytical Toxicology*, CRC Press, Cleveland, OH, 1975, pp. 54-56.

[8] Peoples, A. J., Pfaffenberger, C. D., Shafik, T. M., and Enos, H. F., "Determination of Volatile Purgeable Halogenated Hydrocarbons in Human Adipose Tissue and Blood Serum," *Bulletin of Environmental Contamination Toxicology*, Vol. 23, 1979, pp. 244-249.

[9] Pfaffenberger, C. D. and Freal, J. J., III, "A Convenient Purging Device for Analyzing Adipose Tissue for Volatile Hydrocarbons," *Journal of High Resolution Chromatography and Chromatography Communications*, Vol. 2, No. 10114, Oct. 1979, p. 632.

[10] Pfaffenberger, C. D., Peoples, A. J., and Enos, H. F., "Distribution of Volatile Halogenated Organic Compounds Between Rat Blood Serum and Adipose Tissue," *International Journal of Environmental Analytical Chemistry*, Vol. 8 No. 1, 1980, pp. 55-65.

[11] Wyers, H., "Methyl Bromide Intoxication," *British Journal of Industrial Medicine*, Vol. 2, No. 1, Jan. 1945, pp. 24-29.

[12] Shield, L. K., Coleman, T. L., and Markesberry, W. R., "Methyl Bromide Intoxication, Neurologic Features Including Simulation of Reyes Syndrome," *Neurology*, Vol. 27, Oct. 1977, pp. 959-962.

[13] Johnstone, R. T., "Methyl Bromide Intoxication of a Large Group of Workers," *Industrial Medicine*, Vol. 14, No. 6, June 1945, pp. 495-497.

[14] Ireland, M. W., Ed., *The Medical Department of the United States Army in the World War*, Vol. XIV, Medical Aspects of Gas Warfare, U.S. Government Printing Office, Washington, DC, 1926, p. 82.

[15] Prain, J. H. and Harvey Smith, G., "A Clinical-Pathological Report of Eight Cases of Methyl Bromide Poisoning," *British Journal of Industrial Medicine*, Vol. 9, No. 44, 1952, pp. 44-49.

[16] Butler, E. C. B., Perry, K. M. A., and Williams, J. R. F., "Methyl Bromide Burns," *British Journal of Industrial Medicine*, Vol. 2, No. 30, 1945, pp. 30-31.

[17] Benatt, A. J. and Courtney, T. R. B., "Uraemia in Methyl Bromide Poisoning, A Case Report," *British Journal of Industrial Medicine*, Vol. 5, No. 1, Jan. 1948, p. 21.

[18] Irish, D. D., Adams, E. M., Spencer, H. C., and Rowe, V. K., "The Response Attending Exposure of Laboratory Animals to Vapors of Methyl Bromide," *Journal of Industrial Medicine and Hygiene*, Vol. 22, No. 6, 1940, pp. 218-230.

[19] Rathus, E. M. and Landy, P. J., "Methyl Bromide Poisoning," *British Journal of Industrial Medicine*, Vol. 18, No. 53, 1961, pp. 53-57.

[20] Irish, D. D., "Chemical Effects of Methyl Bromide in the Animal Body in Relation to its Physiological Effects," *Journal of Industrial Hygiene and Toxicology*, Vol. 23, No. 8, Oct. 1941, pp. 408-411.

[21] Miller, D. P. and Haggard, H. W., "Intracellular Penetration of Bromide as a Feature of Toxicity of Alkyl Bromides," *Journal of Industrial Hygiene and Toxicology*, Vol. 25, 1943, p. 423.

[22] Lewis, S. E., "Inhibition of SH Enzymes by Methyl Bromide," *Nature*, Vol. 161, No. 4096, May 1948, p. 692.

[23] Drawneek, W., O'Brien, M. J., Goldsmith, H. J., and Bourdillon, R. E., "Industrial Methyl Bromide Poisoning in Fumigators," *The Lancet*, 17 Oct. 1964, p. 855.

[24] Florida Department of Health and Rehabilitative Services Pest Control Rules, Chapter 10D-55.19 (4), Florida Administrative Code.

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