

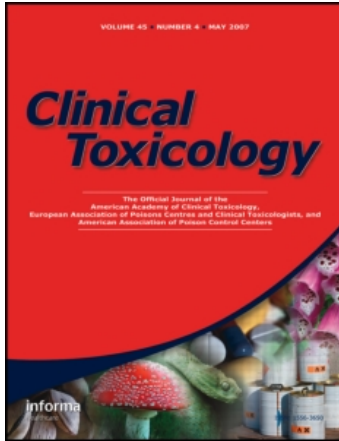
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## Central Nervous System Toxicity and Early Peripheral Neuropathy Following Dermal Exposure to Methyl Bromide

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### ABSTRACT

**Case Report:** We describe a case of early peripheral neuropathy and central nervous system toxicity as a result of acute predominantly dermal exposure to methyl bromide. A 32-year-old male was admitted after an accidental predominantly dermal exposure to methyl bromide while fumigating soil for pest control. The patient suffered dermal burns and vesicles on the upper and lower limbs. One week following exposure, he developed progressive weakness of the lower limbs, ataxia, paresthesiae of both legs and the left arm, hyperactive tendon reflexes in the lower limbs, and left Babinski sign. Nerve conduction velocity testing was compatible with axonal neuropathy. The patient recovered gradually from his burns. Three months postexposure he showed no signs of central nervous system toxicity, but the peripheral neuropathy was still present. **Discussion:** Neurological effects primarily referable to the central nervous system following severe inhalation of methyl bromide have frequently been reported. The patient described in this study developed an unusual early peripheral neuropathy following dermal exposure. Peripheral neuropathy can be an outcome of methyl bromide intoxication, but is usually a late sequela of acute central nervous system toxicity or an aftereffect of repetitively inhaled chronic exposure. In this case, exposure to methyl bromide through abraded skin caused early peripheral neuropathy and central nervous system toxicity.

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## INTRODUCTION

Methyl bromide (MB) is a halogenated aliphatic hydrocarbon used as an insecticide fumigant. It is a colorless, odorless, highly volatile liquid that exists as a gas at ambient temperatures.<sup>1</sup> Signs and symptoms of acute toxicity are associated with the central nervous system (CNS), as well as with the cardiovascular and respiratory systems.<sup>2-4</sup> Dermal exposure may result in intense blisters and severe burns.<sup>2,3</sup> Severe symptoms such as coma and seizures<sup>5</sup> are usually reported after inhalation exposure to MB.<sup>4,5</sup> In this report, we describe a case of acute MB dermal exposure that resulted in mild CNS toxicity and early signs of peripheral neuropathy.

### Case Report

A 32-year-old previously healthy male was admitted to our hospital about 10 hours following exposure to MB via an accidental leakage to his upper and lower limbs while fumigating soil for pest control. He had used protective respiratory gear but its condition was unknown. This was his first exposure to MB and he had no previous exposures to any other pesticides. On admission, the patient was fully alert and well-oriented, but had erythema with multiple vesicles on all 4 extremities. Neurological examination, including cranial nerve function, was unremarkable. The patient's temperature was 37.4°C, blood pressure 120/85 mm Hg, pulse rate 98 bpm, and respiration 17/min. Initial arterial blood gas results showed PO<sub>2</sub> 98 mm Hg, PCO<sub>2</sub> 35 mm Hg, bicarbonate 23 mEq/L, and pH 7.32. White blood cell count was 17800 mm<sup>3</sup>, hemoglobin 15.3 g/dL, platelets 255000 mm<sup>3</sup>, sodium 130 mEq/L, potassium 3.6 mEq/L, urea 15.4 mmol/L (43 mg/dL), creatinine 106 μmol/L (1.2 mg/dL), aspartate aminotransferase 50 U/L, and alanine aminotransferase 37 U/L. Serum bromide levels were not obtained during the first days of hospitalization. Electrocardiogram (ECG) was normal. The patient was treated with intravenous fluids, wet dressings, and topical nitrofurazone 0.2%.

One week following exposure, the patient developed progressive weakness of lower limbs, unstable gait, paresthesiae of both legs and left hand, hyperactive deep tendon reflexes in the lower limbs, and left Babinski sign. He remained fully alert and cranial nerves were intact. Brain and spinal cord computerized tomography scan and spinal myelography were normal. Nerve conduction studies (NCS) of the peroneal nerve revealed a reduction in amplitude of evoked compound action potential (0.5 mV)

with relatively normal NCV (40 m/s), which is characteristic of axonal neuropathy. NCV studies of the left median nerve were normal (amplitude of action potential 2 mV, NCV 45 m/s). Toxic screens for urine lead and mercury were negative. Arsenic was not tested. A serum bromide level obtained 10 days postexposure was 12 mg/L (normal 0.5–2 mg/L). The skin lesions healed gradually within approximately 5 weeks following exposure.

Follow-up observation over the next 3 months showed no paresthesiae of the left hand and the Babinski sign was negative; weakness of the lower limbs and an unstable gait were still present.

## DISCUSSION

MB is a commonly used insecticide fumigant. It is a colorless and odorless volatile liquid with a boiling point of 3.6°C that evaporates in an ambient atmospheric temperature.<sup>6</sup> The neurological manifestations of MB intoxication following respiratory exposure include the insidious onset of headache, vertigo, nausea, and vomiting. In severe intoxication, seizures and CNS depression may occur within 24 hours.<sup>7</sup> The exact mechanism of MB-induced CNS toxicity is not yet clearly understood. MB toxicity results from alkylation of crucial sulfhydryl containing enzymes and proteins in mammalian tissues, and CNS toxicity may be mediated by CNS glutathione depletion.<sup>8</sup> Alternately, in some species, glutathione depletion has inhibited toxicity.<sup>9</sup> Other mechanisms of CNS toxicity as suggested by Granier *et al.* who noted that glutathione transferase activity can vary among ethnic groups according to genotype.<sup>10</sup> The transformation of methyl glutathione (the first metabolic step) into toxic metabolites (methanethiol and formaldehyde) is responsible for the neurotoxicity. Therefore, patients with glutathione transferase activity may be predisposed to greater neurotoxicity, and *N*-acetylcysteine treatment, a glutathione precursor, could enhance neurotoxicity.

CNS toxicity sequelae, including organic brain syndrome, impairment of basal ganglia function, pyramidal tract effects, and peripheral neuropathy, have been reported after inhalation of MB-contaminated air. These manifestations occur as late sequelae following acute CNS toxicity, or in workers chronically exposed to MB by inhalation.<sup>5,11-14</sup>

It is well known that MB is an intense vesicant with the capacity to penetrate protective clothing, including rubber and leather, resulting in severe burns.<sup>2,15</sup> Increased plasma bromide levels and percutaneous absorption of MB have been previously described.<sup>15</sup> The development



in our patient of CNS toxicity characterized by pyramidal signs and hyperactive tendon reflexes, but without clinical symptoms such as impaired consciousness, headache, dizziness, etc., may relate to the slow absorption of MB through the damaged skin. Even though the patient had been equipped with respiratory gear, we have no way of ruling out the possibility that it might have been dysfunctional and that some MB absorption could have occurred through the respiratory tract.

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