

Neurologic Abnormalities in Workers of a 1-Bromopropane Factory

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We reported recently that 1-bromopropane (1-BP; *n*-propylbromide, CAS Registry no. 106-94-5), an alternative to ozone-depleting solvents, is neurotoxic and exhibits reproductive toxicity in rats. The four most recent case reports suggested possible neurotoxicity of 1-BP in workers. The aim of the present study was to establish the neurologic effects of 1-BP in workers and examine the relationship with exposure levels. We surveyed 27 female workers in a 1-BP production factory and compared 23 of them with 23 age-matched workers in a beer factory as controls. The workers were interviewed and examined by neurologic, electrophysiologic, hematologic, biochemical, neurobehavioral, and postural sway tests. 1-BP exposure levels were estimated with passive samplers. Tests with a tuning fork showed diminished vibration sensation of the foot in 15 workers exposed to 1-BP but in none of the controls. 1-BP factory workers showed significantly longer distal latency in the tibial nerve than did the controls but no significant changes in motor nerve conduction velocity. Workers also displayed lower values in sensory nerve conduction velocity in the sural nerve, backward recalled digits, Benton visual memory test scores, pursuit aiming test scores, and five items of the Profile of Mood States (POMS) test (tension, depression, anxiety, fatigue, and confusion) compared with controls matched for age and education. Workers hired after May 1999, who were exposed to 1-BP only (workers hired before 1999 could have also been exposed to 2-BP), showed similar changes in vibration sense, distal latency, Benton test scores, and depression and fatigue in the POMS test. Time-weighted average exposure levels in the workers were 0.34–49.19 ppm. Exposure to 1-BP could adversely affect peripheral nerves or/and the central nervous system. **Key words:** 1-bromopropane, distal latency, nerve conduction velocity, neurobehavioral testing, neurotoxicity, ozone-depleting solvents, postural sway testing, reproductive toxicity, vibration sense. *Environ Health Perspect* 112:1319–1325 (2004). doi:10.1289/ehp.6995 available via <http://dx.doi.org/> [Online 30 June 2004]

Ozone-depleting solvents, such as specific chlorofluorocarbons and 1,1,1-trichloroethane, have been banned since 1996 in developed countries. Because they were used in large amounts in various industries, alternative compounds were introduced to the workplace. One such alternative compound is 1-bromopropane (1-BP; *n*-propylbromide, CAS Registry no. 106-94-5), which is used in the United States and Japan as a cleaning agent for metals, precision instruments, electronics, optical instruments, and ceramics (Ichihara, in press). It is also used in spray form as an adhesive in the United States (Ichihara et al. 2002). *Environ Tech* (2001) estimated the total amount of 1-BP commercially available for sale in the United States in the year 2000 was 1,967.9 metric tons (4,338,583 lb), which is comparable to 9.0, 31.0, and 10.6% of the amount of methylene chloride, perchloroethylene, and trichloroethylene used in adhesive/foam fabrication and metal cleaning in the same year in the United States. In Japan, the amount of 1-BP sold in 2003 was 1,125 metric tons, which is about double the 645 metric tons sold in 1998 (Association of Bromopropane Producers of Japan, unpublished data). In

addition, in the workplace where cases of neurotoxicity had been reported, 1-BP was introduced as an alternative for methylene chloride (Ichihara et al. 2002). The benefits of using 1-BP instead of the chlorinated carbons are not clear. However, under pressure to regulate the use of chlorocarbons, 1-BP has been used as a surrogate, which is encouraged by the lack of measures to define the exposure limits. In this regard, previous animal studies revealed neurotoxicity and reproductive toxicity of 1-BP (Ichihara et al. 2000a, 2000b; Wang et al. 2002, 2003; Yamada et al. 2003; Yu et al. 1998, 2001). Exposure to 1-BP resulted in a dose-dependent limb muscle weakness and reduction of nerve conduction in rats (Ichihara et al. 2000a). It also resulted in myelin degeneration of peripheral nerves and swelling of preterminal axons in the medulla oblongata (Ichihara et al. 2000a). It was also revealed that 1-BP exhibits reproductive toxicity in both male and female rats (Ichihara et al. 2000b; Yamada et al. 2003). Thus, animal studies preceded human studies and warned about the potential neurotoxicity and reproductive toxicity of 1-BP in humans. The most recently reported cases also confirmed the neurotoxicity

of 1-BP in humans (Ichihara et al. 2002; Sclar 1999). However, these case reports have limitations in terms of quantitative analysis. In 1999 we investigated a 1-BP factory, but this investigation was also limited because it was originally oriented to study the effects of 2-bromopropane (2-BP), which targets mainly reproductive and hematopoietic systems (Ichihara et al. 2004).

The aim of the present study was to assess the neurologic function and other health-related changes in workers exposed to 1-BP and compare the results with those of control workers in a beer factory.

Materials and Methods

Factories and workers. The subjects were female workers of a 1-BP production factory located in Yixing, Jiangsu Province, China. The survey was conducted 16–18 January 2001. The same factory mainly produced 2-BP in 1996 (Ichihara et al. 1999), but shifted the main production to 1-BP between 1996 and 1999 (Ichihara et al. 2004), and the product was only 1-BP at the time of the present survey. 1-BP was synthesized by incubating *n*-propranolol and hydrogen bromide under concentrated sulfuric acid. The product was purified by distillation and temporarily stored in ceramic containers. The crude product was then transferred to 20-L plastic vessels through hose pipe from the cock of the container and subsequently neutralized with hydrogen carbonate. The product was finally transferred to 1,000-L drums for storage and transport. The

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