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Leading Work-Related Diseases and Injuries--United States

The National Institute for Occupational Safety and Health (NIOSH) has developed a list of 10 leading work-related diseases and injuries. The first six categories have been described previously (1-6); a discussion of the seventh category, Neurotoxic Disorders, appears below.

NEUROTOXIC DISORDERS

Background. Diseases of the nervous system resulting from toxic exposures in the workplace were known as early as the first century A.D., when Pliny identified palsy as a manifestation of lead poisoning among workers exposed to lead dust (7). In 1557, Jean Fernel linked gingival pigmentation, tremor, and behavioral changes to occupational mercury poisoning (8); in the nineteenth century, Delpech recognized rubber processing as the cause of the bizarre psychoses occurring among French workers who manufactured condoms and balloons in small cottage industries. Later, carbon disulfide was implicated as the specific neurotoxic agent (9).

Industrial hygiene practices have improved in the twentieth century, and some animal models of neurotoxic disease have been developed. In addition, workers who become ill often draw attention to outbreaks of neurotoxic diseases. Despite the prior identification of acrylamide as neurotoxic in animals, its neurotoxicity in humans was first recognized in the 1950s, when several Japanese workers involved in a pilot production project developed peripheral neuropathy (10). During the 1960s and early 1970s, dozens of cases of neuropathy occurred among Japanese and Italian workers exposed to solutions containing n-hexane during the manufacture of shoes (11). Subsequently, high doses of n-hexane were found to be neurotoxic in exposed animals. In the past 15 years alone, outbreaks of serious human neurotoxicity occurred among workers exposed to three substances not previously known to be neurotoxic: the chlorinated hydrocarbon, chlordecone, which caused opsoclonus, tremor, disturbances of gait, and changes in personality (12); and two hexacarbons, methyl-n-butyl ketone and 2-t-butylazo-2-hydroxy-5-methylhexane, both of which caused a predominantly peripheral neuropathy (13,14).

Nature of Neurotoxic Disorders. Neurotoxic disorders are on the NIOSH list of Ten Leading Work-Related Diseases and Injuries (1) because of their potential severity--as exemplified by the neurotoxicity of chlordecone--and because of the large number of workers potentially at risk. A

conservative estimate of the workers exposed full time to one or more neurotoxic agents is 7.7 million (15). The number of potentially neurotoxic chemicals found in the workplace exceeds 850; an abbreviated list of the more commonly used of these chemicals is shown in Table 3 (16).

Clinically, symptoms and signs of neurotoxicity can be diverse. Depending on the intensity of exposure, the molecular configuration of the agent, and the mechanism of toxicity, either central or peripheral neurologic effects may predominate. Most neurotoxic chemicals, however, affect both the central and peripheral nervous systems. Because the symptoms of peripheral neuropathy are more specific and the nerves themselves more directly accessible to precise diagnostic examinations, the effects of neurotoxic agents on the peripheral nervous system are usually more easily identified than effects on the central nervous system (CNS). Early symptoms of peripheral neuropathy may include numbness, tingling, or pain in the feet or hands. As the disease progresses, clumsiness or incoordination due to both sensory and motor changes may develop. Production workers may find their ability to do usual work partially or fully impaired. Chemicals used extensively in industry, which cause peripheral neuropathy when present in sufficiently high and persistent concentrations, include: lead, n-hexane, acrylamide, carbon disulfide, mercury, and methyl bromide (17,18) (Table 4). Several chemicals are known to cause selective impairment of cranial-nerve function, including dysfunction of the fifth cranial nerve (trichloroethylene) (18).

The effects of neurotoxic agents on the CNS present a far wider range of disturbances (16,18,19) (Table 5). At times, the most striking effects are changes in mood and personality (20). High levels of exposure to manganese or carbon disulfide produce psychoses and suicidal tendencies. Delusions and hallucinations may result from exposure to high concentrations of solvents, such as methylene chloride. Manifestations of cognitive dysfunction, such as reduced attention span, lack of alertness, and memory loss, are prominent neurotoxic effects that may occur in addition to personality changes after exposure to many solvents and to asphyxiants, such as carbon monoxide. Other neurologic effects occur under certain restricted conditions of exposure to unique chemical substances (Table 6).

Although research into the neurobehavioral effects of industrial chemicals is relatively new, early results suggest that occupational neurotoxicity may be a larger problem than previously suspected. Sensitive methods for evaluating subtle losses in cognitive function have only recently been applied to the evaluation of exposed workers. Because of the complexity of the nervous system and the variety of potentially neurotoxic exposures, the true scope of this health hazard in the workplace is unknown. Reported by Div of Biomedical and Behavioral Science, Div of Surveillance, Hazard Evaluations, and Field Studies, National Institute for Occupational Safety and Health, CDC.

Editorial Note

Editorial Note: Studies of the neurotoxicity of workplace chemicals demonstrate the problems encountered in recognizing occupational disease in general. Despite occasional large and dramatic outbreaks of neurotoxic disorders, such as those mentioned above, more often small numbers of workers in many workplaces are chronically exposed to neurotoxic agents that subtly and slowly alter nervous-system functions. Several neurotoxic syndromes mimic diseases of nonoccupational and "idiopathic" etiology, e.g., the toxic axonopathy associated with exposure to various metals and solvents, the parkinsonian syndrome of chronic intoxication with manganese, and the organic brain syndrome of chronic solvent intoxication. Because of these similarities to other nonoccupational diseases, such cases are frequently not identified as occupational in origin.

In addition, many physicians are not trained to take an adequate occupational medical history (21). For these reasons, the prevalence of occupational neurologic disease is unknown, and important causal relationships between chemicals and disease remain obscure.

The prevention of neurotoxicity among workers will require strategies such as those suggested in the 1990 objectives for improving the nation's health (22), developed by the U.S. Public Health Service: (1) analyses of structural analogues of known neurotoxic agents in an effort to predict the neurotoxicity of untested chemicals; (2) continuing search for animal models of disease; (3) ongoing research in establishing an acceptable human exposure level for identified neurotoxic agents; (4) epidemiologic evaluations of suspected neurotoxicity;(5) development of simple screening tools for use on asymptomatic populations exposed to known neurotoxic agents; and (6) premanufacture and premarket testing of new chemicals as required by the Toxic Substances Control Act (23). As in the prevention of other work-related diseases, however, the most direct and effective method for preventing neurotoxic illness will continue to be the environmental control of exposures to neurologic chemicals. Such efforts as the substitution of less toxic substances where possible, engineering controls, teaching appropriate work practices, and educating workers about the potential neurotoxicity of chemicals will aid a comprehensive prevention effort.

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