

## Occupational Neurologic Disorders in Korea

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**Received** March 22, 2010

**Revised** April 23, 2010

**Accepted** April 23, 2010

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This article presents a schematic review of the clinical manifestations of occupational neurologic disorders in Korea and discusses the toxicologic implications of these conditions. Vascular encephalopathy, parkinsonism, chronic toxic encephalopathy, cerebellar dysfunction, peripheral neuropathy, and neurodegenerative diseases are common presentations of occupational neurotoxic syndromes in Korea. Few neurotoxins cause patients to present with pathognomic neurologic syndrome. Detailed neurologic examinations and categorization of the clinical manifestations of neurologic disorders will improve the clinical management of occupational neurologic diseases. Physicians must be aware of the typical signs and symptoms of possible exposure to neurotoxins, and they should also pay attention to less-typical, rather-vague symptoms and signs in workers because the toxicologic characteristics of occupational neurologic diseases in Korea have changed from typical patterns to less-typical or equivocal patterns. This shift is likely to be due to several years of low-dose exposure, perhaps combined with the effects of aging, and new types of possibly toxicant-related neurodegenerative diseases. Close collaboration between neurologists and occupational physicians is needed to determine whether neurologic disorders are work-related.

**J Clin Neurol 2010;6:64-72**

**Key Words** occupational disease, neurologic disorders, toxicology.

## Introduction

Chemicals capable of damaging the central nervous system (CNS) are ubiquitous in the environment, and especially in occupational settings. Industrial processes are major sources of some of the most well-known neurotoxicants. According to the United States Environmental Protection Agency, more than 65,000 commercial chemicals are currently used in the US, and 2,000-3,000 new chemicals are added each year.<sup>1</sup> Approximately one-quarter of these chemicals are suspected neurotoxins.

The nervous system is vulnerable to the effects of certain chemicals found in the work environment. Clinical disorders of the CNS have varying presentations, often involving a host of nonspecific symptoms. Multiple syndromes may occur in response to a single neurotoxin, depending on the level and duration of the exposure. For example, acute, high-level exposure to carbon disulfide produces psychosis, whereas chronic moderate exposure causes atherosclerosis-related health effects.<sup>2</sup> Furthermore, few neurotoxins cause patients to present

with pathognomic neurologic syndrome. Symptoms and signs of neurotoxin exposure may be mimicked by various psychiatric, metabolic, inflammatory, neoplastic, and degenerative diseases of the nervous system.<sup>3</sup>

Many occupational neurologic disorders may go unrecognized in Korea. In the absence of a detailed neurologic examination and comprehensive work history, physicians may overlook the possibility of previous or current neurotoxin exposure. The recognition of occupational neurologic disorders is important for clinicians for several reasons: 1) diagnosis can protect the worker from further harm by reducing exposure to the toxin, 2) diagnoses often provide some indication of prognosis, and 3) recognition of occupational exposure can alert the employer to the need for improved hygiene measures that will protect other workers.

South Korea has experienced rapid economic development since the 1960s, a phenomenon that has caused the Korean economy to shift from labor-intensive (i.e., light) industries to machinery-intensive (i.e., heavy) industries such as automobile, petrochemical, shipbuilding, nonferrous metal, machinery, and se-

miconductor industries,<sup>4</sup> in which neurotoxic chemicals are widely used. Most of the carbon disulfide poisoning cases that occurred in Korea in the 1980s presented with severe neurologic disturbances.<sup>5</sup> Some of the cases of poisoning that involved metals and organic solvents in the 1990s and 2000s manifested as mild neurologic disturbances.<sup>6,7</sup> Patients with occupational neurologic diseases in Korea present with clinical features that can vary with the level of exposure.

This article schematically reviews the clinical manifestations of occupational neurologic disorders in Korea and discusses the toxicologic implications of these disorders.

## Methods

We conducted an extensive search of the PubMed and KoreaMed databases for reports of occupational neurologic disorders in Korea through to December 2009, and we evaluated all relevant papers published in Korean and English, and the references therein. In addition, the electronic database on occupational diseases of the Korean Worker's Compensation and Welfare Service (COMWEL) were searched thoroughly, and related materials on occupational neurologic disorders, such as reports or monthly magazines that do not appear on the PubMed and KoreaMed databases, were reviewed critically to identify occupational neurologic disorders.

## Clinical Manifestations and Toxicological Implications of Major Neurotoxic Syndromes in Korea

Various categories of neurologic disorders, such as vascular encephalopathy, parkinsonism, chronic toxic encephalopathy (CTE), cerebellar dysfunction, peripheral neuropathy, and neurodegenerative diseases, were diagnosed and compensated as occupational neurologic diseases by COMWEL. Various heavy metals, organic solvents, or other chemicals were found to be responsible for these occupational neurologic disorders.

### Vascular encephalopathy

Carbon disulfide poisoning is a highly typical and frequently encountered vascular encephalopathy. Mass poisoning by carbon disulfide occurred at a viscose-rayon factory in Korea in 1998. By the end of 2004, 910 workers had been compensated for carbon disulfide poisoning.<sup>8</sup> In 1964, used rayon manufacturing machinery that had been made by the Toray Company (Toyo Rayon) of Japan in 1956 was brought into the factory,<sup>4</sup> which led to the use of carbon disulfide in the spinning process at the factory.

The victims of carbon disulfide poisoning in Korea have exhibited various clinical characteristics, including multiple brain

infarctions,<sup>5,9,10</sup> peripheral neuropathy,<sup>11</sup> retinopathy including microaneurysm of the fundus,<sup>12</sup> hypertension,<sup>13</sup> and glomerulosclerosis of the kidney.<sup>14</sup> These findings indicate that the basic mechanisms underlying the carbon disulfide poisoning cases in Korea involved atherosclerotic changes in blood vessels, consistent with a recent report by Chuang et al.<sup>15</sup> The clinical manifestations of vascular encephalopathy (e.g., hemiparesis and speech disturbance) in cases of chronic carbon disulfide poisoning were similar to those observed in patients with atherosclerotic cerebrovascular disorders.<sup>5,9,10</sup> The main findings of T2-weighted brain magnetic resonance imaging (MRI) in patients with carbon disulfide poisoning in Korea included white-matter hyperintensity and lacunar infarction.<sup>16</sup> Brain atrophy has also occasionally been reported.<sup>15,17</sup> Many cases presenting with acute cerebrovascular stroke-like symptoms, sometimes with hypertension or diabetes, were often misdiagnosed as having suffered cerebrovascular attacks. Thus, the possibility of carbon disulfide poisoning must not be overlooked when physicians make differential diagnoses in patients with vascular encephalopathy.

Comparing the poisoning cases in Korea with those in Japan, from which the rayon industry was transferred to Korea, helps to reveal the toxicological characteristics. Psychosis and peripheral neuropathy due to carbon disulfide poisoning were first reported among rayon industry workers in 1932 and 1934, respectively.<sup>18</sup> In the 1930s, during which the Japanese were the first to produce rayon, carbon disulfide poisoning was the most common occupational disease in Japan,<sup>19</sup> and psychosis, which resulted from very high exposure, was the predominant health problem. Since 1949, rayon manufacturers have collaborated with university researchers in Japan to control carbon disulfide concentrations in the workplace and to monitor the incidence of carbon disulfide poisoning.<sup>19</sup> Therefore, atherosclerosis, which is associated with moderate levels of exposure, was the main type of carbon disulfide poisoning in the 1960s in Japan.<sup>19</sup> Similar clinical features (e.g., atherosclerosis) were observed in Korean victims of carbon disulfide poisoning, probably due to the transfer of the rayon industries from Japan in the 1960s.

Many more cases have occurred in Korea than in Japan, possibly due to a lack of knowledge about the toxicity of carbon disulfide among occupational health professionals and a lack of concern regarding occupational health and safety by employers, governments, and professionals.<sup>4</sup>

### Parkinsonism

Manganism is one of the most typical forms of parkinsonism in Korea. Chronic excessive exposure to manganese can affect the globus pallidus, resulting in parkinsonian signs and symptoms, sometimes with psychiatric features. The mechanism un-

derlying this response to manganese exposure is not clear; however, it is suggested that an initial insult to the globus pallidus during manganese neurotoxicity can result in increased activity in the subthalamic nucleus, which is normally under tonic inhibition by the globus pallidus in the basal ganglia circuitry.<sup>20</sup> Diagnosis of classical manganism requires a history of occupational manganese exposure, typical neurologic findings such as bradykinesia, rigidity, and postural instability, and exclusion of other neurologic diseases related to the basal ganglia, such as Parkinson's disease (PD), and secondary parkinsonism due to traumatic, vascular, or iatrogenic damage, or atypical parkinsonism syndromes.<sup>21</sup>

The differential diagnoses of this disorder can be summarized using clinical features and neuroimaging data (Table 1).<sup>21,22</sup> The pathological lesions caused by manganism are typically degenerative lesions of the globus pallidus, with less-frequent and less-severe injury to the substantia nigra (SN). However, the SNc is typically involved in patients with PD, whereas the pallidostriatal complex is spared.<sup>23</sup>

A manganese-induced, bilateral and symmetrical increase in signal intensity, confined mainly to the globus pallidus, can be observed on T1-weighted MRI, but no alterations are typically seen on T2-weighted MRI or computed tomography (CT) scans. Increased signals on T1-weighted MRI were observed in asymptomatic manganese-exposed workers as well as in patients with experimental or occupational manganese poisoning.<sup>6,24,25</sup> However, the increased signal intensities generally resolve 6-12 months after the cessation of manganese exposure.<sup>25,26</sup> Thus, a high T1 signal on MRI may reflect the target organ dose of recent occupational manganese exposure, but not necessarily manganism in the spectrum of manganese symptomatology.<sup>27</sup>

At lower exposure levels, less-severe, subtle, and preclinical neurobehavioral effects have been widely reported in various occupational and environmental settings.<sup>28,29</sup>

Six typical cases of manganism were reported for the first

time in Korea in 1991.<sup>30</sup> The patients were workers at a factory that employed approximately 20 people and had prepared manganese powder for welding rods by crushing ferromanganese. They were exposed to manganese at a level of approximately 2.1 mg/m<sup>3</sup>.<sup>31</sup> The six workers had complained of parkinsonian symptoms that could be differentiated from PD; gait disturbance (especially backward gait), postural instability, and dystonia were prominent.<sup>30,32</sup> One of the patients, who had worked in the factory for 1 year but had resigned more than 10 years previously owing to tremors and gait disturbances, showed normal <sup>18</sup>F-6-fluorodopa uptake on positron-emission tomography (PET) without a high signal on MRI. Normal fluorodopa PET results were similar to those of previous findings.<sup>22,33</sup> The patient had negative MRI results because the exposure to manganese had ceased more than 10 years previously. These patients were probably exposed to moderate levels of manganese, in contrast to poisoned miners who developed psychosis due to exposure to manganese at levels of up to several hundred milligrams per cubic meter.<sup>34,35</sup> These cases also contrast with those of welders' parkinsonism, who were exposed to low levels of manganese (up to approximately 0.5 mg/m<sup>3</sup>).<sup>6</sup>

Several welders were recently compensated for manganism in Korea.<sup>26,36</sup> These welders exhibited the typical clinical features of PD, such as unilateral rigidity, tremor (predominant resting tremor), bradykinesia, (less-predominant) gait disturbance, and a persistent response to L-dopa. They were concurrently exposed to manganese, which raised concerns about whether chronic exposure to low levels of manganese induces PD.<sup>26,36</sup> In fact, PD is not a single disease, but rather a heterogeneous group of clinically similar conditions. It is possible that some individuals have neurotoxin-related PD; however, these cases are likely to have been overlooked because most cases are not attributable to neurotoxin exposure. The development of PD in the group of welders shows that Korea is confronting a new class of possibly toxicant-related neurodegen-

**Table 1.** Comparison of the features of manganism and PD

Feature	Manganism	PD
Bradykinesia/Rigidity	Typical	Typical
Symmetry	Symmetric	Asymmetric
Resting tremor	Less frequent, mainly action tremor	More frequent
Dystonia	More frequent	Less frequent
Gait disturbance	More frequent	Less frequent
Gait	Cock-walk	Festinating gait
Propensity to fall backward	Typical	Not typical
Response to L-dopa	Poor response	Good response
Signal intensities in globus pallidus in T1-weighted MRI	Bilaterally increased*	Normal
DAT SPECT/Fluorodopa PET	Normal	Markedly decreased

\*A negative MRI signal can occur if manganese exposure ceased at least 6 months previously. PD: Parkinson's disease, DAT SPECT: dopamine transporter-single-photon-emission CT.

erative disorders that differ from typical manganese-poisoning cases. However, whether manganese exposure induces PD or affects the progress of this condition remains to be determined.

### Chronic toxic encephalopathy

CTE is an established, internationally recognized condition that results from excessive occupational exposure to solvents via inhalation or skin contact. In 1985, the World Health Organization published diagnostic criteria for CTE caused by exposure to solvents.<sup>37,38</sup> The most recent International Classification of Diseases document (no. 10) defines the terminology (i.e., CTE),<sup>39</sup> and the Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition<sup>40</sup> lists the condition as a form of substance-induced, persistent dementia.

The severity of CTE is graded as I-III or 1, 2A, 2B, and 3.<sup>37,38</sup> Type I CTE and types 1 and 2A CTE include subjective symptoms relating to memory, concentration, and mood. Type II CTE and type 2B CTE are characterized by objective evidence of attention and memory deficit, decreased psychomotor function,<sup>37</sup> or learning deficits<sup>38</sup> on neurobehavioral testing. Detailed occupational and medical histories, as well as standardized neurobehavioral testing, are the cornerstones of the standard diagnostic process. Workers with a history of repeated episodes indicative of acute solvent intoxication (e.g., light-headedness, dizziness, headache, and nausea) over a period of many years, a history of insidious onset of attention, memory, and mood problems, and objective evidence of impairment on standardized neurobehavioral tests (i.e., deficits in attention, memory, learning, or psychomotor function) should be considered as having met the diagnostic criteria for type II CTE or type 2B CTE. Type III CTE and type 3 CTE are often accompanied by neurological deficits and neuroradiologic findings. The MRI findings in patients with CTE are nonspecific, and hence MRI is useful mainly for making a differential diagnosis of CTE, although slight brain atrophy is associated with CTE. Thus, nonsolvent etiologies should be considered if there are major findings on the brain MRI of a patient with suspected CTE.<sup>41</sup>

Follow-up is also important in diagnosing patients with CTE. Subtle changes in mental functioning due to intoxication often go unrecognized unless the clinician specifically assesses these changes using sophisticated neuropsychologic tests.

Several cases of CTE have been reported in Korea (Table 2),<sup>42-47</sup> with a wide spectrum of clinical signs and symptoms. Two-thirds of the reported cases in Korea are relatively severe, whereas in other countries most cases of CTE are type II or 2B.<sup>48</sup> These toxicological differences may indicate that Korean workers are exposed to higher levels of solvents than workers in other countries. The duration of exposure is rather short compared with the Finnish criteria for CTE, which usually constitutes more than 10 years of daily exposure at work.<sup>49</sup> In

Table 2. Reported cases of CTE

Age (years)	Exposure duration (years)	Job	Causative agent	Neurobehavioral test	Clinical feature	Imaging	Reversibility	Severity	Reference
41	1	Painting	Mixed solvent	Abnormal	Impaired memory & cognition	Normal; CT	Persistent	III	42
38	1	Painting	Mixed solvent	NA	Muscle weakness & difficulty in standing	Demyelination; MRI	Persistent	III	43
40	10	Painting	Mixed solvent	Abnormal	Cerebellar dysfunction	No information	NA	III	44
48	8	Degreasing	TCE	Abnormal	Depression	Normal; MRI	Reversible	II	45
43	15	Painting	Mixed solvent	Abnormal	Depression	Normal	NA	II	46
30	4	Painting	Mixed solvent	Abnormal	Cerebellar dysfunction	Normal	NA	III	47

CTE: chronic toxic encephalopathy, NA: not available, TCE: trichloroethylene

addition, Korean clinicians are not accustomed to the new concept of CTE developed in European countries. Therefore, severe cases were reported in earlier years and milder cases (i.e., similar to cases in developed countries) have been reported more recently.

### Cerebellar dysfunction

Gait ataxia, dysarthria, intention tremor, gaze-evoked nystagmus, dysmetria, and adiadochokinesia result from cerebellar dysfunction. Cerebellar dysfunction is a clinical entity that can be differentiated from solvent-induced CTE or carbon-disulfide-induced vascular encephalopathy. Neurotoxin-induced cerebellar dysfunction is sometimes accompanied by other neurologic findings. If a patient presents with cerebellar dysfunction, a detailed history of his or her occupation and exposure to neurotoxins should be obtained.

### Methyl bromide intoxication

Methyl bromide is a highly toxic gas that is used widely as an insecticidal fumigant for dry foodstuffs and can be toxic to both the CNS and the peripheral nervous system.<sup>50,51</sup> Most neurologic manifestations of methyl bromide intoxication occur as a result of inhalation. Chronic exposure can cause peripheral polyneuropathy, optic neuropathy, and cerebellar dysfunction, sometimes with neuropsychiatric disturbances.<sup>50,51</sup> There have been five case reports of methyl bromide intoxication related to fumigation in Korea.<sup>52-56</sup> Two case reports describe the full spectrum of features of the intoxication (e.g., peripheral polyneuropathy, predominantly axonopathy, optic neuropathy, and cerebellar dysfunction).<sup>52,53</sup> There are two other case reports that describe a patient with peripheral polyneuropathy<sup>53</sup> and resultant erectile dysfunction.<sup>54</sup> A subject with polyneuropathy and cerebellar dysfunction showed a high cerebellar signal on MRI.<sup>55</sup> Another patient experienced cerebellar dysfunction only with cerebellar atrophy, as observed on CT.<sup>56</sup> Patients who suffered from seizures and finally died were reported serially.<sup>57</sup> The common prominent features were cerebellar dysfunction (e.g., gait ataxia, dysarthria, intention tremor, gaze-evoked nystagmus, and adiadochokinesia). In these cases, occupational history was vital to the diagnosis of bromide intoxication.

### Organic tin intoxication

Organic tins, such as the dimethyl and trimethyl compounds, are widely used as polyvinyl-chloride stabilizers, catalysts, and biocides.<sup>58</sup> Selective cerebellar dysfunction is most prominent upon recovery from coma due to acute severe organic tin intoxication.<sup>58</sup> One subject experienced selective residual and persistent cerebellar dysfunction such as gait ataxia, dysarthria, intention tremor, gaze-evoked nystagmus, dysmetria, and

adiadochokinesia after he had cleaned a tank containing organic tins. His brain MRI exhibited cerebellar atrophy, compatible with the findings of <sup>18</sup>F-fluorodeoxyglucose PET/CT.<sup>59</sup> Cerebellar ataxia is sometimes accompanied by limbic symptoms such as decreased memory, hallucinations, and disorientation in cases of moderate organic tin intoxication.<sup>60</sup>

It is easy to make a diagnosis of acute organic tin intoxication in patients whose work history and circumstances of exposure are known and whose signs and symptoms are typical and consistent with those reported in the literature.

### Toxic peripheral neuropathy

Most toxic neuropathies cause symmetric effects, with a prominent distal predilection for sensory and motor symptoms (i.e., “stocking-glove” distribution). Large fibers are commonly involved, and reliable early findings include the unequivocal loss of distal vibratory sensations and reduced or absent deep-tendon reflexes. Most toxic peripheral neuropathies are of the axonal type. Unlike segmental demyelination, axonopathy usually presents with normal nerve conduction velocities and decreased amplitude.<sup>61</sup> However, nerve conduction velocities could be decreased with secondary degeneration of the myelin sheath.<sup>61</sup> Toxic peripheral neuropathies are sometimes accompanied by other neurologic or systemic abnormalities, depending on the extent of exposure to the neurotoxicant. The presence of one or more of these clinical findings helps determine the diagnosis. Improvement over time after cessation of exposure is also helpful in confirming the etiology. In the clinical setting, 10-40% of peripheral neuropathy cases are of unknown etiology.<sup>62</sup>

Occupational history is central to a diagnosis of toxic peripheral neuropathy. Table 3 lists the types of toxic peripheral neuropathy cases reported in Korea.

Most cases of toxic peripheral neuropathy in Korea are sensorimotor-type neuropathies of the feet and/or hands. In an outbreak involving n-hexane intoxication,<sup>63</sup> most of the 13 intoxicated workers complained of significant motor weakness as well as sensory disturbances in the feet and hands, consistent with simulated workplace exposure to very high levels of n-hexane. Eight migratory workers with communication barriers who were exposed to high levels of n-hexane also presented with significant motor weakness as well as sensory disturbances in the feet and hands.<sup>64</sup> N-hexane-induced peripheral neuropathy has been known to produce sensorimotor neuropathy with significant motor weakness; however, recent cases of n-hexane-induced peripheral neuropathy predominantly involved sensory disturbances, probably due to low levels of exposure.<sup>7,65</sup> In addition, 2,5-hexanedione, a metabolite of n-hexane, caused toxic peripheral neuropathy, similar to recent mild cases involving n-hexane.<sup>7,65,66</sup>

**Table 3.** Cases of peripheral neuropathy reported in Korea

Age (years)	Job	Chemical	Duration of exposure (years)	NCV	EMG	Clinical features	Reference
15-49*	Glue adhesion (rubber industry)	N-hexane	0.5-3	NA	NA	s/M	63
19-37†	LCD manufacture	N-hexane	0.3-2.6	Sensorimotor axonopathy+myelinopathy	+	s/M	64
57	Cleansing	N-hexane	3	Sensorimotor axonopathy+myelinopathy	NA	S	7
NA	Cleansing	N-hexane	6	Sensorimotor Neuropathy	NA	S	65
26	Cleansing	2,5-Hexanedione	0.25	Sensorimotor Myelinopathy	NA	S	66
30	Acrylamide production	Acrylamide	2	Sensorimotor Axonopathy	+	S/m	67

Methyl-bromide- and carbon-disulfide-induced peripheral neuropathy was already present in each case.

\*13 workers, †8 workers.

s/M: sensory disturbance with significant motor weakness, S: sensory disturbance with mild motor weakness, NA: not available, LCD: liquid crystal display, NCV: nerve conduction velocity.

The clinical features of acrylamide-induced peripheral neuropathy also include sensorimotor-type neuropathies in the feet and/or hands, which were predominantly axonopathy.<sup>67</sup>

## Neurodegenerative diseases

### Amyotrophic lateral sclerosis

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease with an annual worldwide incidence of 2-4 cases per 100,000 individuals.<sup>68</sup> A few cases have been reported in Korea.<sup>69,70</sup> The association between ALS and exposure to solvents or lead is unclear, with even the best-designed incidence studies producing conflicting results.<sup>71-73</sup>

### Other neurodegenerative diseases

PD was dealt with under the manganism section above, and Alzheimer's disease, the commonest neurodegenerative disease, has not yet been compensated or reported in Korea.

## Other neurologic disorders

### Inorganic mercury poisoning

Inorganic mercury poisoning has been known to produce general weakness, tremors, and neuropsychiatric symptoms such as irritability, poor concentration, anxiety, depression, and emotional lability. These signs and symptoms differ from those caused by organic (methyl) mercury intoxication, which results predominantly in cerebellar manifestations. The symptoms and signs of inorganic mercury poisoning are mimicked by other psychiatric disorders.<sup>74</sup> In Korea, occupations that involve exposure to inorganic mercury include fluorescent lamp or thermometer manufacturing, and industrial waste recycling.<sup>75-77</sup>

### Multiple sclerosis

Many factors, including both genetic and environmental, have been suspected of being associated with multiple sclerosis. Among environmental exposures, sunshine, mean annual temperature, and intake of vitamin D are protective of multiple sclerosis.<sup>78</sup> Conversely, infection with certain viruses, nonbiological factors such as exposure to selected heavy metals or organic solvents, hazardous wastes sites, outdoor air pollutants, and food consumption were found to be associated with higher rates of multiple sclerosis in certain study populations.<sup>78</sup> There are case reports linking solvents or heavy metals to multiple sclerosis in other countries,<sup>79,80</sup> and a few compensated cases due to heavy metal or solvents in Korea were confirmed by the electronic database of COMWEL. However, whether solvents or heavy metals are indeed risk factors for multiple sclerosis has yet to be established.

## Conclusion

CTE, vascular encephalopathy, cerebellar dysfunction, parkinsonism, peripheral neuropathy, and neurodegenerative diseases are commonly encountered presentations of occupational neurotoxic syndromes in Korea. Few neurotoxins cause patients to present with pathognomic neurologic syndromes. The symptoms and signs of occupational neurologic disorders may be mimicked by many psychiatric, metabolic, inflammatory, neoplastic, and degenerative diseases of the nervous system. Detailed neurologic examinations and categorization of the clinical manifestations of neurologic disorders will assist in the diagnosis of occupational neurologic diseases. Physicians must be aware of the typical signs and symptoms of possible exposure to neurotoxins, and they should also pay attention to less-typical, rather-vague symptoms and signs in workers because the toxicologic characteristics of occupational neurologic diseases in Korea have changed from typical patterns to less-typical or equivocal patterns. This shift is likely to be due to several years of low-dose exposure, perhaps combined with the effects of aging, and new types of possibly toxicant-related neurodegenerative diseases. Therefore, taking a patient's comprehensive work history is essential to making a diagnosis of occupational neurologic disease, especially in subjects who may have been exposed to low doses. Close collaboration between neurologists and occupational physicians is needed to determine whether neurologic disorders are work-related.

### Conflicts of Interest

The authors have no financial conflicts of interest.

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