The New Occupational Neurotoxins: Are They for Real?

All of us have had, from time to time, what my mother-in-law refers to as a "senior moment." Whether it is missing an exit on a highway we have taken a hundred times previously, briefly forgetting the name of a loved one, being unable to recall the spelling of a common word, or simply forgetting how to do something which we could perform effortlessly in years past, we all experience memory lapses.

Similarly, we routinely experience a plethora of behavioral and constitutional symptoms such as depressed mood, irritability, headache and fatigue. And, from time to time, we may have trouble with our ability to perform on various tests, learn new things, or successfully complete in a timely manner common, everyday work tasks. Anyone who has had a couple of beers can easily identify the acute symptoms of intoxication. Many others who *did* inhale will also recognize other altered behavior, sensation and cognitive functions.

Over the past several decades, there has been increasing interest in neurotoxic effects, primarily long-term problems from potential workplace, consumer product and environmental exposures. In 1990, the U.S. Congress' Office of Technology Assessment reported that relatively few of the thousands of chemicals in the stream of commerce had been adequately tested for neurotoxicity. It has been estimated by one researcher that 3 to 5 percent of chemicals have neurotoxic potential. Legislative and regulatory actions in this area have been limited, although the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and EPA's activities in handling pesticides are prominent exceptions.

Neurotoxins Old and New

Neurotoxins can affect both the central nervous system and the peripheral nerves. Some of the more well-known neurotoxins include metals, such as lead and mercury. Lead, for example, can lead to extensor motor paralysis in the forearm (a peripheral nerve effect) and also–in high doses–produce acute encephalopathy and eventually death. Mercury causes dementia, *i.e.*, "Mad as a Hatter." Arsenic can produce a peripheral neuropathy, potentially causing a permanent loss of nerve functioning in certain extremity nerves. Wood alcohol, in sufficient, doses will produce blindness, while manganese exposure is associated with a Parkinsonian-like presentation. Various drugs and plants are hallucinogenic.

More recently, complaints have arisen surrounding such unlikely candidates as poor indoor air quality, fragrances (cacosmia: exaggerated response to odors) and routine building pesticide applications. Such complaints have also alleged exposure to electromagnetic fields and biologic agents, including allergic sensitizers. These newer complaints differ from the more severe and well-recognized problems in that frequently all one has to go on are a wide range of vague complaints and the puzzling results of neuropsychological test batteries.

For these new complaints, many questions remain unanswered. What substances produce neurotoxic effects? What levels of which substances produce acute effects? Chronic effects? Are short-term, high-exposure effects reversible? Is there an effect from long-term, high-exposures? Is it permanent? Is there an effect from long-term, low-level exposures ? Does it last?

Do poor indoor air quality, fragrances and routine building pesticide applications cause neurotoxic effects?

Determining a Threshold Dose

Many of the questions center around exposure to commonly used solvents and other concerns such as indoor air pollution. There is evidence that long-term high exposures can produce debilitating neurotoxicity, such as in glue sniffers who receive massive toluene exposures. But the extent to which lower level exposures produce effects is unclear. That is: what is the threshold dose?

Does one have to become "high" and consistently exposed at that level for chronic health problems to occur? Researchers looking at painters in Europe in the 1970s and 1980s reported a number of symptoms and abnormal neuropsychometric test results. In the case of lead exposure in children, some experts have opined that there is no safe dose and that doses over 50 percent lower than what was the average exposure in the United States in decades past produce IQ, behavioral and other neurotoxic effects which are alleged to be irreversible. Other substances, such as ethylene oxide, have been reported under the Toxic Substances Control Act to produce neurobehavioral effects.

While the effects appear reversible, complaints reportedly may take many months or even a year or two to fully resolve, depending on the exposure. NIOSH scientists have reported that, in general, acute solvent neurotoxicity is short-lived.

By Howard M. Sandler, M.D.

Testing

Many neuropsychological tests have been developed over the years to measure brain dysfunction. A number of these tests have been validated. Traditionally performed by clinical neuropsychologists, these tests were first used to identify and shape rehabilitation for problems following stroke, head trauma and other CNS problems. They can grossly identify areas of the brain affected, as well as assess the relative level of dysfunction. In the neurotoxicity area, their use is much more recent.

Some test batteries were devised specifically for the study of neurotoxic effects and focus on visuospatial function, memory and other particular CNS functions which have been potentially identified as neurotoxic in nature. To date, neuropsychological tests have not been routinely used for purposes of medical monitoring and surveillance in the workplace. There are numerous limitations and problems with these tests which limit their usefulness in the evaluation of workers' compensation and litigation cases.

Neuropsychological tests address a range of functional performance areas:

- Grip strength
- Intellectual processes, *e.g.*, verbal and performance
- Receptive and expressive speech
- Sensory perception, *e.g.*, tactile, auditory, visual
- Short and long-term memory
- Emotional functioning
- Attention and concentration
- Academic abilities

In assessing whether a worker suffers from neurobehavioral effects, there are many testing considerations:

- Choosing the right test battery;
- Correlating symptoms and reported functional deficits;
- Predicting the worker's pre-exposure functional level;
- Utility of objective tests such as MRI, CT, NCV, or EEG;
- Accounting for confounders, such as patient psychiatric state or drugs;
- Appropriate examiner interpretation;
- Testing environment, instructions and methodology.

One of the more difficult problems is interpretation of test results for a given individual. Most of us will score poorly on one or more tests or subtests within a validated battery. As test results are dependent on subject effort, motivation, and other factors, it is left to the examiner to assure the validity of the test as well as the impact of other factors which can account for test result abnormalities.

These factors include failure to explain or understand test instructions, fatigue, anxiety, depression, malinger-

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ing and hysteria. Other factors include litigation, ethnicity/culture, native language, attentional difficulties, alcoholism and substance abuse. Still others involve low blood sugar, time of day, antagonism toward examiner, underlying medical/neurological disorders, emotional stressor, pain, allergies, or a history of head trauma.

Once results are tallied, the clinical neuropsychological assessment must be performed in context with other factors ranging from childhood development to medical history to observations of coworkers and family members.

These limitations also greatly impact the ability to interpret the test results of a group of workers. For example, what do these tests mean in regard to everyday functioning? It is hardly surprising that severity is often increased in the litigation setting, where motivation, depression or the stress of legal involvement may account for all or part of the abnormal test findings. This difficulty is underscored by the vast difference in test results frequently found between the examining neuropsychological experts.

Be Aware

While formal testing for neurotoxic effects should not be a routine part of preventive occupational health practice, safety and health staff should become familiar with:

- Potential neurologic agents in their workplace;
- Need to monitor possible exposures to such agents;
- Recognition of potential relationship of injury to neurotoxicity, *e.g.*, loss of attention due to narcosis;
- Strengths and limitations of neurological and neuropsychological testing tools; and
- Need for appropriate individual testing or group screening.

It is critical to note that the ability to "test for" outstrips our current understanding of what the results of various neurological testing means. For example, certain clinicians employ neuro-ophthalmologic testing or SPECT scans or other sophisticated approaches in assessing patients. Such tests frequently have limited assessment potential, *e.g.*, cerebral blood flow. None of these tests are specific for neurotoxic effects. Over all, they should be utilized only in a research capacity for workplace and environmental exposure investigations.

While many workplace agents have the potential to affect the nervous system, we are a long way from understanding and documenting the impact of such exposures. Areas for research include effect type, effect reversibility, dose, objective testing capabilities and differentiation of neuropsychological effect etiologies. Careful research will help prevent neurotoxic exposures, prevent unnecessary concern and manage current neurotoxicity problems. OH

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