Other drugs acting synergistically with dopa include anticholinergics such as trihexyphenidyl hydrochloride and benztropine mesylate. Amantadine hydrochloride may have both short- and long-term benefits, particularly for tremor.

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Electrodiagnosis of Neuromuscular Disorders

ELECTRODIAGNOSTIC TECHNIQUES can be of help in the diagnosis, management, and prognosis of neuromuscular syndromes. Motor nerve conduction is determined by recording the compound muscle action potential, usually from a small intrinsic hand or foot muscle, while the nerve is stimulated at two locations. The distal latency reading is subtracted from the proximal latency reading and the difference divided into the distance measurement. Abnormal latencies and waveforms may indicate axonal loss or the presence of nerve conduction block resulting from demyelination and assist in locating the site of such abnormalities.

The F wave, resulting from electrical stimulation of the motor nerve, is an example of a "late response." It occurs when an antidromically conducted action potential reaches the motoneuron and is fired back out to the periphery. Prolonged latencies of late responses when nerve conduction is normal indicate the presence of proximal neuropathy, usually demyelination (acute Guillain-Barré syndrome). The F wave is conducted over the ventral root and is not a reflex. In some muscles, such as the soleus or flexor carpi radialis, it is possible to record the H reflex, which results from the activation of muscle spindle afferents. The H reflex uses the spinal monosynaptic reflex requiring the dorsal root. Disorders selectively involving the dorsal root can be detected by comparing the F-wave and H-reflex responses.

Sensory nerve action potentials are recorded from the skin or by near-nerve needle recording. Cerebral and spinal evoked potentials can also be recorded after nerve stimulation. These potentials often require signal averaging to record. The technique permits an investigation of disorders of the sensory nerve affecting large myelinated fibers and connections to cerebral cortex.

A repetitive stimulation of motor nerves while recording the compound muscle action potential (CMAP) is used to evaluate neuromuscular transmission. A decline in the amplitude of the CMAP at slow rates of stimulation indicates a postsynaptic defect; the reduced amount of acetylcholine produced following each nerve impulse finally falls below the level sufficient to activate some muscle fibers. A presynaptic defect, as seen in botulism or the Lambert-Eaton syndrome, causes an increase in amplitude with high rates of stimulation (> 10 Hz) as the release of acetylcholine is facilitated by increased levels of extracellular calcium associated with repetitive stimulation. The amplitude of the CMAP from a condition of rest is below normal.

A quantitative analysis of the amplitude, duration, and waveform of the motor unit action potential recorded by a needle electrode can be used to detect signs of motor unit loss, denervation, reinnervation—early and late—and muscle fiber loss. This technique can characterize the extent and severity of neurogenic atrophy as well as of myopathy.

The single-fiber electrode records the potentials of single muscle fibers from within a small electrode recording area. Two or more muscle fiber potentials can be recorded from within the same motor unit. By triggering the sweep of an oscilloscope with the single-fiber potential and delaying the display of action potentials, the synchrony of the firing of fibers and their density within the motor unit can be determined. Such studies are helpful in diagnosing disorders of the neuromuscular junction when the results of other studies are normal.

The latency and amplitude of reflexes can be used to assess central connections important for the reflex and the integrity of each limb. For example, the blink reflex can be used to evaluate an oligosynaptic ipsilateral response of orbicularis oculi muscle in response to stimulation of the trigeminal nerve, as well as a polysynaptic, bilaterally represented later response with pathways in the pons and medulla. Combined with motor conduction studies of the seventh nerve, lesions within the pons can be differentiated from those affecting one limb of the reflex.

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Nervous System Effects of Toluene and Other Organic Solvents

ORGANIC SOLVENTS are industrial compounds that produce neurologic syndromes related to both acute and chronic intoxication. Because hundreds of new organic compounds are introduced each year, many previously unsuspected toxic effects have been recognized. Solvents are highly lipophilic, which explains their distribution to organs rich in lipids, such as the brain. Although extremely high concentrations of all volatile organic solvents produce nonspecific effects, such as encephalopathy, many of these solvents produce relatively specific neurologic syndromes with lower level, longer term exposure. Long-term or persistent specific effects on the nervous system vary with the duration of exposure and whether the central nervous system (CNS) or the peripheral nervous system is primarily affected.

Long-term exposure to the aliphatic hydrocarbons, such as *n*-hexane and methyl butyl ketone, is typically associated with the development of peripheral neuropathy. Animal models developed using these compounds are classic examples of target-organ toxicity affecting the peripheral nervous system. The aromatic hydrocarbons, such as toluene, have been known to cause both acute and chronic CNS toxicity in humans for more than two decades, but because of the lack of an animal model of neurotoxicity and the small number of human cases, understanding the pathogenesis of the CNS effects of toluene has only come recently.

Toluene is the most widely used of the organic solvents

and is a major component in many paints, lacquers, glues and adhesives, inks, and cleaning liquids. As with other solvents, inhalation is the major route of entry, though some absorption occurs percutaneously. Of all the solvents, toluene seems to have the highest potential for abuse, and recent studies of habitual inhalant abusers of toluene-containing products have begun to shed light on its chronic CNS effects.

Acute intoxication with toluene produces euphoria, giddiness, and a cerebellar ataxia. Higher levels of exposure will lead to progressively greater degrees of a nonspecific encephalopathy. With long-term abuse (usually ten years or more of daily use), neurologic impairment will develop in almost two thirds of abusers. Neurologic abnormalities vary from mild cognitive impairment to severe dementia, typically associated with other neurologic signs such as cerebellar ataxia, corticospinal tract dysfunction, oculomotor abnormalities, tremor, deafness, and hyposmia. Cognitive dysfunction is the most disabling and frequent feature of chronic toluene toxicity and may be the earliest sign of permanent CNS injury. A recent magnetic resonance imaging and neuropathologic study of long-term toluene abusers has shown evidence of diffuse CNS white matter changes, suggesting that the primary effect of toluene may be on CNS myelin or myelin-producing cells.

While it is now clear that habitual toluene abuse leads to permanent multifocal CNS injury from effects on white matter, it is less obvious what happens in industry, where workers have exposure to much lower, presumably "safe," levels of toluene and other solvents. Exposure to solvents in the workplace is a particularly common situation. Unlike exposure in cases of abuse, where dramatic clinical neurotoxicity is seen following high-level acute and chronic exposures, studies over the past two decades, primarily from Scandinavia, report a syndrome that develops after low-level chronic exposure. This syndrome has been called the "psycho-organic syndrome" primarily because of the nonspecific nature of the signs and symptoms. The most common symptoms of the syndrome are poor memory, headache, fatigue, concentration difficulties, and personality changes (irritability, depression, emotional lability). The results of the neurologic examination in these persons, as well as neuroimaging and neurophysiologic studies, are normal. Only extensive neuropsychological testing has suggested cognitive dysfunction. Athough these initial studies were uncontrolled, nonrandomized, and unblind, the psycho-organic syndrome was widely accepted as a clinical illness and soon became a major problem for industry, the legal profession, and physicians. Recent studies, however, have cast doubt as to whether or not the syndrome exists. Several recent, well-designed studies, including one by the Danish group that first reported this condition, have shown no neuropsychological differences between workers with or without exposure to solvents.

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Peripheral Neuropathy Associated With Human Immunodeficiency Virus Infection

PERIPHERAL NEUROPATHIES occur in a third or more of patients with human immunodeficiency virus (HIV) infection, with the most common type being distal axonal polyneuropathy in patients with the acquired immunodeficiency syndrome (AIDS). Three other types of peripheral neuropathy are also widely recognized: inflammatory demyelinating polyneuropathy, mononeuropathy multiplex, and progressive lumbosacral polyradiculopathy.

In patients with distal axonal polyneuropathy, sensory symptoms typically develop in the feet as the initial complaint. While a third of patients with AIDS have mild distal numbness or paresthesias, 10% of patients with constitutional symptoms from HIV infection—more often AIDS than AIDS-related complex—present for a neurologic evaluation of painful feet. Depressed or absent tendon reflexes only at the ankle and a decreased perception of sensation in the feet are the predominant abnormalities detected on examination. Although rarely a complaint, mild distal weakness may be present. Nerve conduction studies show decreased amplitude of sensory nerve action potentials as the predominant abnormality, but mild slowing of sensory and motor conduction velocity may also be found. Although patients treated with azidothymidine and other patients without treatment have rarely improved, the condition of most patients continues to worsen despite treatment with azidothymidine, prednisone, or plasmapheresis. Treatment is symptomatic, with the use of tricyclic antidepressants often reducing the severity of pain. The pathogenesis of this neuropathy is unknown, with possible causes including nutritional deficiency, drug toxicity, and infection.

Patients with inflammatory demyelinating polyneuropathy have weakness either acutely—with the clinical features of the Guillain-Barré syndrome—or chronically. In addition to weakness that includes proximal muscles, tendon reflexes are absent. Sensory symptoms and signs are minor. Electrodiagnostic studies provide evidence for an acquired demyelinating polyneuropathy, with severely reduced conduction velocities, multifocal conduction block, or both. Either of these polyneuropathies may be the initial symptom of a patient with undiagnosed HIV infection, so cerebrospinal fluid (CSF) pleocytosis in a patient with inflammatory demyelinating polyneuropathy suggests the need to determine the HIV antibody status. Nerve biopsy specimens reveal segmental demyelination and mononuclear cell infiltration, and an autoimmune pathogenesis is generally accepted. These polyneuropathies usually respond well to treatment with plasmapheresis, either alone in the acute form or possibly together with the use of prednisone in the chronic form.

Patients with mononeuropathy multiplex and HIV infection typically present with multifocal sensory loss that is more prominent than weakness. Cranial nerves, particularly the trigeminal and facial, may be involved. Patients with this neuropathy typically have constitutional symptoms and other features of AIDS-related complex. Electrodiagnostic studies usually provide evidence for axonal degeneration that varies in severity in different nerve distributions. Nerve biopsy specimens contain perivascular and endoneurial inflammatory cell infiltrates and confirm axonal degeneration; an autoimmune pathogenesis is generally accepted. The neuropathy spontaneously remits in half of patients. Some with progres-