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-

sion respond to plasmapheresis or prednisone therapy, with or without the additional features of a chronic inflammatory demyelinating polyneuropathy developing. The remaining patients with progression go on to have more confluent distal symptoms and signs typical of distal axonal polyneuropathy and do not respond to immunotherapies.

Progressive lumbosacral polyradiculopathy occurs predominantly in patients with AIDS. Progressive weakness, numbness, and pain of the legs develop subacutely along with impaired sphincter control. A CSF examination is the most important diagnostic test. In polyradiculopathy due to cytomegalovirus (CMV) infection, the CSF typically has a polymorphonuclear pleocytosis (0.5×10^6 per liter or greater), a low glucose level, and an elevated protein content. Ascending paralysis typically leads to death within two months, but early treatment of CMV polyradiculopathy with ganciclovir has been effective in at least some cases. In one patient with a positive CSF VDRL, antibiotic therapy was curative for a syphilitic polyradiculopathy. Other patients have presented with similar neurologic symptoms and signs but with a CSF that had fewer cells and from which CMV could not be cultured. Some of these patients have had lymphomatous cells on CSF cytologic examination, and these patients have died. Others with normal cytologic findings have shown either continued progression or spontaneous remission; the cause in these cases is unknown.

Thus, peripheral neuropathies are common in association with HIV infection, and each type suggests a particular diagnostic and treatment strategy.

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Diagnosing Heavy Metal Intoxication in Patients With Neurologic Signs

NERVOUS SYSTEM SIGNS are common in acute and chronic cases of heavy metal poisoning. These include peripheral neuropathy from lead, arsenic, organic and inorganic mercury, and thallium; mental retardation or dementia from organic and inorganic mercury and lead; psychosis from arsenic and inorganic mercury; encephalopathy with seizures from lead and arsenic; and visual disturbances or ataxia from organic mercury.

Most toxicology laboratories use atomic absorption spectroscopy to analyze specimens for heavy metals. This method can detect common heavy metals, is accurate and quantitative, and can be done on blood, urine, hair, or other tissues. The toxicology laboratory should be informed which heavy metals are suspected because the instrument must be adjusted for each element analyzed. The choice of specimens to submit depends on how recent the exposure was and the duration of the intoxication. In general, blood is the most useful specimen in acute intoxications (within three days), except for arsenic (where, because of arsenic's short half-life, urine is also helpful). For chronic intoxications (weeks to months), urine or hair provides the most useful information.

Care should be taken in collecting specimens to avoid environmental contamination. Whole blood is preferred over serum for heavy metal analysis because metals often accumulate within erythrocytes. The blood specimen should be collected in a heparinized, trace metal-free glass tube. A 24-hour urine specimen should be collected in an acid-washed container (the inside of a plastic or glass container is washed with a solution of 0.1 molar hydrochloric acid, rinsed with distilled water, and then dried). Hair can be used to detect chronic metal intoxications from arsenic and mercury. For the specimen, 50 to 100 strands of scalp hair are cut close to the scalp. The strands are oriented so that the bases of the hairs are together. The bundle of hair should then be cut into thirds and each group of hair strands separately placed into trace metal-free glass tubes that are labeled proximal, middle, or distal scalp hair. A metal measurement of all three specimens will provide an estimation of the duration of the exposure because hair grows about 1 cm per month. Differences in metal content in the three hair sections also decrease the likelihood that the metal accumulation occurred from external environmental contamination, such as from hair washing.

In interpreting heavy metal analyses, it is important to know the normal values from a particular toxicology laboratory. In general, levels that are consistent with significant heavy metal intoxication are at least twofold to threefold above the normal levels for a laboratory. If borderline levels of lead or another heavy metal occur in a patient thought to have chronic intoxication, a diagnostic challenge with calcium disodium ethylenediaminetetraacetate (EDTA) may be considered. In this situation, a baseline 24-hour urine specimen is collected. A second 24-hour urine collection is started and the adult patient is given EDTA, 1 gram in 250 ml of 5% glucose solution given intravenously over one hour. The EDTA dose is repeated 12 hours later. A pronounced increase in the heavy metal content in the second urine collection, usually threefold to fivefold over the baseline specimen, implies substantial exposure to the heavy metal with increased body burden.

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New Strategies in Stroke Treatment

THE INCIDENCE OF STROKE has decreased significantly in recent decades, due largely to a better management of risk factors such as hypertension. This improvement has not been matched by the results of treating acute stroke, which has been directed at restoring or amplifying altered perfusion and preventing the aggregation of formed elements of blood. Using aspirin reduces the incidence of stroke after a transient ischemic attack, ticlopidine hydrochloride use is under study, and other antiplatelet drugs have not been shown to be effective. Heparin and sodium warfarin administration reduces the incidence of cardiogenic emboli but is not beneficial in