

Chronic

Chronic exposure to low levels of cyanide in cigarette smoke has been implicated as causing visual loss in the tobacco-alcohol amblyopia syndrome. However, many of these patients are malnourished and consume large quantities of ethyl alcohol as well, and the role of cyanide in these conditions remains unproven.

There have been many experimental animal studies of the effects on the central nervous system of acute and subchronic cyanide intoxication. Some were undertaken on the premise that, in addition to the classic pattern of hypoxic-ischemic damage to the brain, cyanide induced primary demyelina-

Recent reports by Brierley and colleagues (13) on rats and primates, in which the physiological state of the animals was carefully monitored, have suggested that pure histotoxic damage to neurons does not occur in cyanide intoxication. As a result of Brierley's work, it now seems likely that many of the neuronal changes, previously attributed to a direct effect of cyanide on nerve cell oxidative metabolism, may have reflected hypotension and respiratory depression in moribund animals.

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MANGANESE

Manganese is used in metal alloys and as an antiknock agent in lead-free gasoline. Mining manganese for these purposes has resulted in a high incidence of chronic manganese poisoning in exposed workers. Many thousands of workers may have developed manganese neurotoxicity and, of

300-400 cases from Mexico, Japan, U.S. Republics and the United States reported (3, 84, 115). Manganese ore enters the body where it passes from the stomach and the brain. The metal is rapidly cleared from the body, excreted in the liver, pancreas, and kidneys principally in mitochondria. Manganese excretion is increased in workers as compared with normal (84). Clinical signs appear in the brain after 6 months to 24 months (manganese poisoning disease, last for 1-3 months). Symptoms include hallucinations, emotional lability, and aberrant behavior. Neurological signs appear later as generalized tremor, slurred speech, and headache. Sexual impotence may occur. Gait is shuffling, impaired coordination, increased muscle tone, and associated movements, tremor. These nonprogressive signs are akin to Parkinson's disease. Permanent. Rigid and hypokinetic. Response to L-dopa therapy and levodopa therapy, facial expression, and me- improves patients with movement was noted in treated with 5-hydroxytryptophan. Prominent pathologic changes in the brain include: damage to the globus pallidus, subthalamic nucleus, and putamen (5). No autopsy and none has attempted neuropathological correlation.

Methanol is a colorless liquid with a boiling point of 65°C. It is a polar solvent, unlike nonpolar solvents as well as being readily metabolized in the body to formic acid.

Methanol is used as a
manufacture of formal
stoves and ovens.

The most common cause of methanol poisoning has followed "moonshine" (58). Acute headache, acidosis, mydriasis, respiratory failure, and treatment is reversal of methanol by intravenous administration of

swelling and scattered small subarachnoid hemorrhages. Individuals who survive the acute episode may be left with residual damage to the CNS resulting from anoxic or hypotensive injury to the brain.

Chronic

There is strong evidence linking chronic exposure to dietary cyanide to the development of an ataxic neuropathy syndrome described in poorer class Nigerians (86, 101). These individuals subsist on food that includes large amounts of cassava, the tuber of the manioc shrub, and other plants known to contain cyanogenetic glycosides. This diet results in significantly elevated plasma thiocyanate levels. Many are also riboflavin deficient and generally in poor health. The disease is slowly progressive and rarely fatal. Initial complaints are painful paresthesiae of the feet followed by numbness in the hands. As the illness progresses, visual loss, diminished hearing, weakness of the lower extremities, and a broad-based ataxic gait appear. Loss of sensation and weakness often have a distal, symmetrical, stocking-glove distribution, and proprioceptive deficits may be severe in the lower extremities. Ataxia is present only in the lower extremities, and probably reflects sensory loss rather than cerebellar involvement. Optic atrophy and visual impairment are prominent features of the illness. Cochlear-type hearing loss is sometimes present but vestibular impairment has not been reported. Nerve conduction is abnormal in the lower extremities. Occasional individuals display signs of corticospinal tract involvement. There have been no postmortem reports or experimental animal models of this condition, and the clinical data permit only a limited clinical-pathological correlation. The symmetrical polyneuropathy, and resemblance of the CNS signs to those of the spinocerebellar degenerations, indicate that the Nigerian syndrome most likely is a distal axonopathy. Plasma thiocyanate levels are significantly elevated in these individuals.

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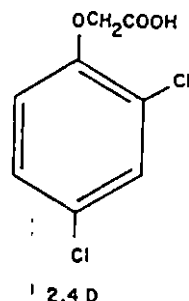
EXPERIMENTAL ANIMAL STUDIES

There have been many experimental animal studies of the effects on the central nervous system of acute and subchronic cyanide intoxication. Some were undertaken on the premise that, in addition to the classic pattern of hypoxic-ischemic damage to the brain, cyanide induced primary demyelina-

tion. Definitive ultrastructural studies by ... and colleagues (63) have dispelled this notion, and indicate that the myelin changes induced in the corpus callosum of rats by cyanide are secondary to axonal degeneration. Furthermore, Levine (76) has suggested that the localization of degeneration to the corpus callosum may reflect a pattern of hypoxic damage and vascular insufficiency.

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2,4-DICHLOROPHENOXY ACETIC ACID



2, 4-Dichlorophenoxy acetic acid (2,4-D) was introduced as a herbicide in the early 1950s. In 1959, Goldstein and co-workers (44) described neurotoxicity in three individuals exposed to the compound by skin contact. Symmetrical polyneuropathy appeared approximately 1 week after exposure. Both motor and sensory deficits occurred initially in the extremities. The lower limbs were affected to a greater extent than upper limbs. Partial recovery was observed over a period of many months. Foisac-Gegoux and co-workers (37) described unilateral sensory loss in the face following 2,4-D exposure. No pathological or experimental animal studies of 2,4-D neurotoxicity have been performed to date.

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300-400 cases from Mexico, Japan, Uruguay, and the United States have been reported (3, 84, 115). Manganese ore enters the body when it passes from the lungs to the blood stream and the brain. The half-life of manganese is rapidly cleared from the body. Manganese is excreted primarily in the urine, but also in the feces. Manganese excretion is increased in healthy workers as compared to those with chronic manganese intoxication (84). Clinical signs appear in humans after exposure for 6 months to 24 months (manganese poisoning), last for 1-3 months, and include hallucinations, emotion lability, and aberrant behavior. Neurological signs appear later as generalized tremor, slurred speech, and head tremor. Impotence may occur in severe cases, and a shuffling gait, impaired coordination, increased muscle tone, and associated movements, tremor, and rigidity. These nonprogressive signs are akin to Parkinsonism. Rigid and hypokinetic features respond to L-dopa therapy and levodopa therapy improves patients with chronic manganese poisoning. Movement was noted in patients treated with 5-hydroxytryptophan. Prominent pathological changes include: damage to the globus pallidus, subthalamic nucleus, and putamen (5). No one has attempted a neuropathological correlation.

METHANOL

Methanol is a colorless liquid with a boiling point of 65°C. It is a nonpolar solvent as well as a readily metabolized in the body to formic acid.

Methanol is used as a fuel in the manufacture of formaldehyde, and in stoves and ovens.

The most common cause of methanol poisoning has followed "moonshine" (58). Acute symptoms include headache, acidosis, mydriasis, respiratory failure, and coma. Treatment is reversal of the toxic effects by venous administration of