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Spencer + Shaumberg -

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 parasthesiae 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.

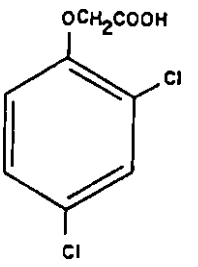
Chronic exposure to low levels of cyanide in cigarette smoke has been implicated as causing visual loss in the tobacco-alcohol amblyopia syndrome. However, many of these patients are malnourished and consume large quantities of ethyl alcohol as well, and the role of cyanide in these conditions remains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

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 demyelination. Definitive ultrastructural studies by [illegible] 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.

Recent reports by Brierly 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.

2,4-DICHLOROPHENOXY ACETIC ACID



2,4 D

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. Foissac-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.

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 manganesium neurotoxicity and, of

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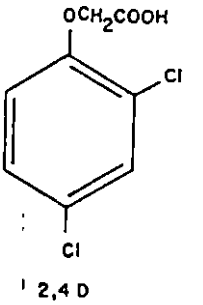

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