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Neurological syndromes produced by some toxic metals encountered industrially or environmentally

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The most important toxic metals affecting the nervous system are classified according to predominant type of disorder resulting from exposure.

I) Peripheral neuropathy:
1 – Arsenic, 2 – Lead
3 – Some organophosphates, 4 – Thallium

II) Encephalopathy:
1 – Lead

III) Optic neuritis:
1 – Arsenic, 2 – Thallium

IV) Cerebellar disturbance:
1 – Organic mercury

V) Parkinsonism:
1 – Manganese

VI) Mental changes:
1 – Tetraethyl lead
2 – Mercury

I – Peripheral neuropathy

1. Arsenic

Accidental exposure to insecticides and weed killers containing arsenic causes a number of deaths every year. Gastrointestinal symptoms are prominent within 6 hours of acute poisoning and death may occur at this stage. Peripheral neuropathy may develop after an interval of 1–3 weeks. Sensory symptoms occur first with burning sensations in the extremities, cutaneous sensations are impaired in a stocking or glove distribution, and tendon and planter reflexes are lost (8).

In chronic poisoning, neuropathy progresses gradually. In mild cases recovery is complete, but slow. Little further improvement can be expected after a year. BAL (British Anti-Lewisite) is the treatment of choice. It is effective in preventing or reversing non-neurological manifestation of arsenic poisoning. However, its efficacy in preventing neuropathy after

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acute poisoning is doubtful. Although there is a latent interval before symptoms develop, neuronal changes leading to neuropathy probably occur early and before BAL can be given. In chronic poisoning, treatment can prevent further deterioration.

2. Lead

Chronic poisoning by inorganic lead in adults leads to anaemia, colic and in more severe cases peripheral neuropathy. Neuropathy is entirely motor and predominantly affects the most exercised muscles. These are frequently the finger and wrist extensors. Weakness is commonly bilateral, but one side is affected before the other (2). Neuropathy reaches its maximal intensity within several days or weeks. With removal of exposure and institution of proper treatment complete or nearly complete recovery takes place. For treatment, many chelating agents can combine with lead, but D-penicillamine given orally is the least toxic of these.

3. Some organophosphates

Poisoning usually occurs following accidental ingestion of a single dose, and triorthocresyl phosphate has been the substance most usually implicated.

Most organophosphates have an acute anticholinesterase effect producing headache, abdominal pain, vomiting, sweating, miosis, muscular twitching and convulsion. The neurotoxic organophosphates, for example TOCP, DFP (diisopropyl-fluoro-phosphate) and mipafox, also produce different and delayed neurological effects. A latent interval of 10 to 20 days occurs after exposure before neurological symptoms begin. Distal sensory disturbances occur first, followed by limb weakness, beginning distally. Symptoms may progress for about a month. Damage occurs to both peripheral nerves and spinal cord. During the acute stage, peripheral neuropathy dominates the clinical picture, but recovery is usually only partial and residual signs are mainly due to spinal cord damage.

Atropine in large doses is important in controlling acute anticholinesterase effects. 2 mg should be given intramuscularly or subcutaneously and repeated if necessary. Cholinesterase reactivators, for example 2-pyridine aldoxime methiodide (PAM), 1 g intravenously should be given in severe cases. There is no specific antidote for the delayed neurotoxic effects.

4. Thallium

Acute poisoning occurs with symptoms of gastrointestinal irritation symptoms, followed by numbness and weakness of extremities within 2 to 5 days. Delirium, convulsions, cranial nerve palsies and blindness may also develop.

In the chronic form, alopecia and optic neuritis or generalized polyneuritis are the commonest symptoms, Paraesthesia in extremities, motor weakness, loss of reflexes with little or no impairment of cutaneous sensibility are characteristic of thallium polyneuropathy. Complete recovery of polyneuritis is the rule in the chronic form (16).

II – Encephalopathy

1. Lead

Lead poisoning in children usually causes encephalopathy. Anorexia and irritability are followed by ataxia and vomiting. Within few days convulsive fits of focal or generalized nature may occur. Any type of neurological signs may develop, including cerebellar ataxia, hemiplegia or decerebrate rigidity. Facial or oculomotor paralysis may appear. Temperature is normal but hyperpyrexia with convulsions in terminal stages of the disease. Papilloedema is common, which may end in optic atrophy. Anaemia is usual, as raised CSF protein.

Whereas until recently a mortality of 25 % was to be expected, with active modern treatment, the mortality can be reduced to 5 %. After recovery from the acute phase 25 % have longterm sequelae of fits, mental retardation or behaviour disturbances.

For treatment, rapid removal of lead is of prime importance. A combination of EDTA (ethylene diamine tetraacetate) and BAL, in the maximum safe dose of each, has been recommended (5). More lead is removed this way than when either agent is given alone. Paraldehyde is the safest and most effective drug to control fits in the first few days. The increased intracranical pressure is alleviated by lumbar puncture, hypertonic solutions per rectum or intravenously, or by subtemporal decompression (6, 12, 15).

III – Optic neuritis

1. Arsenic

Usually follows administration of any of the pentavalent arsenicals, particularly tryparasamide. The onset of symptoms is sudden in both eyes within 2 to 12 hours after administration of the drug. Transient impairment of vision occurs in 15–20 % of cases, but permanent damage results in approximately 4 %, in the form of reduction of visual acuity and constriction of peripheral field of vision (9).

2. Thallium

Blurring or dimness of vision develops after several weeks or months of the use of drugs containing thallium. There is loss of central vision and constriction of peripheral fields. After removal from exposure, there may be improvement of vision, but with reduction of visual acuity (16).

IV – Cerebellar disturbances

1. Organic mercury

Methyl mercury is much more toxic than inorganic mercury. Several large outbreaks of poisoning have occurred in Japan. These have followed the discharge of mercury in industrial waste into the sea. Biotransformation of inorganic to organic mercury occurs and methyl mercury concentrates in fish which are therefore poisonous when eaten. Other outbreaks have occurred in Iraq, when grain treated with methyl mercury as fungicide was eaten instead of being sown (3). Paraesthesiae occur in

the limbs and also in and around the mouth after a latent interval of a few days or weeks, Paraesthesiae may be caused by damage to the CNS. The cerebellum and occipital cortex are also affected producing ataxia and visual failure. Visual symptoms usually consist of concentric constriction of the visual fields with preservation of central acuity, but complete blindness may occur. Ataxia is often the most disabling manifestation of poisoning (10). Muscle atrophy, fibrillations, signs of involvement of pyramidal tract are reported by *Kantarjan* (11). Acute encephalitis occurs with exposure to alkyl mercury (7).

V – Parkinsonism

1. Manganese

Manifestations of poisoning rarely occur, except in workers of manganese mines. Industrially, manganese is mostly used as an alloy in steel, but exposure in the manufacturing process is mild, and no cases of poisoning have been reported. Psychotic symptoms may precede overt signs. These consist of sleep disturbance, emotional instability, irritability and spontaneous laughter. Frank psychosis may develop. Extra-pyramidal signs are characteristic. Rigidity, abnormalities of gait and mask-like facies are more obvious than tremor. Pyramidal signs are common (14). The occurrence of parkinsonian symptoms in a middle-aged or elderly male who is exposed to manganese raises a difficult medico-legal problem, as it is indistinguishable from that which develops due to pathological causes (1). When the patient is removed from exposure, he always recovers from the mental disturbances, however, neurological abnormalities rarely improve except in mild cases. It has been reported that administration of EDTA (calcium salt) increases the excretion of manganese, but it is doubtful whether any clinical improvement follows.

VI – Mental changes

1. Organic lead

Large quantities of tetraethyl lead are added to motor fuel as anti-knocking agent. Toxic symptoms have occurred in men petrol storage tanks. Mild and early cases develop sleep disturbances and nightmares. Following severe exposure acute psychosis develops, characterized by excitement and mania. After a single exposure there is always a latent interval varying between a few hours and 10 days before symptoms develop. No long term sequelae are recognized. Sedation during the manic phase is important. Chelating agents have little effect on the prognosis (4).

2. Inorganic mercury

Occasional cases of poisoning have been encountered with workers making scientific instruments or persons using amalgams for making gilding or in dental filling. However, hygienic precautions have reduced their number considerably. Stomatitis and excessive salivation are early symptoms. Erethism is the name which has been given to the mental disturbance produced by mercury. This consists of emotional instability,

apprehension, depression, outbursts of anger and insomania. Coarse tremors with jerky movements occur later. The site of damage responsible for the tremors is unknown. Health status testing, using psychomotor and neuromuscular tests should be considered for any person routinely exposed to mercury, when the blood concentrations exceed approximately 100 μg/l. Removal from exposure showed reversal of the subclinical changes detected by these tests (13). Treatment with chelating agents, such as BAL or D-penicillamine are effective in removing mercury and improving symptoms and signs.

Summary

Toxic metals encountered industrially or environmentally may produce the following syndromes:

1) Peripheral neuropathy: which is mainly sensory in arsenic and entirely motor with inorganic lead, organophosphorus compounds and tallium produce a mixed form of peripheral neuropathy.

2) Encephalopathy: usually with lead poisoning where ataxia and hemiplegia or optic atrophy may occur.

3) Optic neuritis: transient or permanent impairment of vision in arsenic poisoning and blurring of vision followed by field fedects with thallium poisoning.

4) Cerebellar disturbances: in the form of ataxia in organic mercury.

5) Parkinsonism: extrapyramidal signs occurs in manganese poisoning shown as mask face and rigidity of muscles.

6) Mental changes: as acute psychosis in organic lead and erethism in organic mercury.

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