The image contains a page from a medical publication discussing melanocytic tumors of the nervous system. The text appears to be discussing the histopathological features of melanocytic lesions, particularly emphasizing lentiginous melanomas and their involvement in the trigeminal nerve. The text includes references and figures illustrating nerve involvement and histopathological findings.

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**Propranolol in startle induced epileptic seizures**

Startle epilepsy is a rare but severe seizure disorder, most often seen in patients with severe brain damage and neurologic or mental handicap, but occasionally in patients without signs of cerebral dysfunction. Epileptic seizures of predominantly tonic, tonic-clonic, or tonic-clonic convulsions precipitated by sudden, unexpected, intense acoustic or visual stimuli are the constituent features of this condition. The frequency of seizures is high, with daily attacks in most patients, and falls are common. Spontaneous seizures also occur.

Treatment is difficult. Carbamazepine and benzodiazepines such as clonazepam have been found to be effective in some patients, whereas valproate seemed to be of less value and phenytoin or phenobarbital were ineffective.

In the Epilepsy Center, Bethel, 24 adult patients with startle induced seizures have been studied and treated since 1980. Twelve of them received clonazepam and 20 received propranolol. As a new approach, propranolol was investigated in 11 patients. This was after experimental studies had shown an accentuation of the startle reflex by adrenergic substances, and some anticonvulsants. Kolbinger et al had demonstrated the efficacy of metoprolol in a case of startle epilepsy.

We started treatment with 80 mg propranolol, increasing the dose gradually up to 160 mg per day (in two patients up to 240 mg). With propranolol, one patient had no more startle induced seizures, two patients had a greater than 50% reduction in seizure frequency, and eight showed no improvement. There were no side effects and no development of tolerance. The three successfully treated patients remained on propranolol for 82, 19, and 120 months. In the remaining eight patients the drug was withdrawn after treatment failure was apparent. With clonazepam and carbamazepine, one and three patients remained free from startle induced seizures respectively, and one further patient with each drug showed a reduction of more than 50%. Five of seven patients with an initial response to clonazepam developed complete tolerance within two to 16 weeks.

Mean follow up for all patients who were successfully treated was 55 (range 12-120) months. The overall therapeutic outcome was poor. In only 21% of all patients (five out of 24) was a complete control of startle induced seizures achieved. Clonazepam and carbamazepine did not show better results than propranolol. We conclude that propranolol seems to be an additional and safe drug in the treatment of startle epilepsy with efficacy comparable with the standard regimen, but further experience is required.

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**Subcutaneous nerve showing perineural infiltration with cytologically malignant cells** (arrowed). Immunocytochemistry showed S-100 positivity (insert).
Methyl bromide induced neuropathy: a clinical, neuropathological, and morphological study

Methyl bromide is a colourless, odourless gas used as a fumigant to disinfect soil, grains, and warehouses. Due to its high volatility, dangerous concentrations can accumulate rapidly in working areas. Inhalation is a main route of exposure. Dependent on dose and duration of exposure, methyl bromide can cause both acute CNS symptoms and chronic peripheral sensorimotor neuropathy. Optic atrophy has also been described.

A 23 year old Moroccan man working in Italy as a methyl bromide fumigator in greenhouses was admitted because of painful leg numbness. His personal history was unremarkable and he denied alcohol misuse. He had worked for the previous seven months (eight hours a day), wearing a protection mask irregularly. Neurological examination showed asymmetric lower limb weakness and areflexia, stepping gait, and sensory loss for pin prick, position, and vibration. Upper motor and cranial nerve signs were absent. Mental state was intact. Laboratory tests excluded diabetes, hepatic and collagen diseases, syphilis, tuberculosis, HIV, and Lyme related disease. Vitamin B12 and folate concentrations were normal. CSF was normal. Organophosphate and lead poisoning were excluded. One month after cessation of exposure urinary lead and mercury were normal. Methyl bromide was 0.01 ppm. A colour vision test (Farnsworth-Munsell 100-test) showed defective perception of all colours, especially in the red-green axes. Eye fundi and evoked responses were normal.

Electrophysiology showed a severe motor neuropathy of axonal type confined to the legs. The right peroneal muscle action potential was reduced and unrecordable from the extensor digitorum brevis muscle. The bilateral right peroneal nerves had reduced motor conduction (−2.7 and −3.1 SD from mean control value) and muscle action potential amplitude (0.2 and 1.0 mV). Sensory findings in the sural nerve were normal. An EMG showed denervation and loss of motor units in distal muscles.

Tibialis anterior muscle biopsy showed neurogenic changes. A sural nerve sample was examined. Light microscopy showed that the endoneurial area and total fibre density were within the normal range. Multifocal scattered loss of myelinated fibres (4689 × 5000–9500 in normal subjects) was detected, with a prominent loss of fibres larger than 7 μm (1321 × 1650–3300), and relative sparing of the smaller axons. Degenerated fibres were seen. The frequency of clusters fell within the normal range and there was no inflammatory infiltrate. On teasing, 38% of the fibres had signs of segmental remyelination; 15% had shortening of all internodes, suggesting regeneration, whereas the incidence of demyelination multifocally distributed along the fibre length was 8%. Electron microscopy showed ongoing degeneration of both myelinated and unmyelinated fibres. Numerous Schwann cell subunits were devoid of axons. Many nodes of Ranvier showed segregated axonal microtubules (figure).

The patient received B1, B6, and B12 vitamins, folate acid, and amytropine (50 mg/day). When re-examined two months later, muscle strength was normal, whereas limb numbness was still present. Peroneal muscle action potential (0.3 mV) was recordable and there were no signs of denervation. Two coworkers, similarly exposed, had no clinical signs or electrophysiological signs of neuropathy, despite slightly altered colour vision.

The clinical history and laboratory data of this patient excluded known causes of peripheral neuropathy, suggesting that exposure to methyl bromide was responsible. The neurological time course corresponded with previous descriptions, where symptoms appeared after several months of exposure and the patients mostly recovered six to eight months after cessation of exposure.

It has been proposed that methyl bromide causes a distal axonopathy. We report here morphological evidence for nerve abnormalities after exposure to methyl bromide. Loss of large axons and degeneration of both myelinated and unmyelinated fibres were found in the sural nerve. Spared myelinated and regenerating large fibres might account for the normal amplitude and maximal velocity of the sural action potential.

The presence of segregated microtubules in the nodes of Ranvier suggests that methyl bromide impairs axonal flow. As in most types of exogenous intoxication, methyl bromide may cause degeneration of axons with a dying-back-like mechanism, more evident at the distal nodes. This neurotoxic agent may either alter the metabolism of the neuronal perikaryon or interfere with the dynamics of axonal transport. A metabolic mechanism for methyl bromide intoxication has recently been proposed. Based on neuropathological similarities with Wernicke's disease, methyl bromide intoxication has been correlated with an altered glycolysis and pyruvate oxidation.

Our patient and two healthy coworkers showed an acquired type of polyneuropathy. This may be a first sign of optic neuropathy, which precedes electrophysiological abnormalities. We therefore propose to use the Farnsworth-Munsell 100-test to screen workers exposed to methyl bromide.

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