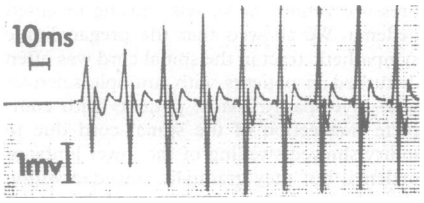

Figure Incremental increase in the compound motor action potential of the left abductor digiti minimi on repetitive stimulation of the ulnar nerve at 50 Hertz.

normal in two nerves; c) CMAP ratio from proximal and distal stimulation less than 0·7 in the right median and left ulnar nerves recorded on day 21; d) A reduction of both ulnar sensory action potential amplitudes below 80% of the lower limit of normal; d) F wave latency prolongation from day 7, increasing to 120% of the upper limit of normal by day 21.

Repetitive stimulation of the left ulnar nerve was performed, with the active surface recording electrode over the midportion of the abductor digiti minimi muscle. The CMAP at rest was compared with the highest amplitude CMAP on stimulation. On the third hospital day supramaximal stimulation at 3 Hertz gave an increment of 18%, and stimulation at 50 Hertz gave an abnormal incremental response of 81% (normal mean increment = 2·4%; upper limit of normal = 42·4%[1]) (figure). The incremental response decreased over the next 10 days (table).

The patient was intubated. She was started on guanidine, 240 mg every six hours. Slow improvement began by the twelfth hospital day, but eye movements took over a month to return to normal. The patient started to walk after two months and subsequently made a complete recovery.

An incremental response to repetitive stimulation is characteristic of impairment of presynaptic release of acetylcholine (ACh), as seen in the myasthenic syndrome, botulism, and also with some drugs and with certain types of arthropod envenomation. In the myasthenic syndrome it appears very likely that an antibody, probably IgG, interferes with ACh release. In botulism, the botulinus toxin also decreases ACh release.[1]

Although the progression of signs in our patient was similar to that seen in botulism, the normal pupils and inability to detect *Clostridium botulinum* or botulinus toxin were against botulism. The raised CSF protein is very atypical for botulism and the finding of abnormal motor and sensory nerve conduction and F wave prolongation are strongly in favour of GBS.[2] A clinical picture resembling botulism is known to occur as a variant of GBS.[3]

There is increasing evidence for a humoral role in GBS. Antibodies to several myelin antigens have been found in GBS and complement fixing antibodies to peripheral nerve myelin appear to be involved in myelin destruction.[4] The titre of these antibodies is highest when neurological symptoms first occur[4] and the abnormal incremental response early in the course of our patient's illness fits this pattern. The finding of an incremental response to repetitive stimulation in our patient with GBS suggests the presence of an antibody directed against the presynaptic terminal, interfering with ACh release.

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1 Oh SJ. *Electromyography. Neuromuscular transmission studies.* Baltimore, MD: Williams and Wilkins;1988:69.
2 Ropper AH, Widjicks EFM, Shahani BT. Electrodiagnostic abnormalities in 113 consecutive patients with Guillain-Barré Syndrome. *Arch Neurol* 1990;47:881–7.
3 Ropper AH. Unusual clinical variants and signs in Guillain-Barré syndrome. *Arch Neurol* 1986;43:1150-2.
4 Koski CL, Gratz E, Sutherland J, Mayer RF. Clinical correlation with anti-peripheral myelin antibodies in Guillain-Barré syndrome. *Ann Neurol* 1986;19:573-7.
5 Miller RG, Kuntz NL. Nerve conduction studies in infants and children. *J Child Neurol* 1986;1:19-26.

Putaminal necrosis after methanol intoxication

Optic neuropathy and putaminal necrosis are the two main complications of methanol poisoning,[1 2] generally occurring in combination after severe intoxication of either suicidal or accidental origin. Surviving patients usually show permanent sequelae consisting of bilateral blindness and motor dysfunction including rigidity, hypokinesis, and other Parkinsonian-like signs, occasionally associated with limb polyneuropathy. Brain pathology has been documented in earlier studies showing the specific involvement of the basal ganglia, especially the putamen. This unusual lesion site was more recently confirmed in reports including brain imaging data, either with CT or MRI.[3] We report a new case study in which repeated CT and MRI examinations may help elucidate the specific putaminal damage.

A 40 year old depressive woman was admitted to hospital after attempting suicide by methanol ingestion, having drunk nearly one litre of methylated spirits several hours earlier. On admission, she was comatose with generalised hypotonia, non reactive pupils and hyperventilation. Her vital signs were: apyrexia, blood pressure 120/60, pulse rate 110 bpm, respiration 30/mn. The main laboratory findings included : pH 6.8; serum methanol : 180 mmol/l. Treatment by intravenous infusion of sodium bicarbonate and 4-methyl pyrazole was initiated and the acidosis was overcome within a few hours. Two days later, she regained consciousness and reacted to verbal commands. On examination, bilateral extensor plantar response, blurred vision, rigidity, and distal postural tremor, were noted. The right pupil was unreactive and optic fundi examination showed bilateral oedema. CT carried out five days after intoxication showed a bilateral, symmetrical area of low density involving the basal ganglia region (fig a). One week later, the patient was well-oriented and cooperative without apparent intellectual deterioration. Tremor and rigidity were of left predominance and hypokinesia persisted with amimic face and dysarthric, monotonous speech. Sensory examination revealed symmetrical loss of superficial and proprioceptive sensation of the lower extremities with hyperpathia. Motor conduction velocities and distal latencies were normal, but distal sensory latencies of both sural nerves were decreased.

Brain MRI was performed with a 0.5 T superconductive magnet three weeks after intoxication (fig b, c). The core lesion (fig b) centred on the putamen, surrounded by a large hyperintensity (fig c), suggested major oedema. Two months later she remained almost totally blind with optic atrophy on fundus examination. Signs of moderate bilateral sensory neuropathy and extrapyramidal syndrome persisted. Neuropsychological evaluation was within normal limits. Repeat CT and MRI examinations showed residual bilateral putaminal cavities.

Our report illustrates the usual consequences of massive methanol intoxication on the nervous system.[2] After a short comatose period, severe bilateral blindness and moderate extrapyramidal syndrome were found in association with lower limb axonal neuropathy.

The relationship between methanol-induced blindness and damage to the retina and optic nerve was the first feature to be well documented in early clinical-pathological works. Subsequently, several necropsy studies of the brain revealed symmetrical haemorrhagic necrosis of the putamen or prominent hyperaemia in the basal ganglia[4] as the specific neuropathological outcome of human methanol intoxication. Selective putaminal locus of lesions was confirmed in

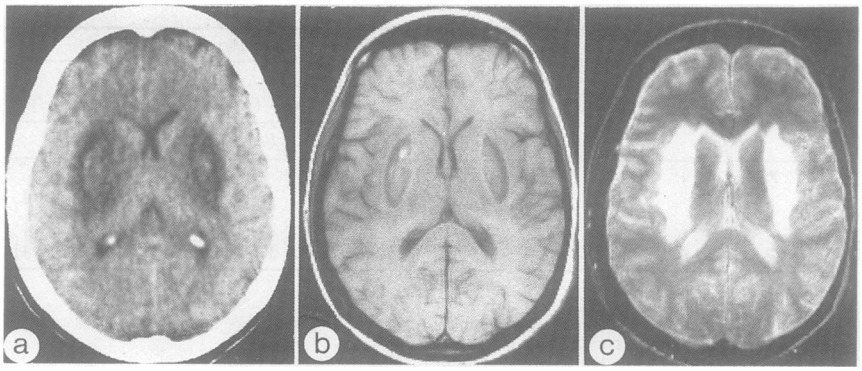

Figure 1 (a) First non injected CT scan five days after intoxication. Bilaterally symmetrical, low density lesion in the putaminal region with central isodense zone possibly suggesting microhaemorrhages; (b) MRI scan: T1 weighted axial section (TR = 450ms; TE=28ms). Bilateral putaminal lesions; (c) T2 weighted sequence (TR = 2000ms, TE = 120ms). High signal intensity of the basal ganglia and the periventricular white matter suggesting major oedematous participation.

vivo with CT and MRI examination. Initial CT may be normal but evidence of prominent putaminal destruction generally appears a few days post onset. Residual bilateral putaminal hypodensity is common.[3] Since symmetrical necrosis of the putamina has not been observed after other intoxications, such CT findings may be of special diagnostic value.[3] MRI findings in our case suggest the usefulness of this method for accurate delimitation of lesion boundaries, especially with partial recovery technique, as well as for evaluating the extent and importance of oedema on spin-echo images.

The mechanism of methanol toxicity seems to be indirect, related to the effect of formic acid generated from methanol by alcohol dehydrogenase. Accordingly, studies in monkeys have shown that ocular toxicity could be prevented by 4-methyl pyrazole, an alcohol dehydrogenase inhibitor. Several reports have insisted on the relationship between symptoms of poisoning or neurological sequelae and the degree of metabolic acidosis and level of blood formate. The main unresolved issue remains that of the mechanism of the putaminal damage, and, specifically, the significance of this part of the striatal complex being selectively involved. Orthner[4] proposed that the putaminal necrosis resulted from decreased venous outflow through the veins of Rosenthal. Another suggestion was that formic acid may achieve higher concentrations within the putamen than in other brain structures.[2] Having observed some similarity between optic lesions and brain white matter changes in their cases, Sharpe *et al*[1] proposed that methanol could provoke a specific histotoxic anoxia with myelinoclastic effect. However, white matter damage is not the rule in most cases of methanol intoxication. Rather, as previously emphasised, the necrotic process appears to involve primarily the grey matter of the putamen.

CT and MRI findings are compatible with ischaemic necrotic lesions. From an anatomical point of view, the arterial supply of the putamen is provided by the lateral lenticulostriate arteries, originating from the proximal middle cerebral artery. The lesion site in our case, as in most similar reports in the literature, is restricted to the putamen, whereas, in usual deep MCA infarcts, the caudate nucleus is generally involved, whatever the mechanism, haemodynamic or occlusive.

Finally, bilateral putaminal necrosis has also been reported in other conditions such as Wilson's disease, striatal degenerations, anoxic strokes and Leigh's disease.[5] This part of the basal ganglia may be particularly susceptible to various pathological processes. Moreover, massive bilateral oedema has been shown on MRI (fig c) and strongly suggests disruption of the blood-brain barrier, possibly facilitating the diffusion of toxic formate molecules into the adjacent putamen.

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1 Sharpe JA, Hostovsky M, Bilbao JM, Rewcastle NB. Methanol optic neuropathy: a histopathological study. *Neurology (Ny)* 1982;32: 1093-1100.
2 McLean DR, Jacobs H, Mielke BW. Methanol poisoning: a clinical and pathological study. *Ann Neurol* 1980;8:161-7.
3 Koopmans RA, Li DKB, Paty DW. Basal ganglia lesions in methanol poisoning: MR appearance. *J Comput Assist Tomogr* 1988; 12:168-9.
4 Orthner H. *Die methylalkohol vergiftung*. Berlin: Springer Verlag. 1950.
5 Berkovic KJ, Karpati G, Carpenter S, Lang AE. Progressive dystonia with bilateral putaminal hypodensities. *Arch Neurol* 1987;44:1184-7.

Reversible myeloneuropathy resulting from podophyllin intoxication: an electrophysiological follow up

Podophyllin used mainly as a vegetable cathartic has been known for over 100 years. In 1942, Kaplan introduced the use of topical podophyllin in the management of condyloma acuminatum.[1] Although widely used, however, there are scant reports concerning the toxic effect of this compound and it is not generally appreciated that podophyllin may produce systemic and neurological toxicity. The earliest systemic toxicity includes nausea, vomiting and watery diarrhoea. Bone marrow suppression and disturbance of hepatic function may appear in the first week. Neurological toxicity can produce peripheral neuropathy with or without encephalopathy. Autonomic neuropathy and ataxia have also been described.[2] Previously, ataxia has been attributed to the central nervous system toxicity of podophyllin;[1 2] however, a patient with severe sensory ataxia was reported by Gorin *et al*[3] who described the first case of podophyllin intoxication resulting in profound loss of proprioception. They ascribed ataxic gait and aimless limb movement to loss of position sense resulting from dorsal radiculopathy.

In our country, powder of roots and rhizome of *Podophyllum peltatum* is an expensive herb used for treatment of liver diseases and soft tissue pain. We describe a 51 year old woman whose systemic and neurological symptoms appeared rapidly soon after ingesting *Podophyllum peltatum* for relief of soft tissue rheumatism. One hour later, she developed headache followed by nausea and watery diarrhoea. The next day, she could not sit or stand without support. Incoordination of all her limbs and rapidly spreading numbness rendered her severely ataxic. On the fourth day after ingestion, she was admitted to our hospital for further evaluation. On admission, her vital signs and general physical examination were unremarkable. Her mental status and cranial nerves were normal. Tendon reflexes could not be elicited. There was mild muscle weakness, predominantly distal. Plantar responses were flexor. Proprioception and vibration sense were lost at the level of the elbow and inguinal region. Fine touch sensation was impaired below T8 level. In contrast, cutaneous sensation was minimally involved. There was marked dysmetria and truncal ataxia which was increased by obliteration of vision. Neither orthostatic hypotension nor other autonomic dysfunctions were observed.

Routine blood, urine and stool chemistry, as well as serology, immunology and CSF tests were normal.

Two months later, there was a marked improvement of kinaesthetic sensibility and the deficits of position and vibration sense dropped to the level of the wrist and ankle. She could walk with a cane, but there was obvious wasting of the hand and foot muscles.

Electrophysiological assessments were performed on day 6, 17, 28, and 57 after ingestion. Motor and sensory conduction studies were performed using standard techniques of supramaximal percutaneous stimulation and surface recording. F response latencies were recorded as the minimal latencies following median and peroneal nerve stimulation. Electromyography was performed using standard concentric needle electrode. Somatosensory cortical evoked responses, referred to Fz, were recorded from 2·5 cm behind the vertex (Cz') following posterior tibial nerve stimulation at the ankles and from a point just posterior to C3 (C3') on the 10–20 system, following median nerve stimulation at the wrists. Erb's point and spinal recording (Cv2) were also made but are not shown. Stimuli sufficient to cause a small muscle twitch were delivered at 3 Hz and two trials of 500 responses were averaged. Sensory nerve action potential amplitudes of median and sural nerves reduced progressively from 18 and 13 μV, respectively, to no response on day 6 to day 28. Compound muscle action potential amplitudes of thenar and extensor digitorum brevis muscle decreased from 11 and 5 mV, respectively, to 8 and 0·5 mV from day 6 to day 57. Conduction velocity of peroneal nerve over the leg segment decreased from 32·5 m/s to 23·9 m/s. F response latencies were prolonged or responses blocked at wrist and ankle stimulation. EMG showed mildly decreased recruitment patterns without spontaneous activity on day 6 and moderate denervation with fibrillation potentials in the distal muscle on day 57, but the proximal muscle revealed normal patterns of recruitment throughout follow up. A series of cortical evoked potentials of median and posterior tibial nerves is shown in the figure.

Our patient presented acutely with symptoms and signs of spinal cord and peripheral nerve disease soon after exposure to podophyllin. Electrophysiological studies correlated well with clinical features which predominantly involve the sensory system. From the initial series of assessments, ataxia was best ascribed to dysfunction of the posterior column. However, as her symptoms progressed the residual disturbance of the posterior column played a minor role and neuropathy appeared to have largely contributed to her ataxia.

One interesting aspect of electrophysiology is the dramatic improvement of central conduction accompanied by deterioration of peripheral nerve function. The rapid improvement of abnormalities of cortical evoked potentials is of considerable interest and suggests remyelination of the affected axons in the posterior column once the exposure to podophyllin ended. Regarding the pathology of the peripheral nerves, sequential electrodiagnosis suggests axonal degeneration with sensory predominance.

The clinical and electrophysiological features of our patient are similar to those of nitrous oxide abuse,[4] except for the acute as opposed to chronic onset. It is well known that the pathology of nitrous oxide abuse is demyelination of posterior and/or lateral column with axonal neuropathy.[4] The pathology of our patient was similar to that of nitrous oxide abuse.