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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## 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.

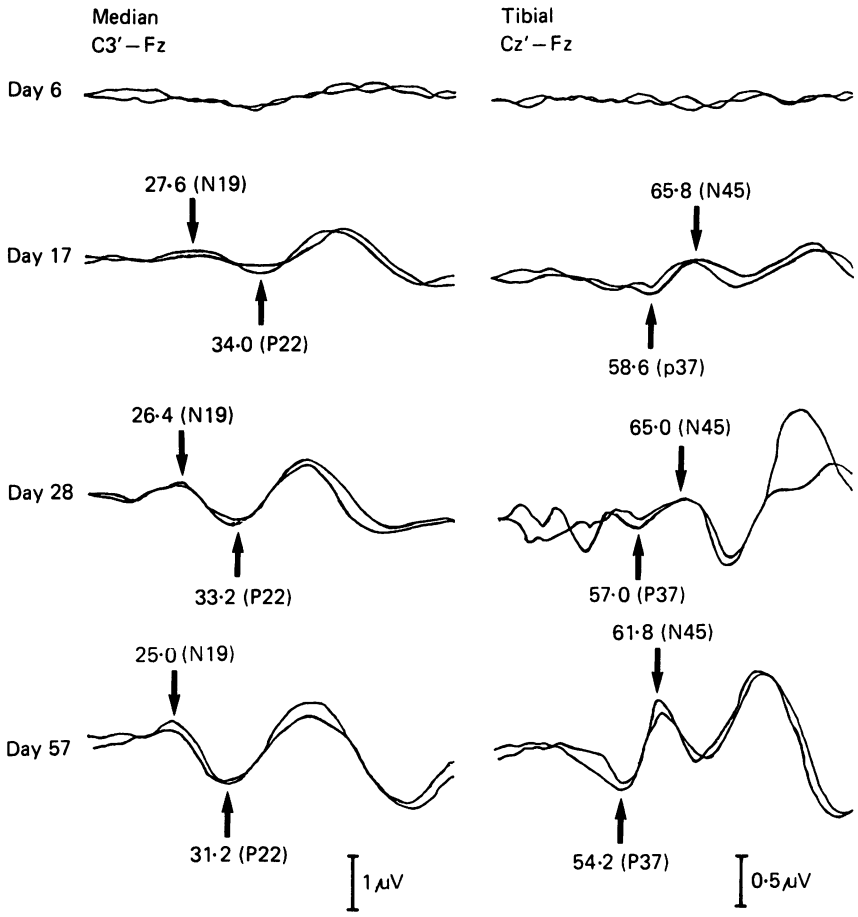
Two months later, there was a marked improvement of kinaesthetic sensibility and the deficits of position and vibration sense dropped to the level of the wrist and ankle. She could walk with a cane, but there was obvious wasting of the hand and foot muscles.

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 $\mu$V, 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.




*Cortical evoked potentials (N19 & P37) show dramatically increased amplitude and decreased latency over the period of 2 months. The rapid improvement suggests demyelination resulting in abnormal central conduction.*

In neurotoxic disease, exposure to different levels of the same substance may result in dramatically different clinical pictures, but a certain toxin associated with structural damage to the nervous system produces a similar pattern of disease, commensurate with the dose and duration of exposure.[5] Podophyllin is considered to be one of the neurotoxins belonging to this group. From a previous reported case[3] and our patient, it appears that podophyllin destroys the sensory system selectively from peripheral nerves to posterior column resulting in deafferentation. It thus appears that podophyllin can provide an experimental model for investigating deafferentation.

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## Paroxysmal hemidystonia induced by prolonged exercise and cold

Paroxysmal choreoathetosis is a rare usually familial disorder. Depending upon the age of onset, frequency and duration of the attacks, trigger factors and response to treatment, three subgroups are identified:[1] (1) Paroxysmal dystonic choreoathetosis;[2] (2) Paroxysmal kinesiogenic choreoathetosis;[3] (3) Intermediate type.[4 5]

In this sporadic case of the intermediate type there were previously unreported features.

This 18 year old cobbler, was seen in February 1988 with a nine month history of paroxysmal involuntary movements affecting the right half of the body. His first attack involved two trigger factors. He was caught in a sudden shower of rain while he was returning home from a nearby village. After running two kilometres in about 10 minutes he started to experience a dragging sensation in the right shoulder which was immediately followed by strong irregular jerky movements. This spread rapidly to the whole of the right half of the body. He assumed it was the effect of "cold" and tried to "rub it down." He did not experience any pain in the affected part and remained fully conscious during the attack which lasted about 10 minutes. His speech remained normal. The attack faded as he changed into dry clothes. He had no motor or sensory deficits after the attack. Since then, he has experienced similar attacks whenever he runs for more than six to 10 minutes and also when taking cold baths. The frequency of the attacks varied from two to three per month.

A month later, whilst working at the anvil, he experienced an attack of involuntary movements similar to the previous ones. It also started at the right shoulder and spread to involve the right half of the body and lasted about 10 minutes.

He had not previously experienced such attacks with sudden movements, startle or fatigue. They were also not precipitated with cold drinks, tea or coffee. He did not drink alcohol or smoke. There appeared to be no diurnal variation in the attacks. He received no treatment.

He was born of non-consanguineous parents and there was no relevant past or family history.

Detailed and neurological examination was unremarkable. Attempts were made to induce the attacks and the results were video recorded and studied.

Running and treadmill exercising induced the attacks in about eight minutes each. Striking of a hammer against a stone, using the right hand, induced an attack in about six minutes. However, similar exercise with the left hand did not provoke an attack. Passive movements, application of a vibrator to the limbs, sudden movements and startle did not induce an attack. A cold water shower (temperature 15°C) and exposure to cold breeze blowing from an air cooler, induced the attacks within three to four minutes. A warm water shower did not induce an attack. Figures 1 and 2 show the patient during attacks induced by treadmill exercising and a cold shower, respectively.

All observed attacks were similar in nature and lasted about 10 minutes each. An attack started with the patient experiencing a dragging sensation in the region of the right shoulder. The involuntary movements, started within five to 10 seconds thereafter. During the period of the attack the arm was generally extended at all the large joints while the leg generally took the posture of flexion at the large joints. While the fist remained partially closed the foot was extended (fig 1). There were repeated brisk irregular jerky and sometimes bizzare movements at the various joints. These produced repeated extension, abduction and lateral rotation of the arm, extension and supination of forearm, extension and lateral deviation of the hand, flexion and medial rotation of the thigh, flexion of the leg and flexion-inversion of the foot. Frequent mild irregular jerking movements were seen affecting the trunk, neck and face on the right side. Each attack usually increased in intensity in the initial two minutes, and after five to six minutes tapered down over another two minutes and stopped. The patient remained fully alert and oriented during the attacks. His speech remained completely normal and he experienced no pain during the attack. There was no postictal deficit. The left half of the body remained unaffected.