in all patients. The average disability score for blepharospasm after pretarsal treatment was 0·6 (0·5) ($P < 0·001$). The mean duration of the clinical effect was 67·2 (17·2) days.

All the patients complained of a slight, but definite, increase in pain during pretarsal injections (compared with orbital injections); most patients had ecchymoses at the injection sites. Ptosis or diplopia were not seen after pretarsal injections.

This study shows that pretarsal BTX injections resulted in a pronounced symptomatic improvement of blepharospasm in patients who failed to benefit after standard orbital injections.

Lack of efficacy of orbital BTX treatment is not usually related to antibody production.[2] Our study shows that all the patients responded favourably to BTX when it was injected either at orbital or at pretarsal sites. All these patients had a typical blepharospasm and did not meet the clinical criteria for a diagnosis of apraxia of eyelid opening or of levator palpebrae inhibition; these have been reported to respond to pretarsal but not to orbital treatment.[6]

As pretarsal injections may be effectively used to treat patients affected by blepharospasm who do not improve after orbital injections, this raises the question as to whether all patients with blepharospasm should be regularly treated at pretarsal sites. We think that this technique should be employed in all cases of blepharospasm, either alone or in combination with orbital infiltration. A slight increase in pain during treatment and in the incidence of ecchymoses are counterbalanced by higher clinical efficacy, immediacy of benefit, and reduction of dose and cost.

This study was supported by Comitato Promotore Telethon grant E113 to AA.

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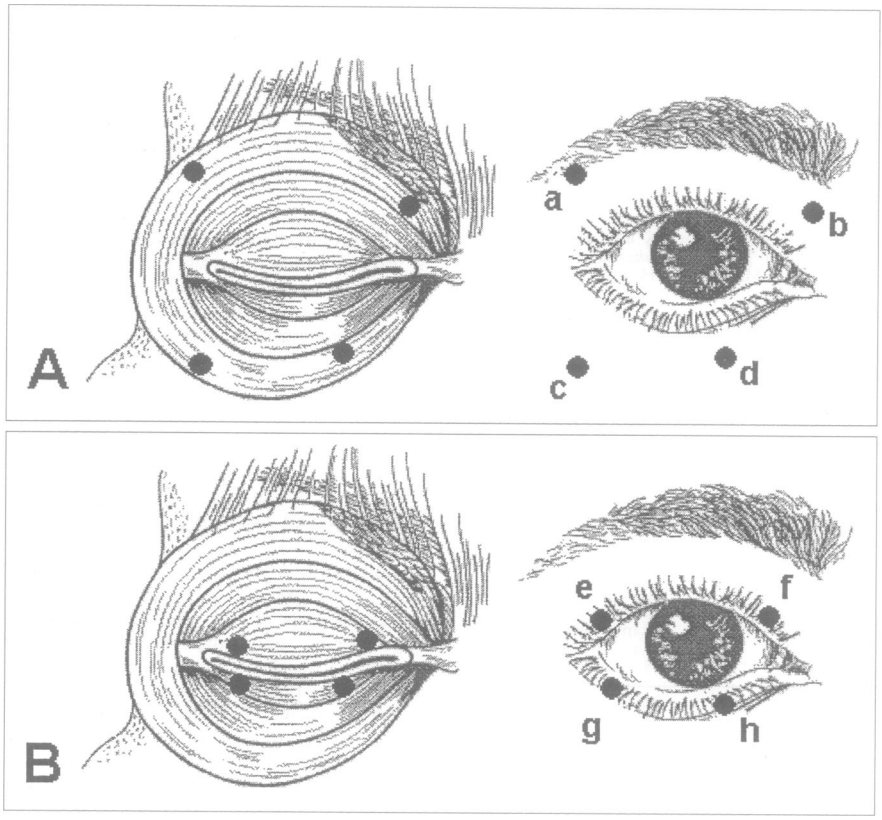



*Common sites for BTX injection into the eyelids. The orbital, preseptal, and pretarsal portions of the orbicularis oculi muscle are shown in the left panels. (A) Orbital injections: a, lateral upper lid; b, medial upper lid; c, lateral lower lid; d, medial lower lid. (B) Pretarsal injections; e, lateral upper lid; f, medial upper lid; g, lateral lower lid; h, medial lower lid.*

## Leucoencephalopathy after inhalation of heroin: a case report

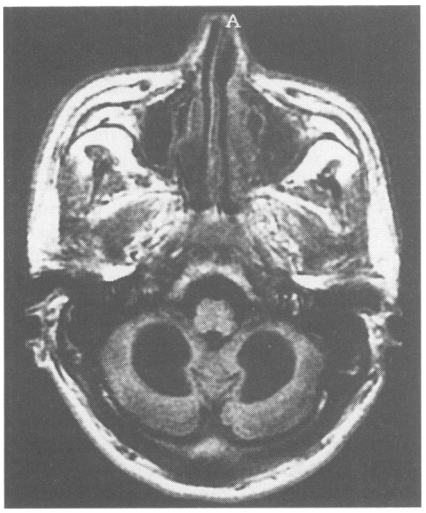
The use of heroin, a diacetyl derivate of morphine, is common among drug addicts. Heroin may be taken in different ways; intravenously, subcutaneously, smoked, sniffed, or inhaled. As well as psychosocial degeneration, common medical complications of heroin addiction are encephalopathy, transverse myelitis, myelopathy, cerebral infarctions, meningitis, cerebral abscesses, mycotic aneurysms, myopathies, and plexopathies. A subacute leucoencephalopathy showing spongiform neuropathological changes has been reported as a rare complication to inhalation of preheated heroin.[1–7] Clinical, radiological, and neuropsychological findings in a patient with this syndrome are presented here.

A 36 year old Moroccan man living in Norway for 16 years was referred for neurological examination. He had no history of neurological or psychiatric illness. Drug misuse started six years previously with sporadic misuse of cannabis, increasing to daily cannabis in the past two years. Heroin misuse began two years previously. The heroin was most often inhaled as a white smoke (pyrolysate) after preheating on tinfoil, occasionally smoked mixed in tobacco, or sniffed, but never intravenously injected. During the six months before the onset of symptoms he used heroin daily in doses from 250–500 mg; he used no other illicit drugs or medication and alcohol consumption was moderate. Over a few weeks he developed increasing dysarthria and ataxia as major symptoms. Drug misuse was terminated, and his symptoms remained unchanged until he was referred for neurological examination four months later.

The clinical neurological examination disclosed psychomotor retardation, pronounced scanning dysarthria, bilateral cerebellar ataxia, dysdiadochokinesia, intention tremor, and dysmetria. There was a general hyperreflexia with right sided predominance; plantar reflexes were neutral. Apart from retardation of the tongue, the cranial nerves were normal. Motor function showed no abnormalities except for those that could be ascribed to cerebellar dysfunction, and sensory examination was normal.

Cerebral CT showed non-enhancing hypodense areas symmetrically in both cerebellar hemispheres. Cerebral MRI showed corresponding areas with decreased signal intensity on T1 weighted images (figure) and increased signal intensity similar to CSF on T2 weighted images. No lesions were seen in the brain stem or cerebral hemispheres, and there was no contrast enhancement. Somatosensory and brainstem evoked potentials and EEG were normal. Visual evoked potentials were normal on the right side and inconclusive due to an earlier eye lesion on the left. The CSF (cell count, total protein, and agarose electrophoresis) was normal.

The patient was admitted to a rehabilitation unit for physical and cognitive therapy. Neuropsychological examination was performed eight months after onset of symptoms with the Wechsler adult intelligence scale (WAIS), Halstead-Reitan neuropsychological test battery, and other selected tests. The patient showed a pronounced and generalised impairment of cognitive, motor, and sensory-perceptual functions reflected by a Halstead impairment index of 0·9, corresponding to a T score of 13, representing



*Cerebral MRI performed six months after onset of symptoms showing areas with decreased signal intensity on TW1 in both cerebellar hemispheres.*

more than 3 SD below the expected level. Comparing his test results with age and education corrected norms, he showed specific dysfunctions regarding speed of information processing, motor speed, visuomotor coordination, and tactual-perceptual functions. On these tests he performed between 2 SD and 4 SD below the expected level. There was also a discrepancy between verbal and non-verbal intellectual capacity with a pronounced decrease on the performance IQ score of 64 compared with his verbal IQ of 89. The motor tests and some of the sensory-perceptual tests showed a left-right discrepancy of more than 1 SD with right hand performance better than the left. On tests for verbal intellectual functions, memory, and other higher cortical functions, he performed within the normal range.

The rehabilitation therapy was terminated after four months. At this time his general functioning was moderately improved, but objective signs on neurological examination were essentially unchanged. Re-examination 24 months after the onset of neurological symptoms showed unchanged clinical findings on neurological examination, whereas cerebral MRI showed regression of the cerebellar changes. Neuropsychological re-examination showed some improvement, with a Halstead impairment index of 0·6, an improvement of 1·5 SD from the initial examination. The improvement was most obvious in time and motor dependent tests, but was also evident in tests for non-verbal cognition and sensory perceptual functions. The left-right discrepancy seen initially on some tests was now less obvious.

The clinical and radiological findings in our patient are consistent with the previously reported cases of leucoencephalopathy after inhalation of heroin.[2-6] Unlike most of the reported patients however, our patient managed to terminate his drug misuse and was accessible for follow up examinations. In the previously reported cases there has been a symmetric hypodensity of both cerebellar hemispheres on cerebral CT; in some cases CT has also shown hypodensity of cerebral white matter. Neuropathological studies have shown oedema of the cerebral and cerebellar white matter, and to a lesser degree also of the grey matter. This condition has been termed spongiform leucoencephalopathy because microscopic investigations have shown that the myelin sheats were swollen and vacuolated, and some were totally destroyed. The axons were spared.[2-4]

Spongiform leucoencephalopathy after inhalation of heroin pyrolysate is a rare complication, and so far only 56 cases have been reported in Europe.[2-6] In south east Asia, where this mode of heroin intake is common, the condition has never been reported. In Europe it seems that when it occurs several cases are affected as a small epidemic. It has therefore been suggested that the aetiology, which is still unknown, is related to the heroin batch and could perhaps be a toxic effect of one or more of the heroin additives. In our case it was not possible to obtain any sample of the heroin batch used by the patient for analysis. This has, however, been done in other reports, and none of the common heroin additives detected, such as caffeine, phenobarbitone, methaqualone, procaine, piracetam, and lignocaine, is known to cause this kind of encephalopathy.[2 6]

Spongiform leucoencephalopathy has so far been almost entirely related to inhalation of heroin. One reason may be that the dose aquired by direct inhalation is much greater than the doses obtained by smoking or sniffing. Another explanation is that the process of heating creates a new compound from either the heroin or one of the additives, and which in turn causes the leucoencephalopathy. Because this leucoencephalopathy tends to occur as small epidemics it seems more likely that it is related to one of the irregularly occurring additives. Other modes of heroin intake do not seem to be associated with this complication, with the possible exception of a two and a half year old boy recently reported.[7] In this case the mode of intake was unknown, but inhalation was considered improbable. With this exception it therefore seems that inhalation is essential for the development of this state.

The heroin inhaled by our patient originated, according to his own statement, mainly from the same batch. He shared the heroin with his Norwegian girl friend, who usually required greater doses than our patient to reach the same effect. The girlfriend never developed any symptoms and showed normal findings on neurological examination. This suggests that the aetiology is not only related to toxicity of the heroin or its additives, but also to an individual disposition.

Severe neuropsychological deficits are seldom seen in ordinary opiate abuse. A previous study of seven patients receiving injections of high doses of pharmaceutical heroin for an average of 32 years, showed minor or no cerebral CT abnormalities and only slight cognitive impairment in terms of reduced verbal memory function and speed of information processing.[8] To our knowledge none of the previously reported cases of spongiform encephalopathy after inhalation of heroin have been neuropsychologically examined. Our patient had pronounced neuropsychological impairment not typically seen in heroin addicts. Whereas his motor and coordination problems are fully consistent with the cerebellar abnormalities seen on MRI, the cognitive and sensory-perceptual deficits must have a cerebral origin, and the verbal performance discrepancy and the neuropsychological test profile might indicate a relatively more severe affection of the right hemisphere. The sensory perceptual and cognitive deficits could be explained by affection of cerebral white matter.

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## Sixth nerve palsy from a CNS lesion in chronic inflammatory demyelinating polyneuropathy

Evidence of demyelination of the CNS has been found in half of the patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as shown by MRI, but only a few patients show clinical evidence of CNS involvement.[1] Sometimes a relapsing multifocal course resembling multiple sclerosis precedes CIDP.[2] Involvement of cranial nerves is uncommon in CIDP, but cranial nerve impairment may be the first manifestation.[3] Although an immune attack on nerve myelin sheaths is a likely explanation, a central cause should also be considered. We report a patient with CIDP who developed unilateral sixth nerve palsy associated with a pontine white matter lesion.

In March 1993 a 48 year old man developed tingling in his hands and feet followed by progressive weakness of the legs leading to walking impairment after three weeks. In June severe weakness of all limbs was present; tactile, vibratory, and pain sensations were decreased in the hands and feet, and there was areflexia. Analysis of CSF showed a raised protein content of 1·0 g/l (normal <0·4). Nerve conduction studies fulfilled the criteria for CIDP. In the sural nerve biopsy some axonal degeneration was found with a normal density of myelinated nerve fibres (6048/mm$^2$); CD3 positive T lymphocytes were scattered throughout the biopsy. The patient recovered gradually after a five day course of intravenous immunoglobulin treatment (IVIg 0·4 g/kg/day). In November 1993 his condition seriously deteriorated, to improve again after treatment with IVIg. In both relapses there were increased concentrations of mutant T lymphocytes in peripheral blood; values returned to normal during remission.[4]

In January 1995 he suddenly experienced diplopia while driving his car. On examination there was a complete paralysis of the left abducens nerve but no signs of a relapse