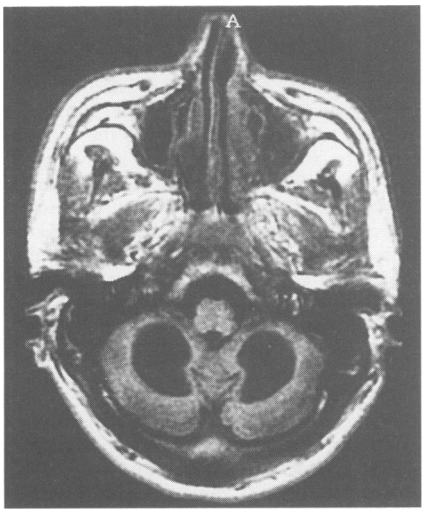

Cerebral MRI performed six months after onset of symptoms showing areas with decreased signal intensity on TW1 in both cerebellar hemispheres.

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]

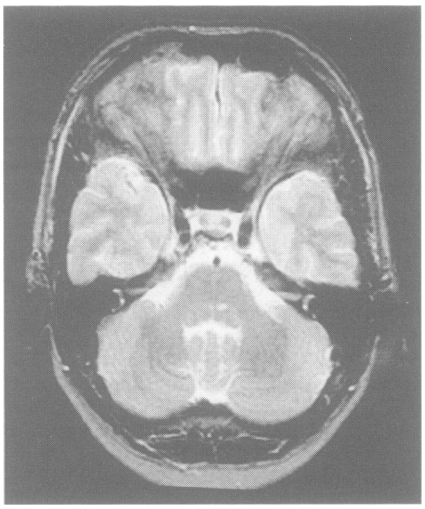
In January 1995 he suddenly experienced diplopia while driving his car. On examination there was a complete paralysis of the left abducens nerve but no signs of a relapse

of the neuropathy. After three months the diplopia had disappeared. The CSF showed 6 × 10^9/l mononuclear cells and a protein content of 0·88 g/l; some oligoclonal bands were present, but the IgG index was normal. Brain MRI showed multiple abnormalities of periventricular white matter. Some of these enhanced after intravenous administration of gadolineum, suggesting active CNS inflammation. In the pons an area of high T2 signal intensity was seen in the proximal part of the fila radicularia of the left abducens nerve, providing substantial evidence for a sixth nerve palsy of CNS origin (figure).

Although a vascular origin cannot be fully excluded, the distribution of the lesions was typical for plaques seen in multiple sclerosis. Moreover, the enhancing white matter lesions were present several weeks after onset of the sixth nerve palsy, making a coincidental vascular lesion unlikely. Lesions without enhancement may reflect older lesions. Nevertheless, multiple sclerosis could not be diagnosed, as other white matter abnormalities in the CNS were asymptomatic.

Previous studies have suggested that cranial nerve lesions in CIDP may be related to CNS lesions.[1 5] However, MRI abnormalities were not more common in patients with cranial nerve involvement than in those without.[1] The enhancing pontine lesion in our patient is suggestive of active CNS demyelination and therefore probably responsible for a central origin of the ocular palsy, which interestingly occurred independent of peripheral nerve involvement at that time. Previous information on white matter abnormalities in the CNS in this patient was not obtained as MRI is not a routine diagnostic procedure in CIDP. Yet these abnormalities may occur in a disproportionate number of patients.[1 3 6 7]

There may be several explanations for the combined occurrence of central and peripheral myelin dysfunction. Firstly, coincidence seems unlikely, as so many patients with CIDP show evidence of involvement of central white matter. Secondly, the process of demyelination in itself may lead to ongoing generalised demyelination through activation of cytokines. Finally, central and peripheral myelin may share common antigens which trigger an immune response. The occurrence of isolated sixth nerve palsy in our patient stresses the relevance of MRI in patients with CIDP and cranial nerve dysfunction.



T2 weighted transaxial spin echo MR study (TR 2653, TE 100). At the level of the middle cerebellar peduncles an isolated lesion of high signal intensity is present below the floor of the fourth ventricle, close to the median plane, corresponding with the proximal part of the fila radicularia of the left abducens nerve.

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Capture-recapture methods for precise measurement of the incidence and prevalence of stroke

Capture-recapture methods, originally developed for wildlife censuses, are increasingly being used in epidemiology to estimate the incidence and prevalence of disease in the population.[1] The principle is that two or more censuses are taken, with the people or animals being identified and marked on each occasion, and knowledge of the degree of independence of these censuses is used to estimate the proportion of the total population that has been missed. This allows an estimate of the size of the total population under study. Capture-recapture results have been published for a wide range of medical conditions including myocardial infarction,[2] but not yet for stroke. The method is attractive because maintaining community based registers that are "as complete as possible" is an expensive exercise.

Using the capture-recapture method, at least two independent sources of cases need to be identified. The number of cases that are common to both sources is calculated (m), as are also the total numbers of cases from the first and second samples (M and n respectively). A simple capture-recapture estimate of the total number of cases, N, is given by the equation:

$$N = \frac{(M + 1)(n + 1)}{(m + 1)} - 1$$

LaPorte has used the capture-recapture method to estimate the number of cases of myocardial infarction in six communities in Sweden,[2] with the myocardial infarction registry as the first source (M = 5832) and the hospital discharge index as the second source (n = 6582), and noted an overlap of m = 4746. The capture-recapture estimate of 8088 cases implies that 5% of the cases of myocardial infarction had been missed by both sources of notification. The fact that cases may be missing from the individual sources need not be an important drawback when the capture-recapture method is used, as the pattern of overlap allows these missing cases to be inferred.

In a preliminary analysis we have attempted to apply capture-recapture to a previously published study of the incidence of first time stroke among those aged under 75 years.[3] This was carried out in three districts of south east England (two inner city and one rural) in 1989–91 and used notifications from hospital ward registers, general practitioners, rehabilitation staff, and death certificates. The main difficulty we met was the lack of independence between sources of notification, which would be due partly to strokes of different degrees of severity being likely to be registered by the different sources. (This is known as "variable catchability" from the corresponding situation in wildlife surveys, in which some categories of animal are more likely to be caught in one census than in another.) In our study, an example of variable catchability is that the most serious strokes would most likely be registered only as death certificates, and the mildest strokes only as general practitioner or rehabilitation staff notifications.

Secondly, when planning a study in which capture-recapture methods are not intended, it is natural to encourage sources of notification to be complementary rather than overlapping. For instance, in our study general practitioners were asked to record all cases of stroke but to take particular care to record those not admitted to hospital.

A further difficulty, especially in inner city areas, is the high mobility of the overall population—that is, those people resident in the study districts and at risk of stroke. The overall annual population mobility in central London is estimated at around 30%, but this would be lower for the older people more likely to have a stroke.

Log linear modelling is now the most common statistical method for analysing capture-recapture data. It is flexible but does not allow for variable catchability, therefore the analysis should be stratified—that is, the different types of case (for example, mild, moderate, and severe) should be identified and separate estimates made of their respective sizes. Calculating confidence intervals for incidence estimates is not straightforward, but the "bootstrapping" computational technique has been used.[4]

In our incidence study a total of 639 strokes were registered, representing a crude annual rate of 0·68 patients with first time stroke per 1000 population (aged under 75 years).[3] The corresponding crude rate from the Oxfordshire Community Stroke Project, some 10 years earlier, was 0·93 with 95% confidence interval 0·82–1·04.[5]

Our initial capture-recapture estimate of the total number of strokes, obtained using log linear modelling, was 1999, corresponding to 2·13 cases per 1000 person-years. This rate is more than twice that of the Oxfordshire study and, considering the thor-