mean (SD) dose of levodopa : 595 (88) mg, mean (SD) stage of Hoehn and Yahr : 3.2 (0.3) with waning efficacy of levodopa and who were requiring an increase in PD treatment. The second group included 11 other patients, mean age, 61 (2) years, mean (SD) duration of PD : 12 (1) years, mean (SD) dose of levodopa : 857 (92) mg, mean (SD) duration of levodopa therapy : 10 (1) years, mean (SD) stage of Hoehn and Yahr : 3.0 (0.3) with levodopa-induced peak-dose dyskinesias most of the day. In both groups, ifenprodil (Vadilex), (20 mg three times daily orally, the dose currently used in clinical practice) was added in an open design without changing the previous usual treatment. These two kinds of PD patients were selected to investigate if the NMDA antagonist could improve Parkinsonian symptoms (group 1) or modify dyskinesias (group 2). Parkinsonian symptoms were evaluated in the morning (10 am) according to the Unified Parkinson's Disease Rating Scale (UPDRS) before and after 1 month of treatment. Each new assessment was made blind, without the previous scale score in front of the physician. Patients of group 2 were assessed in the "on" condition.

Add-on therapy with ifenprodil did not modify the Parkinsonian symptoms in any group. The total UPDRS motor examination score did not change significantly in group 1 18.6 (3.5) vs 20.2 (3.2) or group 2 [9.4 (2.3) vs 8.6 (2.4)]. The UPDRS subscores for cardinal extrapyramidal symptoms (tremor, rigidity, bradykinesia) or for daily activities did not change (data not shown). The dyskinesia score remained unchanged in group 2. Side effects were palpitations and sedation (1 patient) and feeling of nasal congestion (1 patient).

Our study is the first to investigate the clinical effects of an NMDA antagonist in the treatment of PD. It failed to demonstrate any relevant anti-Parkinsonian effect of ifenprodil. These negative results must, however, be considered with caution. We used the daily dose of ifenprodil recommended for the treatment of intermittent claudication but the pharmacokinetic profile of the drug is poorly known. No published data are available about its plasma half life and brain distribution. It is thus possible that other NMDA antagonists with a better pharmacokinetic profile may exert more potent effects in PD. Since the polyamine modulatory site is only a part of the NMDA receptor complex,^{6,7} it is also difficult to give a precise biochemical interpretation of our result. Our work does not exclude a definite role for NMDA antagonists in PD. Further studies should be conducted with other NMDA antagonists when available in humans.

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Central pontine myelinolysis in a patient with AIDS

Central pontine myelinolysis (CPM) has been associated with rapid correction of hyponatraemia¹ as well as an acute rise in serum sodium even from normonatraemic levels.² CPM has also been linked with hyperosmolality.³ The rate of change in the osmolality, the length of time that this rate of change persists, and the clinical condition of the patient are all important factors.⁴ We describe a case of CPM in a 49 year old HIV positive homosexual man who had a normal serum sodium and osmolality throughout his illness.

The patient had been HIV positive for at least six years. In 1989 he developed increasing hepatosplenomegaly and uncontrollable thrombocytopenia. A splenectomy was performed and histology showed only non-specific changes associated with HIV. After an initial stormy postoperative course, he made an excellent recovery and returned to work.

Seven months later he presented with a short history of malaise, anorexia, and fevers. The only abnormal finding was a pericardial rub. Investigations showed that he was mildly anaemic, and hypoalbuminaemic with a serum albumin of 19 g/l. Liver function tests and clotting studies were normal. Initial investigations were all negative apart from demonstrating a pericardial effusion and a small pleural effusion. On rescanning for pericardiocentesis, however, the effusion had resolved. A small pleural effusion was aspirated and found to contain numerous lymphocytes suggesting a lymphoma. Immunocytochemistry was unhelpful. Bone marrow examination and 24 h urine protein excretion were normal. He had no gastrointestinal symptoms. Thirteen days before his death he developed diplopia and was found to have a right sixth nerve palsy. A CT brain scan showed no abnormalities. A lumbar puncture showed clear CSF with 10 lymphocytes and a protein of 0.78 g/l. No pathogens were isolated and he was cryptococcal antigen negative. Cytology of the CSF was normal. A trial of high dose steroids made no difference to his deterioration. He became progressively

Figure Myelin stained section of the pons showing the area of circumscribed pallor in the base characteristic of CPM.

weaker, developed right-sided ptosis and dysarthria and died a few days later.

Necropsy examination demonstrated disseminated lymphoma, including large ulcerating deposits in the stomach. Postmortem examination of the brain showed the typical appearance of CPM with a large well defined focus of myelin loss in the base of the mid-pons and upper-pons (figure). Focal infiltrates of lipid containing macrophages were present in the area of myelinolysis but there was no inflammation otherwise associated with this lesion. Axons were partly preserved. There was some mild cerebral atrophy, mild diffuse myelin pallor in the cerebrum and slight lymphomatous infiltration of the meninges.

To our knowledge there have been no previous reports of CPM in association with HIV. The only significant biochemical abnormality was the hypoalbuminaemia which developed in the month preceding his death. This may have been due to gastro-intestinal losses as well as to his underlying condition. His serum sodium remained normal throughout his stay in hospital, and he received no intravenous fluids. His albumin remained at 19 g/l until he died. CPM has been described in liver transplant recipients and in severe burns cases, as well as in association with alcoholism and malnutrition. It has been thought that the rapid correction, or over correction, of hyponatraemia was the crucial factor in causing CPM in most cases. This is obviously not the only cause. In a series of CPM in severely burnt patients, hyponatraemia was not a feature, whereas each patient who developed CPM had had a prolonged episode of extreme hyperosmolality. Our patient did not have an episode of serum hyperosmolality, but had one month of hypoalbuminaemia. A low serum albumin may be a significant factor in the development of CPM. This could be a feature common to our patient and the groups of patients described above in which CPM had been reported. Another possibility is that CPM may be a primary effect of HIV, representing yet another neuropathological manifestation of this virus. The p24 HIV protein was detected immunocytochemically in rare perivascular macro-

phages in the brain stem in this case, at and beyond the margin of the area involved with CPM. No multinucleated cells were seen.

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Could midbrain "resting" tremor be caused by postural maintenance at rest?

James Parkinson described resting tremor suggesting that tremor in Parkinson's disease (PD) persists even when the patient no longer has to maintain limb posture. So-called midbrain or rubral tremor characteristically includes resting, postural, and intention tremor. Gordon Holmes¹ noticed that midbrain resting tremor ceased when the limb was completely at rest. Holmes' observation suggests that midbrain resting tremor, contrary to resting tremor in PD, is caused by postural maintenance. We describe a patient with presumed midbrain tremor showing evidence that PD resting tremor and midbrain resting tremor may have a different neurophysiological background.

At the age of 63, a 67 year old man was suddenly struck by a left-sided third nerve palsy and a right-sided hemiparesis which disappeared after a few weeks. After this period resting, postural, and intentional tremor appeared in the right arm. He developed coarse, irregular myoclonic head shaking to the right and frequent generalised shuddering tremor lasting a few seconds. The patient was unsuccessfully treated with Sinemet. With orphenadrine 50 mg four times daily the tremor diminished, as did the shuddering attacks. Four years later the patient noticed that the entire limb tremor would disappear if he pushed firmly on the upper edge of the homolateral trapezius muscle.

On physical examination the right arm showed a complex resting tremor (Webster grade 2-3) with flapping flexion-extension at the wrist and elbow, and pronation-supination of the forearm. In our patient the first finger was beating against the thumb, though the classic "pill-rolling" movement of the thumb against the first finger, was absent (According to Denny-Brown² these movements of our patient's first finger and thumb differentiate midbrain tremor from PD tremor). The tremor amplitude increased on stretching the arms out and performing the finger-nose test. With distraction, when the patient was at rest or lying on a bed the tremor sometimes disappeared. The right

arm was hypokinetic (grade 1) and rigid (grade 2).

EMG showed regular 5 Hz bursts in the trapezius, supraspinatus and splenius capitis muscles, with the trapezius muscle constantly discharging 10 to 20 ms before the supraspinatus muscle. There were alternating 5 Hz bursts in the biceps and triceps muscles. CT head scan did not reveal any focal abnormalities.

The resting and action tremors were completely abolished by local intramuscular injection of 10-20 cc bupivacaine-adrenaline solution into the supraspinatus and the adjacent part of the trapezius muscle. The effect on the tremor lasted for days to weeks, although it diminished after the first few days. The patient was treated 17 times with intervals of two weeks to three months. Unfortunately the 17th injection caused a troublesome pneumothorax, so that the patient refused further injections.

Although we do not have direct anatomical proof of a mesencephalic lesion in our patient, the clinical picture consisting of acute ipsilateral third nerve palsy and contralateral hemiparesis warrants a diagnosis of Benedikt's syndrome as a result of mesencephalic stroke. In these patients a so-called midbrain tremor, that is, combined resting, postural and intentional tremor, may develop.

Direct evidence that postural maintenance rather than rest was involved in our patient was provided by local intramuscular anaesthetic infiltration after which both action and resting tremor disappeared. Although we cannot explain why the beneficial effect was so long lasting, the effect itself is well known. According to Rondot,³ postural tremors may spread from one muscle to the other muscles of the limb. Intramuscular anaesthesia of the muscles in which the rhythmic activity originates stops the rhythmic phenomena in all muscles of the corresponding limb. This procedure was neither effective in suppressing the resting tremor in 3 of our PD patients with classic resting tremor, rigidity and hypokinesia at the injected side, nor in PD patients elsewhere, Rondot *et al*³ and Rondot (personal communication).

Sabra and Hallett⁴ argued that in cases of severe tremor appearing on postural maintenance, Holmes' term "rubral tremor" should be avoided; "severe postural cerebellar tremor" is more appropriate because it is mainly the superior cerebellar peduncle which is involved. The most typical vascular form of this postural tremor is associated with a contralateral third nerve palsy.⁵ Antagonist muscles in these patients showed Parkinson-like alternating activity. Both findings are also present in our patient. Although Sabra and Hallett mention only one of their 32 patients having a tremor at rest, our case suggests that postural tremor at rest may be part of such postural tremor.

We cannot exclude the possibility that, depending on the site and extent of the lesion, other patients with so-called midbrain tremor show the characteristic resting tremor of PD. Dopa responsive midbrain tremor^{6,7} may belong to this group. Patients with midbrain tremor will be studied carefully in an attempt to resolve this issue.

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Transcutaneous phrenic nerve stimulation

Transcutaneous phrenic nerve stimulation, with measurement of the terminal latency of the nerve, is a well recognised technique for assessing phrenic integrity. The technique used is essentially that described by Newsom-Davis in 1967,¹ with measurement of the diaphragmatic compound muscle action potential (CMAP) using surface electrodes placed over the chest wall. The exact position of the electrodes has been the subject of some discussion. Newsom-Davis originally recorded from the eighth intercostal space in the anterior axillary line. In other studies the fifth and sixth spaces, also in the anterior axillary line, the eighth space and the xiphisternum, and the seventh or eighth space near the costochondral junction have been used.² Most recent studies have used the seventh or eighth intercostal spaces just anterior to the costal margin.^{3,4}

In some papers, notably Newsom-Davis's original work,² there was slight concern over the possibility of stimulating nerves other than the phrenic, especially those supplied by the brachial plexus, and producing a CMAP that did not reflect diaphragmatic contraction. This was not borne out clinically and brachial plexus stimulation, while common (especially in children⁴), does not affect the CMAP seen. Other muscles which also may be stimulated, such as latissimus dorsi, lie too far away from the electrodes to affect the signal. Stimulation of the serratus anterior muscle was also suggested as a possible confounding contraction² but anterior placement of the electrodes should avoid this as the origins of the muscle are from the lateral borders of the upper 8-10 ribs.

We are involved in a prospective study of phrenic nerve function in children having cardiac surgery, and over the period of a year have successfully studied over 250 children before and after surgery. Chest electrodes are placed over the seventh intercostal space and over the eighth rib in the anterior axillary line. In a small number of children we are now recognising an artefactual trace which was initially thought to be part of the diaphragmatic CMAP; we now recognise that it is clearly not. Figure 1 shows the preoperative trace of a normal five year old boy, with latency measured at 5 ms. Post-operatively his trace was that seen in figure 2. This shows an apparent latency of 2.6 ms with a normal appearance to the CMAP.