chronic myoclonic jerks that affected the face and limbs. Tactile and auditory stimuli produced generalised myoclonic jerks. Fundoscopy and pupillary reactions were normal and oculocephalic, corneal and gag reflexes were present. Muscle tone was normal. Generalised myoclonic jerks were produced when deep tendon reflexes were tested. Both plantar responses were flexor. Formal assessment of muscle power, sensation and coordination was not possible.

General examination revealed third and fourth heart sounds and a soft ejection systolic murmur.

Initial biochemical investigation showed: plasma potassium 7.9 mmol/l, bicarbonate 17 mmol/l, urea 47.8 mmol/l, creatinine 1504 μmol/l, glucose 7.5 mmol/l, arterial blood pH 7.24, pCO2 43 mm Hg, pO2 104 mm Hg, oxygen saturation 97%. The haemoglobin level was 97 g/l and the leucocyte count 10.8 × 10⁹/l. Cardiomegaly was present on a chest radiograph. Three sets of blood cultures and a midstream urine specimen were sterile.

Three hours of haemodialysis did not affect the patient's neurological status. A generalised tonic/clonic convulsion occurred less than 10 minutes after administration of naloxone, 0.2 mg. Recurrent hyperkalaemia (7.5 mmol/l) was treated with oral sodium resonium. Electroencephalography revealed generalised theta and delta activity of moderate to high amplitude, intermixed with multifocal spike and sharp waves at a frequency of 1–2 per second. Intravenous injection of clonazepam, 0.5 mg, resulted in immediate cessation of myoclonic jerks and reduction of spike and sharp activity. Lower amplitude semirhythmic 3–4 Hz activity appeared. Myoclonus and hyperkalaemia did not recur. The pethidine level in the plasma stored from the time of admission was <10 μg/l and the norpethidine level 114 μg/l. Haemodialysis did not affect the rate of fall of plasma norpethidine levels which were logarithmically related to time (correlation coefficient, r = −0.82; P < 0.05). The elimination half life of the metabolite in our patient was 25 hours.

The initial metabolism of pethidine occurs in the liver where hydrolysis to pethidinic acid and N-demethylation to norpethidine, followed by hydrolysis to norpethidinic acid, occurs. While repeated administration of pethidine in patients with cancer 14 or sickle cell anaemia may result in norpethidine accumulation, more rapid accumulation after fewer doses occurs in renal failure. Norpethidine is a central nervous system excitant with less potent depressant effects than pethidine. The progression of excitatory effects, from nervousness and tremors to agitated delirium, multifocal myoclonus and seizures, in a group of cancer patients treated with pethidine, correlated with the plasma level of norpethidine as well as the ratio of norpethidine to pethidine in the plasma.2

It is likely that the myoclonus and generalised convulsions in our patient were related to norpethidine accumulation. Normal muscle tone and marked stimulus sensitivity do not usually occur in a phentozpine (procyclorperazine) induced syndrome. In our patient, the effect of uraemia on the threshold for central excitation, resulted in lower norpethidine levels producing myoclonus and seizures compared to the levels required in cancer patients (424–1856 μg/l).3

In both uraemic and norpethidine related myoclonus, the involvement of not only the distal muscles of the stimulated limb, but also proximal muscles and other limbs in the myoclonic response to peripheral stimuli, suggests that the myoclonus was a reticular rather than a cortical reflex type. The former has been described in uraemia,4 hypotnarrayaemia and post anoxic encephalopathy.

Because of norpethidine's long half life in uraemic patients, neurological abnormalities may persist for several days after cessation of pethidine. In the presence of renal failure, repeated muscle contraction may result in life threatening hyperkalaemia and urgent control of myoclonus and seizures becomes necessary. Clonazepam was very effective in this case and is also dramatically effective in controlling post-anoxic myoclonus, where diazepam, phenytoin and phenobarbitone may have been ineffective.5 In another reported case of myoclonus due to presumed norpethidine toxicity, clonazepam was ineffective but the route of administration was not recorded. Naloxone, by completely antagonising the depressant effects of pethidine and norpethidine but only partially antagonising the latter's excitatory effects,6 may unmask seizure activity when used in norpethidine intoxication. From our data, norpethidine appears to be difficult to remove by dialysis.

In uraemic patients requiring narcotic analgesia, agents such as pethidine and dextropropoxyphene with toxic metabolites should be avoided. While morphine and codeine may result in unusually severe and prolonged respiratory depression and sedation in renal failure, their cautious use at lower dosage, with careful clinical monitoring, is to be preferred.

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Intramedullary spinal cord metastasis following a slowly progressive course

Sir: Intramedullary spinal cord metastasis is a well known but rare complication of cancer.1 In the majority of patients it occurs in conjunction with widespread systemic disease and progresses rapidly.2 We report a patient in whom the condition was the only indication of relapse and whose signs and symptoms progressed slowly.

A 54 year old woman was referred to our department because of difficulty in walking, burning sensations in the thighs and low backache, slowly progressive over the past year. At the age of 52 an adenocarcinoma of the lung had been detected and a lobectomy of the left lung had been performed.

Examination showed proximal paresis of the legs, MRC grade 3–4/5, more pronounced on the right side. Distally, the strength was nearly normal. Superficial pain and
temperature sensations were disturbed below the level of L2 in both legs. Sensation of vibration was impaired below the hip on the right side and below the knee on the left side. Tendon reflexes of the legs were decreased. Plantar responses were equivocal. Cerebrospinal fluid (CSF) contained 8 leukocytes per mm³; no tumour cells were found at repeated lumbar punctures. The protein and β-glucuronidase content were increased to respectively 1.46 g/l (normal value: 0.20–0.50 g/l) and 37 mU/l (normal value: 9–27 mU/l). Myelography on the first occasion did not show a significant abnormality but three months later showed widening of the spinal cord at level T10–T11. Magnetic resonance imaging (MRI) revealed an intramedullary lesion with prominent enhancement after intravenous administration of gadolinium (fig). Other metastases were not detected and an exploratory operation was performed. After laminectomy, a local tumorous enlargement of the spinal cord at level T10–T11 was found, with diffuse widening of the spinal cord for two centimeters cranially. The dorsal surface of the spinal cord looked normal and there were no signs of leptomeningeal involvement. After incision, the partly necrotic intramedullary tumour was removed as radically as possible. The histological appearance of the removed tissue was identical to that of the lung tumour. The patient received radiotherapy to the site of the metastasis. Strength and sensation in the legs improved.

For nine months her clinical condition remained stable but the strength in her legs then declined again. Myelography showed recurrence of the tumour. Radiotherapy induced a second remission for four months after which she developed an almost complete neurological deficit below the level of Th10.

Intramedullary spinal cord metastasis usually has an abrupt onset. Untreated, the neurological symptoms evolve within one month to full deficit and more than 80% of the patients die within three months after seeking medical attention. Our patient and the few other examples published2,3 show that the condition can follow a slowly progressive course and hence should be included in the differential diagnosis of a patient with a slowly progressive myelopathy.

As initially in our patient, myelography fails to show an abnormality in about 40% of cases2 and MRI is likely to be superior. Patients with intramedullary spinal cord metastasis have variable, sometimes virtually normal, CSF findings.4 In some patients it contains identifiable tumour cells but in such cases meningeal carcinomatosis is likely to be present. The slight elevation of β-glucuronidase content noted in our patient may also reflect leptomeningeal involvement, although slight elevations of cerebrospinal β-glucuronidase activities occur with parenchymal metastases.5 Radiation therapy can be an effective treatment and lead to neurological stabilisation or improvement and disappearance of pain. Operative treatment has been used rarely6 but, as in our patient, can be temporarily beneficial when the condition is slowly progressive.

Fig MRI T1 weighted image after intravenous gadolinium showing intense signal intramedullary at T10–T11.
Intramedullary spinal cord metastasis following a slowly progressive course.
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