

two months after a small infarction in the left thalamus. She stated that the pain was constant, burning, and unbearable. There was pronounced allodynia to light touch and cold stimuli. Pinprick showed hyperaesthesia. At first we gave 50 µg of baclofen intrathecally, with no pain relief. The dose was gradually increased to 150 µg but she reported no pain relief. There was transient urinary retention.

Case 4

A 62-year-old man had central pain due to cerebral haemorrhage in the left corona radiata. His pain was in the distal parts of the right upper and lower extremities. There was no allodynia. Hyperaesthesia to pinprick was noted in the right half of his body. A bolus of 50 µg of intrathecal baclofen resulted in considerable pain reduction in an hour (1-2/10), that developed in the upper and lower limbs at the same time. The effect continued for about 12 hours. This response was confirmed three times with repeat intrathecal injections of the same dose. There was no sensory change with the injection.

Case 5

A 47-year-old woman had had disabling central pain for the past two years. The pain was in the right half of her body including the face. This pain started two months after a hypertensive haemorrhage in the left putamen. Although there was no allodynia, hyperaesthesia to pinprick stimuli was noted in the right half of the body. About one hour after intrathecal baclofen (50 µg), pain relief developed in the face first, and then in the arm and leg. She reported pain scores of 4-6/10. We gave the injection five times and the pain relief was consistent. Relief was always associated with suppression of hyperaesthesia. Placebo did not relieve the pain.

All the patients except one (case 3) reported that no other treatment had been as effective as intrathecal baclofen. Although the present study was not double-blind, we do not consider that the result is merely a placebo effect or is due to observers' bias. The pain relief was always associated with baclofen and placebo was ineffective. Although the patients were not informed of the possible course of pain relief, it was constant for each individual patient. After the study period of intrathecal baclofen, we gave oral baclofen (30-60 mg/day) to all patients; no pain relief was achieved.

Baclofen, an agonist of γ -aminobutyric acid (GABA) receptors, has antispastic effects and its intrathecal use relieves severe spasticity.² Furthermore, intrathecal baclofen is known to have an antinociceptive effect in experimental animals, which is not reversed by naloxone.^{4,5} Intrathecal baclofen also suppresses allodynia induced by prostaglandin $F_{2\alpha}$ in mice.³ Recently Herman *et al*¹ reported that intrathecal baclofen relieves central pain in patients with spinal lesions. In their report, even a patient with a C3 lesion showed suppression of leg pain with lumbar intrathecal baclofen.

The mechanism of suppression of central pain after a stroke with lumbar intrathecal baclofen is difficult to explain. In the first two patients, pain relief started from the leg. Therefore we considered that the effect was

segmental and due to a direct effect of baclofen on the GABA receptors in the spinal cord. This supports the hypothesis that the loss of dorsal horn interneurons containing GABA and glycine in humans leads to an allodynic or hyperaesthetic state,⁵ and it should be studied further if such loss of spinal interneurons occurs in central pain syndrome of supraspinal origin. In two patients, however, relief developed in the arms and legs at the same time and even facial pain was relieved. This is not explained by the spinal segmental effect of baclofen. Therefore, we also consider that there might be a GABA-receptor related pain suppression system that ascends from the spinal cord to a higher level.

This preliminary study indicates that a controlled clinical trial of continuous baclofen infusion is feasible for patients with central pain of supraspinal origin.

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Effect of immobilisation on position and movement sense of the knee

It has been suggested that joint position and movement sense can be improved by practice or by specialised therapeutic techniques such as weight-bearing exercises.¹ Also, motor imbalance after immobilisation may be attributed to proprioceptive deconditioning. To investigate these theories we used established measurement techniques² to test normal knees in 18 patients after a minimum two weeks of immobilisation. Ten patients had been immobilised in a full length leg plaster after fractures of the ankle region and eight were on strict bed rest due to injuries of the untested leg. Results were compared with those of 30 controls with no history of immobilisation.

Movement sense was tested by determining the threshold of perception of slow joint movement at a velocity of 0.5° per second. A motor extended or flexed the knee (starting position 35° flexion) via a system of pulleys connected to the seated and blindfolded subject by a canvas sling wrapped around an inflatable boot. Four randomised tests were carried out in flexion and extension ranges. Subjects signalled

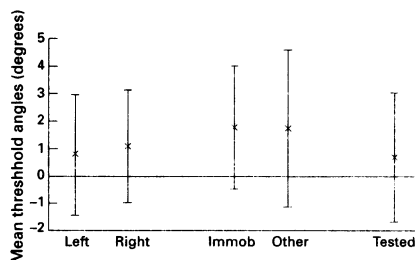
appreciation of knee joint movement by depressing a hand-held switch. The range of movement traversed before detection (threshold angle) was extrapolated from the output of potentiometers placed in parallel with the main pulley circuit.

Position sense was tested by measuring the margin of error in the reproduction of previously held knee joint positions. Tests were carried out within the range 20°-50° of knee flexion—the normal arc of movement during walking. Three conditions operated—namely, active reproduction of an active movement, active reproduction of a passive movement, and passive reproduction of a passive movement. Tests involving active movement were not carried out on the plaster group because of potential effects of muscle weakness and lack of coordination on results. Achievement of target positions was signalled by depressing a hand-held switch.

Results were recorded directly onto computer disc and analysed with two-tailed *t* tests and one way analysis of variance. Tests of movement sense did not show any significant differences either between or within groups (figure). Movement was detected within a mean of 2°.

There were no significant differences in results for position sense either between or within groups. Subjects were accurate to within a mean of 4°. There was a trend, which reached significance in controls ($n = 13$, $p < 0.001$), for greater inaccuracy in active reproduction of a passive movement compared with active reproduction of an active movement and passive reproduction of a passive movement.

In conclusion, results for controls were comparable with those of other studies on the knee joint.^{2,3} No significant differences were detected in position or movement sense between the knees of subjects experiencing altered mobility and weight-bearing conditions and normal controls. The applicability of the results of these tests to normal functional movement is uncertain and warrants further investigation. Results suggest, however, that functional deficits in non-neurological subjects after a period of altered weight-bearing and mobility of the knee joint may be due to factors other than adaptation of position and movement sense mechanisms. Position and movement sense seem to be resistant to changing physical states. The rationale of therapeutic techniques that purport to improve position and movement sense in neurologically intact patients should be reconsidered.



Geometric mean threshold angles in extension range. Right and left = right and left legs of the control group ($n = 30$); immob and other = the previously immobilised leg and the other leg in the immobilised plaster group ($n = 10$); tested = the unaffected leg in the bed rest group ($n = 8$).

As well as this central finding, the results of our study provide further support for a role of muscle afferents in proprioception.⁴ Controls were significantly less accurate in reproducing knee joint position when initial test movements differed from subsequent target seeking movements. This has possible implications for the common physiotherapeutic practice of re-educating active movement through the medium of passive movement.

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Worsening of myasthenia gravis on treatment with imipenem/cilastatin

Myasthenia gravis may be exacerbated by a number of antibiotics which impair neuromuscular transmission, including the aminoglycosides, tetracyclines, and the polypeptide group.¹ Several reports have suggested that ampicillin and erythromycin may have similar effects.^{2,3}

We describe here the worsening of myasthenia gravis on treatment with imipenem/cilastatin. Imipenem is a member of a new class of β lactam antibacterial drugs: the carbapenems. It is combined with cilastatin, a renal dehydropeptidase inhibitor, to inhibit renal degradation and has a wide spectrum of activity against Gram positive, Gram negative, and anaerobic bacteria, and against many multi-resistant strains of bacteria.

CASE REPORT

A 45-year-old man presented with a three week history of progressive diplopia, facial weakness, and respiratory difficulties. Myasthenia gravis with malignant thymoma had been diagnosed 10 years previously; thymectomy was performed at that time and histology showed a mixed lymphocytic/epithelial cell tumour. He had a left upper lobectomy for pleural based metastases three years later. For the next seven years he remained well, requiring only 120 mg of pyridostigmine bromide daily.

At presentation mechanical ventilation was necessary. He was treated with azathioprine, steroids were gradually added to a dose of 60 mg prednisolone daily, and he received a course of plasma exchange.

Two months after admission he was extubated. At this stage he was receiving 150 mg pyridostigmine every three hours, azathioprine 150 mg each day, and prednisolone 60 mg on alternate days. Plasma

exchange was continued with an exchange of two litres on a fortnightly basis. Six weeks after extubation a catheter was inserted into the right subclavian vein for easy venous access. He improved slowly. His forced vital capacity (FVC) increased from 0.3 l on admission to 2.4 l with moderate fatigue of the ocular and bulbar muscles. He subsequently developed superficial cellulitis at the site of the catheter. *Staphylococcus aureus* was grown and he was treated with flucloxacillin 500 mg intravenously three times a day. *Serratia marcescens* was grown on a routine sputum specimen taken two weeks previously and thus imipenem/cilastatin 500 mg intravenously four times a day was added.

His myasthenia deteriorated dramatically over the next 48 hours. His FVC decreased to 1.8 l with diplopia, marked bilateral facial weakness, and severe bulbar weakness. He also noted increased weakness in his arms and proximal leg muscles and had difficulty in walking. Serum calcium, urea, and electrolytes were normal. He responded positively to edrophonium 10 mg intravenously, with an improvement of the ocular bulbar and limb weakness. His FVC increased to 2.3 l. The imipenem/cilastatin was discontinued and the other drugs were left unchanged. Plasma exchange was not repeated at this stage due to the presence of infection; despite this, he improved over the next 24 hours and after 48 hours was back to his baseline state. The cellulitis resolved after six days and the flucloxacillin was discontinued after two weeks.

Various antibiotics may interfere with neuromuscular transmission and the mechanisms of action may include: a pre-synaptic effect leading to impaired release of acetylcholine, a post-synaptic curare-like blockade of the acetylcholine receptor, or a combination of the two mechanisms. The aminoglycosides act pre-synaptically and post-synaptically, while the tetracyclines have a curare-like action.¹ The mechanisms of action of ampicillin, erythromycin, ciprofloxacin, and the polypeptides are unclear.^{2,4}

A discussion with staff at Merck, Sharp and Dohme showed that one case had been reported to their adverse event database of myasthenia gravis developing in a patient receiving imipenem/cilastatin. To our knowledge there has been no published case. Our patient developed a worsening of his myasthenia while receiving this drug. His concurrent cellulitis may have been an additive factor, but this persisted long after the patient returned his to baseline state.

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Acceptability of electroconvulsive therapy to patients with Parkinson's disease

Some patients with Parkinson's disease have been shown to respond to electroconvulsive therapy (ECT).^{1–3} It is not currently offered as a treatment for Parkinson's disease in the UK as clinicians do not consider it acceptable because of the stigma surrounding what may be seen as a psychiatric treatment and a fear of ECT by the patients based on a lack of information. This is surprising as non-drug treatments such as fetal tissue transplantation are more invasive and carry a higher risk than ECT. A consultant neurologist, while canvassing the opinions of patients attending a movement disorder clinic to assess the feasibility of a trial, found that patients were not keen to consider ECT as a treatment.

We decided to investigate this further with a larger group of patients in a standard manner using a questionnaire. Patients were asked a series of questions, including whether they would give consent to ECT if it were of definite benefit and, if so, would they agree to ECT as they were at that time or only if their disease became worse. Their opinion on consent to stereotactic transplantation was also sought.

All respondents were current patients selected from the Parkinson's disease register based at the department of neurology at the Institute of Psychiatry. Sixty-five questionnaires were distributed, of which 50 were completed. Twenty-six of these were administered to patients waiting in the outpatient department and 24 were sent out and returned by patients through the post. The mean age of the patients completing the questionnaire was 66.3 years and the mean duration of illness was 7.9 years. Twenty-eight of the respondents were men and 22 women. Fifty per cent of respondents had no other coexisting medical disorder. Twenty-eight per cent of respondents said they would consider ECT as a treatment at their present stage of illness if it was definitely known that ECT was of benefit in Parkinson's disease. A further 32% said they would only consider ECT if their illness became worse, and 36% said they would never consider it.

When asked about stereotactic transplantation, 16% of respondents said they would consider it at their present stage of illness and 28% only if their illness became worse. Fifty-two per cent said they would not consider it under any circumstances.

We conclude that patients with Parkinson's disease are more likely to accept ECT as a potential treatment than stereotactic transplantation. Had the patients been counselled or given further information about ECT, the proportion of respondents in this study agreeing to have it may have been greater. We suggest, in the light of these findings, that although ECT is not yet of proved value, it could potentially be a safe and effective option in Parkinson's disease, and that it is acceptable to a sizeable minority of patients. Those patients for whom drug treatment is proving unsatisfactory or in whom depressive features are prominent may benefit the most from ECT, but there is still a need for a definitive trial and our findings will have a bearing on the design of such a trial.

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