potential of 5 mv over the right and 2 mv over the left biceps with an onset latency of 4.1 ms and 4.2 ms respectively. Antidromic sensory stimulation of the lateral cutaneous nerve of the forearm evoked a potential of 5 uV at a peak latency of 2.8 ms on the left; the corresponding values for the right were 18 uV and 2.5 ms.

The patient was referred to a physiotherapist for restrengthening exercises. By 10 February, when last seen, she had further improved.

The modern history of brachial plexopathy dates from Spillane's 1943 study of "acute brachial radiculitis" among 46 British soldiers, 26 of whom developed the characteristic pain and neurological deficits while convalescing from other illnesses.⁴ The term "neuralgic amyotrophy" dates from 1948, when Parsonage and Turner described 136 British army personnel with this condition.³ In this study, "66 of the 136 were in hospital with other conditions when the shoulder-girdle symptoms began, and others had recently recovered from illnesses. In 98 of the cases there was evidence of some precipitating factor".³ Later the same authors offered follow up data on 82 patients, and noted that several nerves, most notably the anterior interosseous, were involved individually.⁵ The prognosis was good, most attacks resolving completely in two years, but "in a few cases second attacks may occur many years after the first attack".

More recently, the spectrum of clinical presentation of this entity and its electrophysiological patterns of involvement have broadened. A familial form, associated with the pathological changes of tomaculous neuropathy, may be separate from the common sporadic form in which this pathological picture does not occur. The familial form does not have a recurrent pattern. With the sporadic form, precipitating conditions have included serum sickness, polio vaccination, tetanus and typhoid vaccinations, malaria, typhus, diabetes mellitus, rheumatic fever, tuberculosis, trauma, hepatitis, and systemic lupus erythematosus.

The electrophysiological picture may show any of several described mononeuropathies or mononeuropathies multiplex or affections of the brachial plexus proper.¹ Isolated musculocutaneous nerve involvement, as seen in our patient's second episode, has only rarely been recorded.

Other inflammatory disorders of the nervous system have been associated with the puerperium. McCombe *et al* studied 61 patients with chronic inflammatory demyelinating polyradiculoneuropathy, nine of whom became pregnant. In all nine, either the onset of the neuropathy or a relapse of pre-existent neuropathy coincided with the pregnancy.² They hypothesised that cross-reactivity between fetal and maternal neural antigens or an immune response due to pregnancy itself might explain this association.

To our knowledge, our patient is the first described in which recurrent alternating unilateral brachial plexopathy coincided with successive pregnancies or puerperal periods. The two quite different clinical and electrophysiological patterns which our patient's two attacks manifested conform to the diversity seen by others already cited in this entity. We have no explanation for the alternating, unilateral pattern of involvement in our patient.

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Negative HTLV-I serology in "undiagnosed" myelopathy in North West England and North Wales

Peter Rudge¹ discusses the wide geographical and ethnic distribution of HTLV-I myelopathy which includes cases occurring in the United Kingdom. The similarities between this syndrome and the chronic progressive myelopathy of multiple sclerosis (MS) has led to the recommendation that HTLV-I antibodies should be sought in any patient with an "unexplained" spastic paraparesis.² While a diagnosis of tropical spastic paraparesis (TSP) should invariably be pursued in patients of West Indian origin, the majority of white patients in the United Kingdom with a non-compressive myelopathy and abnormal magnetic resonance (MRI) signals in the cerebral white matter, would be assumed to have MS. Nevertheless, occasional cases with an identical clinical and radiological picture, diagnosed as MS and living in non-endemic areas in Europe with no risk factors for infection, have been found to be HTLV-I positive.^{2,3}

The prevalence of HTLV-I serology in myelopathy has not been systematically studied in non-endemic areas, but a recent survey from France identified 10/37 (27%) sero-positive cases in patients with a myelopathy of uncertain aetiology ("possible MS").⁴ The majority of these were black, born in the French West Indies and presumably similar to the TSP/HTLV-I patients described in other reports from endemic areas. However, one was a white patient born and living in France. A similar finding in a white Italian woman has been reported recently.³ It has been suggested that surveys should be carried out to identify possible high risk areas in western countries.

In a prospective study based in a regional neuroscience unit responsible for the neurological care of approximately 3.2 million people in NW England and North Wales, we aimed to identify all new patients presenting with an isolated non-compressive myelopathy that could be due either to MS,

or to HTLV-I. Of 2104 sequential myelography patients screened in our neuro-radiology department during a 36 month period from 1985-88 we identified 69 cases whose spinal cord disease remained undiagnosed after routine neurological investigations, and in whom there were no other complicating medical illnesses. The patients (27 M, 42 F, mean age 40 years, range 18 to 58) could be classified as "suspected" (11 cases), "latent" (17 cases) or "progressive possible" (41 cases) MS, on the McDonald and Halliday criteria. All 69 patients were white and the majority had been born and lived all their life in this region. A few had been born elsewhere in the UK or in other Commonwealth countries.

After study entry, the diagnostic usefulness of evoked potentials (EP), CSF studies, neuroimaging and HTLV-I assay, were evaluated. Seventy four per cent had abnormal high signal areas in the white matter on T2 weighted MRI, consistent with demyelination, with or without abnormal EPs or oligoclonal bands in the CSF.

All sera were tested with a uniform passive gelatin particle agglutination test. Gelatin particles coated with HTLV-I antigen were exposed to a 1:16 (final) dilution of each specimen. Each plate included microwells dedicated to a carefully selected array of accredited control materials, plus two or three specimens with a broad range of HTLV-I antibody levels confirmed by Western Blot analysis, collected from control cases of West Indian origin with a presumed clinical diagnosis of TSP. Agglutination of the particles after three hours at room temperature was deemed to signal the possible presence of antibodies. All sera from patients in the study yielded uniform and clear negative results in all ways identical to the negative controls (that is, no detectable anti-HTLV-I antibody). There were no equivocal agglutination patterns. Positive controls and specimens from the TSP patients were invariably positive in all test runs. The sensitivity to antibodies of the commercially available test packs has been questioned, but "false-positives", rather than "false-negatives", are the rule.⁵

Our findings in a representative sample of white patients with non-compressive myelopathy, with or without paraclinical evidence of demyelination, parallel the negative HTLV-I antibody studies reported in patients with "clinically definite MS"⁶ and provide no support for the routine use of this test in such cases, at least in this region of the United Kingdom.

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Failure of oral administration of single rising doses of bromocriptine to produce acute anti-Parkinsonian effects

The optimal dose of bromocriptine in the treatment of Parkinson's disease has remained controversial. While most investigators have used daily doses of above 40 mg several reports have since claimed success with oral dose regimes of less than 20 mg/d.^{1,2} The United Kingdom Bromocriptine Research Group has recently confirmed the puzzling finding that with a fast introductory regime higher doses of bromocriptine are needed than with a slower titration schedule to produce similar degrees of clinical improvement in de novo patients with Parkinson's disease.³

We have studied the acute anti-Parkinsonian effect of single rising doses of bromocriptine in an open experimental study in seven patients admitted to hospital with fluctuating Parkinson's disease (three females, four

males; mean age 57.7 (41-69) years; mean duration of disease 10.9 (8-15) years; mean daily dose of levodopa 1014 (500-1400) mg) plus peripheral decarboxylase inhibitor (PDI). All but two had never been treated with bromocriptine.

In one patient concomitant bromocriptine (30 mg/d) was discontinued one day before the study while a second had received bromocriptine (40 mg/d) as an adjunct to levodopa over a 14 months period until one year previously. All showed a predictable wearing-off pattern in response to oral levodopa and during the study period the first daily dose of 200 mg of levodopa was taken at 8 am after a minimum drug free period of eight hours and one hour after a standard hospital breakfast. On alternate days this morning dose was replaced by single rising doses of bromocriptine following the dose schedule depicted in the figure, and oral domperidone (20 mg) was added if nausea and/or hypotension had occurred at the previous dose level. Efficacy assessments of levodopa or bromocriptine test doses were performed using the motor score (section III) of the Unified Parkinson's Disease Rating Scale (UPDRS) beginning 30 minutes before dosing with half-hourly ratings until acute drug effects had worn off or up to a maximum of four hours.

The results are shown in the figure. While 200 mg of oral levodopa led to a mean 50% reduction of the UPDRS motor score, usually within 30 to 45 minutes, there were no acute anti-Parkinsonian effects following any of the single oral doses of bromocriptine employed in this study. The only exception was the patient to whom bromocriptine had been given as a chronic treatment for up to one year before the study. The patient experienced an acute switch on with complete cessation of a coarse resting tremor and moderate peak dose chorea 120 minutes following a single 12.5 mg

dose of bromocriptine and lasting for 115 minutes.

Using a similar single rising dose substitution model, acute anti-Parkinsonian effects have been demonstrated for the non-ergot dopamine agonist PHNO⁴ and also for the ergot derivative CQA 209-291, which is structurally related to bromocriptine.⁵ The lack of effect of bromocriptine seen in the majority of patients in this study may indicate that the doses employed were subthreshold for anti-Parkinsonian efficacy.

It is, however, remarkable that several clinical studies have demonstrated the effectiveness of bromocriptine monotherapy with chronic administration at doses of between 12.5 and 25 mg/d,¹⁻³ that is, daily doses in the range of the upper dose levels employed in this single dose trial. A possible explanation for this apparent discrepancy might be that bromocriptine is capable of inducing delayed effects with chronic treatment, possibly via modulatory effects on central dopamine receptors. Such delayed effects have been noted in one patient in this study (case 7, who received combined treatment with bromocriptine until 24 hours before the study). He complained of increased severity of levodopa-induced dyskinesias on the days following bromocriptine challenges of 10, 15, 20 and 25 mg and experienced enhanced dyskinesias for another week after the end of the study when receiving his pre-study daily levodopa regime. But even this patient failed to show acute anti-Parkinsonian effects from single bromocriptine doses as high as 25 mg.

Other reasons for the observed failure of single bromocriptine doses to induce acute effects could lie in the pharmacokinetics of the drug. Thus the extensive first pass effect of bromocriptine means that only about 8% of the parent drug will appear in the systemic circulation, and its high lipophilicity could further reduce the free concentration of bromocriptine in the extracellular space. Only after saturation of the lipid compartment following repeated dosing might active biological concentrations be attained within the soluble compartment. Accordingly bromocriptine exerts acute effects in the Ungerstedt rat model only following high oral doses of above 9 mg/kg, but with repeated dosing response latencies of a given dose decrease with simultaneous augmentation of efficacy (R Markstein, personal communication). Whether such pharmacokinetic properties of bromocriptine or pharmacodynamic receptor changes in the CNS form the pathophysiological basis for the different dose requirements with "fast" versus "slow" introductory regimes of bromocriptine remains unclear.

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Figure Bromocriptine single dose challenges in seven patients. Each patient represented by one symbol indicating minimum scores (UPDRS part III) over a four hour rating period following each dose. Mean minimum scores for each dose level represented by horizontal bars. Effects of a single oral dose of 200 mg levodopa are shown for comparison.

*. . . p = 0.001 for comparison between baseline ("off") and drug scores.

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