more than I accepted. Flicking or oscillating the hand (or by extension, making other similar movements) in response to questions about the patient's way of relieving paraesthesiae occurred in 45 of the last 48 patients (94%) with documented CTS seen in my laboratory compared with a positive Tinel sign in 54% and a positive Phalen's sign in 52%; informal feedback from other physicians has confirmed my belief that patients with CTS very frequently move their hands to relieve paraesthesiae while those with other neural lesions of the arm do so only seldom. Why the occurrence of the sign should vary between regions I too am at a loss to explain but will have to accept regretfully that the flick sign is as influenced by some unknown population factor as are other clinical evidences of CTS. I too consider electrodiagnosis necessary before surgery is contemplated for CTS but still consider that a reliable diagnostic sign would be valuable if electrodiagnosis is unavailable. The findings from Duke University make it unlikely that the Flick Sign will qualify.

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Coincidence of Wilson's disease with other movement disorders in the same family

Sir: Dr Parker describes a fascinating Australian family in whom 22 members inherited various manifestations of torsion dystonia, apparently as an autosomal dominant trait.[1] Within the same family, a mother who exhibited blepharospasm, whose own mother and grandmother also were affected, gave birth to one child who developed generalised torsion dystonia, two others who developed spastic dysphonia, and two other siblings who developed Wilson's disease. There was no suggestion of consanguinity in this branch of the family. This is a striking coincidence, but it is not unique. We have encountered a similar family in which Wilson's disease was diagnosed in one individual, but another movement disorder without the biochemical characteristics of Wilson's disease appeared in another family member.

JP, a 36-year-old lady (kindly referred by Dr G Harwood), complained of progressive forgetfulness and slowing of movement over the previous seven years. More recently she had begun to fall, her speech had become quiet, and she had had some difficulty with swallowing. Her parents were unrelated. Examination revealed a Parkinsonian gait, generalised rigidity, a flexed posture, and severe bradykinesia and akinesia of all movement. The optic discs, retinae, eye movements, tendon reflexes, and plantar responses were normal. There was left-sided visual inattention and a left-sided hemisensory impairment for all modalities. She was orientated for time and place, was of average intellectual ability, but exhibited considerable defects of both verbal and visual memory. Extensive investigation failed to reveal the cause for this akinetic-rigid syndrome. Full blood count, routine biochemistry, serology, thyroid function tests, CSF examination (including search for oligoclonal bands), serum B12 and folate concentration, plasma lactate, cortisols and amino acids were normal. Leucocyte enzymes (arylsulphatase A, B-galactosidase, and hexosaminidase) were normal. The urine contained a normal pattern of amino acids and sugars and no excess mucopolysaccharides. CT scan showed mild enlargement of the cortical sulci, but no other abnormality. MRI scan revealed symmetrical lesions affecting the heads of both caudate nuclei and the anterior parts of both lentiform nuclei. The nature of these changes was not clear. An EEG showed generalised disorganisation of alpha activity but no specific abnormality. Visual, brainstem, and sensory evoked potentials showed no definite abnormality. Nerve conduction study (Dr P Payan) showed normal amplitude, form and latency of sensory action potentials, but a raised threshold to sensation of the stimulus to the left leg. A bone marrow aspiration was normal, as was a rectal biopsy. Her serum caeruloplasmin was 1·2 μmol/l (normal range 1·3–2·9), and serum copper was 15·0 μmol/l (normal 12·5–19); urinary copper excretion varied from 0·34 μmol/24 h to 1·0 μmol/24 h (normal range less than 1·25 μmol/24 h). A liver biopsy specimen showed normal histology with no stainable copper, and a copper content of 5·24 mg/100 g dry weight. Slit lamp examination showed no Kayser-Fleischer ring.

JB, her younger brother, had died at the age of 24 years of Wilson's disease. He had presented at the age of 18 years (to Dr KJ Zilkha) with a 5 year history of progressive difficulty with walking and speech. Subsequently he had developed a tremor of his right hand and deterioration in school performance. Examination revealed an expressionless face with a constant facile grin. There was marked generalised bradykinesia and akinesia, severe generalised rigidity and tremor of the right arm. There was no evidence of liver disease, but early Kayser-Fleischer rings were present. Biochemical investigation revealed a low serum copper (7·8 μmol/l) and caeruloplasmin (0·7 μmol/l), and excessive urinary excretion of copper (8 μmol/24 h). Administration of 1 g of penicillamine increased urinary copper to over 12·5 μmol/24 h (normal range less than 4·7 μmol/24 h). He was treated with penicillamine and initially showed some improvement. However, he subsequently deteriorated, despite addition of potassium sulphide and BAL.

While our patient's brother clearly had Wilson's disease, she did not. Although presenting with an akinetic-rigid syndrome and cognitive deficit, biochemical studies of copper metabolism were not diagnostic of Wilson's disease. The slightly low serum caeruloplasmin may indicate that she was a heterozygote for Wilson's disease, but this is not certain.

We have encountered two other patients presenting with movement disorders who have exhibited abnormalities of copper metabolism to suggest that they may be heterozygotes for Wilson's disease.

KM, a 16-year-old girl (kindly referred by Dr R Thomson), developed progressive disturbance of speech from the age of about 10 years, followed by increasing tremor of the hands and head, and muscle spasms affecting the head and left arm and foot. School performance had not deteriorated. There was no family history of any similar disorder and her parents were unrelated. On examination she had severe spastic dysphonia, torticollis with the head deviated to the left, dystonic adductor spasms of the left arm at rest or on action, and dystonic posturing of the left foot on walking. The optic discs, retinae, and eye movements were normal. Muscle power, the tendon reflexes, the plantar responses and sensation also were normal. Investigation failed to reveal the cause of her progressive dystonic illness. Full blood count, routine biochemistry, plasma amino acid content, urinary amino pattern, mucopolysaccharide content, leucocyte enzymes, fasting pyruvate and lactate levels were all normal. Bone marrow examination and jejunal biopsy were normal, as was a rectal biopsy. Electroretinograms suggested an abnormality of cone-mediated responses. Serum copper content (17·7 μmol/l) and caeruloplasmin (2·1 μmol/l) as well as urinary copper excretion (0·42 μmol/24 h) were normal. However, a liver biopsy specimen, while showing no definite pathological change and no stainable copper, contained an excess

copper content of 51·5 mg/100 g dry weight (normal less than 30 mg%). There were no Kayser-Fleischer rings on slit lamp examination of the eyes. No explanation for the high liver copper content was established. She was not taking drugs when the biopsy was undertaken, and there was no clinical or biochemical evidence of liver disease.

SW, the other patient, is a 14-year-old boy (kindly referred by Dr J Pilling). The product of a normal birth from unrelated parents, he was well until the age of 11 yr, when his mother noticed that his head turned slightly to one side when he ate. Over the next 3 years his dystonia progressed until, when examined by us at age 14, the following features were present: marked laterocollis and also thoraco-lumbar scoliosis concave to the right, intermittent blepharospasm and oromandibular dystonia, dystonic writer's cramp of the right hand and mild dystonia of the left hand and both legs. The remainder of the neurological and general examination (including slit-lamp examination of the eyes) was normal. Full blood count, plasma and urinary amino acid screen and routine biochemistry were normal, with the exception of a raised alkaline phosphatase of 402 IU/l (normal range below 16 years 40–280 IU/l; the patient was taking primidone for his dystonia with no benefit). CT scan showed slight symmetrical dilatation of the lateral ventricles with some widening of the Sylvian fissures. Levels of serum copper and caeruloplasmin were low (8·4 μmol/l and 0·4 μmol/l) respectively. However, 24 hour urinary copper excretion was only 0·4 and 0·5 mmol/24 h. A previous liver biopsy at Addenbrooke's Hospital (Dr JM Walshe) had shown normal histology and a liver copper content of 41·4 μg/g wet weight. Although this was above the normal range (10 μg/g wet weight) for that laboratory, it was not clearly in the range (more than 60 μg/g wet weight) expected in their series of neurological Wilson's disease with preserved liver function.

It seems possible that non-Wilsonian movement disorders may occur in relatives of patients with proven Wilson's disease, or in individuals with abnormalities of copper metabolism perhaps suggesting that they are heterozygotes for Wilson's disease, more often than one would expect by chance. At present, the evidence does no more than hint at this possibility. However, if this suggestion is confirmed by more reports of such an association, then some explanation may be required. Perhaps the inheritance of one gene for Wilson's disease, while insufficient to cause the neurological complications of that illness by itself, may do so if another gene for neurological illness also is inherited.

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Delayed neuropathy after trichlorfon intoxication

Sir: We have read with interest the studies of delayed neuropathy after organophosphorus poisoning by Vasilescu *et al*[1]. We now report nine cases of delayed neuropathy after trichlorfon (Flibol-E) intoxication.

We observed 70 cases of trichlorfon intoxication (mainly suicide attempts) between 1971 and 1983. Twenty five of them were re-examined in 1984. In 12 cases (48%) no sign of delayed polyneuropathy developed. Four former patients had complaints (paraesthesiae, weakness of hands) after 2–3 months of poisoning but at the time of the re-examination they were healthy. Eight patients had serious delayed polyneuropathy. All of them, except one, consumed alcohol prior to or at the same time as the poison. After 1·5–9 years from the time of intoxication seven patients showed footdrop, difficult gait, distal muscle atrophy of the peroneal and small foot muscles, abolished Achille's reflex. The peroneal nerve was unexcitable in all seven patients; electromyography revealed marked distal denervation of the lower limb muscles. One patient had very brisk knee jerks, patellar clonus and Babinski's sign 2 years after poisoning. His lower limbs were so spastic that he was nearly unable to walk. One patient had severe gastrointestinal haemorrhage and pneumonia ten days after the organophosphorus poisoning. Therefore he was excluded from the study. (He has muscular rigidity and Parkinsonian tremor beside the distal polyneuropathy.)

In conclusion, 36% of our re-examined patients had severe residual signs of delayed polyneuropathy mainly distal motor type. In one case signs of CNS lesions have persisted.

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Reference

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Ineffectiveness of phenoxybenzamine in essential tremor

Sir: Mai and Olson[1] reported that the alpha-adrenergic blocking drug, thymoxamine, given intravenously, significantly suppressed essential tremor in four patients and suggested that alpha-adrenergic blockers may be useful in the treatment of essential tremor. We investigated the effect of phenoxybenzamine, a alpha-adrenergic blocker, in five patients with essential tremor. Average age was 59·6 years and average tremor duration was 18·5 years. The drug was administered orally with an increase in dose of 10 mg a week to 30 mg/day. Tremors were measured with an accelerometer and amplitude and frequency determined by spectral analysis. Tremorgrams were recorded before treatment and after two weeks on the 30 mg/day dosage. The patients reported no subjective improvement in their shakiness or in their functional abilities. Tremor amplitude increased by an average of 8% with therapy as compared to pretreatment. Tremor frequency was unchanged. One patient complained of dizziness and confusion while taking phenoxybenzamine. The results from this study did not support a role for alpha-adrenergic blockers in the treatment of essential tremor.

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