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methylprednisolone, and considering in selected cases the administration of this drug at home, thus avoiding the expense and inconvenience of a hospital admission. Given the prevailing ignorance regarding the pathogenesis of multiple sclerosis in general, and the effects of steroids in particular, the mechanism of the observed beneficial effects of intravenous methylprednisolone remain speculative.

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Neuropathy after organophosphorus compounds poisoning

Sir: I read with interest the report by Senanayake: Tricresyl phosphate neuropathy in Sri Lanka: a clinical and neurophysiological study with a three year follow up.[1] However, in the table there is an error: terminal latency is not measured in m/s, but in ms. In fig 2, either the diagram or the legend should specify the terminal latency values measured in ms. As the author shows, the cases presented display a series of important differences from triorthocresyl phosphate (TOCP) neuropathy.

In our 12 patients who had accidentally ingested TOCP-polluted alcohol, the paralysis began slowly in the lower limbs (15–30 days) and later (5–10 days) spread to the upper limbs.[2,3] In the acute phase the patients displayed flaccid paralysis mainly in the lower limbs. After 2–3 months there were signs of both peripheral and central nervous system lesions, i.e., pyramidal signs. The patients showed a good recovery from the peripheral nerve lesions, 1–2 years after TOCP ingestion, but not from the deficits due to the pyramidal lesions. The latter not only failed to improve, but even extended more distally, especially in the lower limbs. We presume that these signs of CNS lesions were present in the distal zones before examination (1–2 years after intoxication), but became evident only after improvement of the peripheral nerve lesions, which had masked them. On reexamination of two patients 13 years after TOCP ingestion, we found a tendinous retraction of toes I–V and fingers II–V in flexion, and of knees both in flexion and adduction. The gait was spastic. At the same time there was a marked weakness distally, especially in the feet.

Two to three months after intoxication all the patients showed concurrent peripheral and central nervous system signs of lesions, predominantly in the distal portions of the axons, especially the longer ones, which indicated that the process characterising neuropathy by TOCP is of the "dying-back" type, as described first by Cavanagh.[4] However, the clinical picture in five patients was of a mixed, particularly motor and distal, polyneuropathy. Reexamination performed 13 years later in two of five patients with a predominantly neuropathic disorder showed mainly pyramidal signs. There was marked improvement of peripheral nerve lesions and poor improvement of central lesions in both cases which made the initial predominantly neuropathic form pass into the predominantly spinal form of neuropathy with a clinical and electrophysiological picture resembling amyotrophic lateral sclerosis. This finding is in agreement with the observation of Morgan and Penovich[5] who showed that the TOCP lesion described as delayed neurotoxicity was not a neuritis but rather a spinal cord syndrome. Our electrophysiological findings suggest that a mixed process of axonal degeneration and secondary demyelination underlies this predominantly neuropathic form. We assume that in our patients the secondary demyelination occurred in fibres which had already undergone degeneration followed by regeneration, as shown by Dyck *et al*[6] in uraemic neuropathy. In the remaining seven patients, pyramidal signs prevailed, objective sensibility was not disturbed, and motor conduction velocity was normal. These patients thus had a predominantly spinal form of neuropathy. The electrophysiological data suggest that this form of neuropathy was mainly an axonal degeneration.

We also studied two cases of poisoning with organophosphorus insecticides, Dipterex and Divipan, in which there was footdrop, distal weakness especially in the lower limbs, abolishing of the Achilles reflex, and mild pyramidal signs. Electrophysiological findings suggest that this neuropathy also was a distal axonopathy.[3]

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The significance of the incidental finding of basal ganglia calcification on computed tomography

Sir: Harrington *et al*[1] state that "basal ganglia calcification identified radiographically has been associated with any one of 24 conditions". However, their list omits a relatively recently described group of disorders in which mitochondrial abnormalities have been found, the signs and symptoms of which may be of some interest when compared with those described in their series of patients. The definition of such an underlying disorder may not be completely academic as there is some indication that treatment, particularly by dietary manipulation or steroid therapy, may be beneficial in some patients.[2,3]

Many patients have now been described, presenting with a wide variety of neurological symptoms, in whom a characteristic feature is the presence of structurally and/or functionally abnormal mitochondria identified on muscle biopsy. Although myopathy is usually a prominent feature, hence the term "mitochondrial myopathy", there is increasing evidence that the mitochondrial disorder is not confined to muscle and the term "systemic mitochondrial disorder" may be more appropriate. How frequently the mitochondrial abnormality is primary as opposed to a non-specific secondary change, is still open to debate[4] and in only a few of over 100 cases reported of suspected mitochondrial abnormality, has a specific biochemical lesion been determined.[2] However it is now possible to study many aspects of *in vivo* biochemical function with the technique of ^{31}P nuclear magnetic resonance (NMR)[5] and this will almost certainly contribute to

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the non-invasive study of this interesting group of patients.

Basal ganglia calcification has been reported in association with an abnormality of carnitine metabolism[6] and in two patients with lactic acidaemia and myopathy presumed to be due to disordered mitochondrial metabolism.[3 7] It has also been reported in the Kearns-Sayre syndrome[8] and it is interesting to note that in addition this patient had hypoparathyroidism, an association recorded elsewhere.[9] We are at present investigating a 42-year-old woman with a suspected mitochondrial disorder who presented with epilepsy, intellectual deterioration, deafness, pigmentary retinopathy, peripheral neuropathy, ataxia and myopathy. She has bilateral basal ganglia calcification, a resting lactic acidosis and ragged-red fibres on muscle biopsy. Preliminary NMR examination has shown no specific abnormality (personal communication, Oxford Clinical Magnetic Resonance Laboratory). Further biochemical studies are being performed.

Apart from myopathy, many other abnormalities have been noted in patients with known or suspected disorders of mitochondrial function. These include various forms of epilepsy, dementia, mental retardation, optic atrophy, pigmentary retinopathy, cataracts, neurosensory deafness, ataxia, peripheral neuropathy, growth retardation and heart conduction defects. The first seven of these were noted either in isolation or in combination in many of the 26 patients reported by Harrington *et al*[1] and it is interesting to speculate whether any of these patients may in fact have an underlying mitochondrial disorder. The apparent absence of myopathy does not preclude this possibility, as it may be very mild or appear as a late manifestation of the disorder.[2 10]

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Reply letter

Sir: We are interested in the points Dr Hilton-Jones makes concerning disorders with mitochondrial abnormalities and clearly these would be added to our list of conditions associated with basal ganglia calcification. The associated clinical abnormalities in patients with mitochondrial disorders were often found in our own patient group but many were also present in our control group. While the apparent absence of myopathy does not exclude mitochondrial disorder, it is significant that none of our patients had any clinical suggestion of muscle weakness or ophthalmoplegia. We cannot provide more factual information because we did not study mitochondrial antibodies or muscle histology in either our patient or control group.

From our original study we felt that the main practical value of radiographic basal ganglia calcification was as an indicator or treatable parathyroid disease that had not come to attention previously. We have identified a further ten patients incidentally and chose to review them clinically because the two identified during our study were recognisable with hindsight on clinical grounds to have parathyroid disease. One patient had all the features of idiopathic hypoparathyroidism; this was confirmed biochemically and she is now on specific therapy. This suggests an important principle for the incidental basal ganglia calcification found on computed tomography: all patients should be reviewed clinically with regard to parathyroid diseases and in this way a steady trickle of treatable disease will be picked up, much as happens from following up incidental abnormalities of blood calcium in hospital patients. Three cases out of 36 in our population are a worthwhile reward, but clearly these numbers are too small to generalise.

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The significance of the incidental finding of basal ganglia calcification on computed tomography.

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*J Neurol Neurosurg Psychiatry*1982 45: 942-943
doi: 10.1136/jnnp.45.10.942-a

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