

Of the original 52 subjects, 26 (50%) responded by a 50% reduction in fit frequency. Thirteen (25%) failed to respond to clobazam 30 mg daily and a further 13 were withdrawn because of adverse effects. Of the 26 responders, 20 (77%) developed tolerance to the anti-epileptic effect at a median of 3.5 months (range 1–8 months), three (11.5%) showed no tolerance at 12 months and three (11.5%) dropped out (two due to adverse effects and one was lost to follow up).

The respective antiepileptic drug levels (mean  $\pm$  SD,  $\mu\text{mol/l}$ ) for the 1–2 month period prior to and at the development of tolerance were: phenytoin  $48.7 \pm 8.2$  and  $46.3 \pm 9.2$ ; carbamazepine  $27.5 \pm 3.2$  and  $26.9 \pm 2.9$ ; phenobarbitone  $93.3 \pm 28.0$  and  $88.3 \pm 13.0$ ; sodium valproate  $492.0 \pm 106.9$  and  $495 \pm 119.6$ ; clobazam  $0.3 \pm 0.3$  and  $0.27 \pm 0.3$  and desmethyloclobazam  $61.6 \pm 35.2$  and  $62.1 \pm 32.7$ .

The development of tolerance is a major limiting factor in the use of benzodiazepines in the chronic treatment of epilepsy.<sup>2</sup> Gastaut<sup>3</sup> reported a 50% incidence of tolerance in patients treated with clobazam and Martin<sup>4</sup> reported a median time to tolerance of 6.5 months. Our study confirms this finding, but we are unable to explain the development of tolerance by changes in the levels of concomitant antiepileptic drugs, clobazam or desmethyloclobazam, which did not vary significantly. Clobazam had to be withdrawn in 29% of the 52 patients because of adverse effects (mainly sleepiness, unsteadiness and irritability). This is a higher incidence than previously reported but the different populations studied may explain the discrepancy. On discontinuation of clobazam withdrawal fits were a problem in some patients, but they occurred less frequently than in our previous study and status epilepticus was not encountered. The rate of reduction was not more than 10 mg every seven days.

Although the development of tolerance is a major drawback to the use of clobazam, we would still advocate its use, with caution, in otherwise intractable cases. A significant number of our patients had a useful reduction in their seizures, albeit for a limited period. One long term resident, moreover, has been able to leave the Centre because of the complete cessation of tonic clonic seizures. There should be adequate follow up to ensure that the drug is discontinued carefully if it becomes ineffective, in order to avoid the hazards of unnecessary polypharmacy. We feel that patients should be advised, before treat-

ment is started, of the possible development of tolerance, otherwise false hopes may be raised. We have, however, been able to manage tolerance successfully in a few patients, by discontinuing clobazam completely for a month and then reintroducing it at the same dose.

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#### Juvenile muscular atrophy of distal upper extremities

Sir: In 1959, Hirayama *et al*<sup>1</sup> reported 12 young patients from Japan with unilateral hand and forearm wasting which was termed "juvenile muscular atrophy of unilateral upper extremity." Since then, at least another 100 patients have been described.<sup>2–13</sup> The other main features were: predominant male involvement, insidious onset, stationary stage after a progressive course, absence of sensory and pyramidal tract involvement, normal CSF and radiological findings, neuropathic changes in the EMG and muscle biopsy. Though patients from Western Europe<sup>2,4,11</sup> and Australia<sup>10</sup> has been described, the majority of the cases in fact came from Japan<sup>1,5–7,13</sup> and India<sup>3,12</sup> suggesting an ethnic predisposition to the development of the disease. Malaysia is a multi-racial country, the ethnic composition in the peninsular is made up of 50% Malay, 37% Chinese and 11% Indian. The University Hospital, Kuala Lumpur, Malaysia is one of the two centres in the country providing neurological service and its patients come from all over the peninsular. I would like to

report here 19 similar patients seen in this centre since 1967.

Fourteen of the patients were male and five were female. The age of first onset ranged from 11 to 34 years with an average of 20.7 years. The average age at presentation was 22.9 years. The racial composition was eight Malays, seven Chinese and four Indians. The patients came from diverse background with no contact with known toxins. Five were factory workers, four were students, two were clerks and two were housewives. One each was in the various occupations as follows: staff nurse, farmer, soldier and teacher. None has a family history of similar illness. There was no evidence of clustering with 10 of the patients from the state of Selangor, three from Penang, two from Johor and four from the other states.

The onset of the illness was usually insidious, with muscle wasting and weakness developing over several months and then becoming static. Fourteen patients had one hand affected only; with 10 involving the right hand and four the left hand. Five patients had both hands involvement which was asymmetrical over both sides. In four patients, the right hand was predominantly involved and in one patient, the left hand was more severely affected. All except two patients were right handed. Among the two left handers, one has unilateral involvement of left hand only. The other patient has both hands asymmetrically involved with the right side more severely affected.

The illness always started as wasting and weakness of small muscles of one hand. The involvement was not always global. In three patients, the thenar muscles were relatively spared. Tremor of fingers was an early symptom in some and was seen on out-stretched in 12 subjects. The forearm was affected in all the patients, but always less severe than the small muscles of the hand. In eleven patients, the flexor muscles were selectively or predominantly involved. The upper arm muscle was mildly affected in five patients. The weakness and wasting here did not follow any obvious segmental distribution. The opposite hand, when involved, followed the same pattern. Muscle fasciculation was seen in six patients and clawing of the fingers was seen in three patients. Most patients showed mild hyporeflexia of the bicep and supinator jerks over the same side. Sensory examination was normal and the plantar response was flexor in all the patients. We were impressed with the good functional ability in majority of our subjects.

Further investigations including full blood count, ESR, VDRL, blood sugar, chest and cervical spine radiographs, myelography, CSF examinations done were all normal. All the patients showed normal sensory nerve conduction study. Six patients involving seven nerves showed prolongation of motor distal latency greater than  $2\frac{1}{2}$  SD. The range for the median nerve from wrist to APB was 3.5 to 5.9 ms. ( $N \pm SD = 3.5 \pm 0.5$  ms); and for the ulnar nerve from wrist to ADM, it was 3.2 to 4.9 ms ( $N \pm SD = 3.1 \pm 0.7$  ms). All the motor nerve conduction studies was normal. The range for the elbow to wrist segment of the median nerve was 48 to 67 m/s ( $N \pm SD = 58.6 \pm 4.2$ ); and 52 to 71 ms ( $N \pm SD = 56.8 \pm 4.9$ ) for the same segment of the ulnar nerve. Electromyography showed a neuropathic picture in all with varying combinations of fibrillation, positive sharp wave, giant motor units, and isolated interference pattern.

The total duration of illness from date of first symptom to last date of follow up was 15 years in one patient, 8 years in two patients, 6 years in four patients, 5 years in two patients, 3 years in one patient, 2 years in four patients and less than 1 year in five patients. No progression of the illness was seen in those with total duration of illness for 2 years or more.

We agree with Loong *et al*<sup>9</sup> and O'Sullivan *et al*<sup>10</sup> that the anterior horn cell is the most likely site of pathology. This is supported by the segmental distribution seen clinically, the absence of sensory abnormality, the relatively normal motor nerve conduction study and the presence of "giant motor units" which may sometimes be seen in the EMG examination. The aetiology of this condition remains an enigma. The predominance of cases reported from Japan and India, suggest an ethnic predisposition to development of the disease. Malaysia is a multiracial country, the main racial group in the peninsular are Malay, immigrant Chinese and Indian. The three races are ethnically distinct. It is interesting to note that when they are exposed to the same environment, all three groups showed the same apparent prevalence of the disease. The predominance of right hand involvement was noted also by Hirayama *et al*<sup>6</sup> and Hashimoto *et al*.<sup>5</sup> It was suggested that the use of the limb is a factor in the development of the disease.

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## The effects of magnetic resonance imaging on different types of microsurgical clips

Sir: Magnetic resonance imaging (MRI) is a very attractive modality since it does not use ionising radiation and is sensitive to a wide range of pathology. However, a hazard may exist when a microsurgical clip is exposed to strong magnetic fields since these may induce heating or cause a force sufficient to move the clip or even dislodge it from a vessel.

We have investigated these hazards and have tested 47 microsurgical clips in a 0.15 Tesla MR system based in the Queens Medical Centre, Nottingham. Each clip was suspended on a length of cotton 40cm from the magnet bore and any movement caused by the magnetic field measured in degrees. Each clip was then detached, placed within the head coil and subjected to 10 minutes of radiofrequency energy thus simulating the conditions used in human head scanning. Temperature measurements were made before and after radiofrequency exposure. The results are displayed in table. No measureable temperature rise was observed.

The potential hazard posed by the movement of a microsurgical clip especially when attached to an aneurysm is obvious and this risk increases proportionately with

Table *Magnetic properties of various microsurgical clips*

Clip	Numbers tested	Ferromagnetic (that is moved within the magnetic field)
Scoville Lewis	6	Yes
Schwarz	2	Yes
Mayfield	13	Yes
Drakes	2	Yes
Sundt Kees	4	Yes
Heifetz	4	Yes
Kerr	1	Yes
McFaddens	2	Yes
Liga	2	No
Yasargil	2	No
Sugita	2	No
Olivecrona-Norlen	3	No
Cushing-McKenzie's	2	No
Silver Brain	2	No
Weck	2	No
Ferromagnetic (moved within magnetic field) = 34		
Non-ferromagnetic (did not move within magnetic field) = 13		