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improvement in both hand and leg tremor, but the beneficial effect was only sustained for about 3 months. Clonazepam was started at a dose of 2 mg/day and increased to 4 mg/day over a 2-month period. Amplitude and frequency of hand and leg tremor was measured objectively (see ref 8 for method) throughout incremental dosing and again 6 months after reaching the optimal dose. Leg tremor showed a marked dose-related decrease in amplitude on clonazepam by objective measures (fig) and by the patient's own reports. Hand tremor was unchanged, objectively and subjectively, by clonazepam.

Involvement of the legs is not uncommon in essential tremor. In a survey of 185 consecutive essential tremor patients we found leg tremor to be present in 29 (15.7%) although isolated leg tremor (that is, in the absence of hand tremor) was found in only 4 (2.2%) (unpublished data). Essential tremor of the legs is generally present during any voluntary muscle activity but is often exacerbated on standing.

In a single case study, Thompson et al. noted that 16 Hz orthostatic tremor of the legs was not present during all types of voluntary muscle activity thus tremor occurred when standing or pressing the feet against the floor as if preparing to stand, but was absent when the patient was seated and extending the leg horizontally against gravity. The authors concluded that orthostatic tremor arose from an abnormality in the organisation of the motor program for standing. Deuschl et al., however, described a patient with a similar, 16 Hz leg tremor which was present during all kinds of muscle activation in sitting, lying or standing positions.

The pathophysiology of essential tremor and orthostatic tremor is not known. Interpatient variability in the clinical appearance of essential tremor and in its responsiveness to drugs suggests that essential tremor is not a homogenous disorder although, as yet, there are no definitive criteria for the classification of sub-types.

Some studies have shown differences in pharmacological responsiveness of essential tremor of different body parts. Essential tremor of the head or voice has been reported to be more resistant to propranolol treatment. Primidone was found to be effective in hand tremor but ineffective in head tremor in the same patients.

Furthermore, clonazepam, reported to be of little benefit in classical essential tremor, was found to be effective in a "kinetic-predominant" variant of essential tremor (that is, minimal tremor on sustained posture which was exacerbated by voluntary movement).

The patient we described was diagnosed, on the basis of clinical presentation, spectral analysis of tremor and family history as having essential tremor of the hands and legs. Leg tremor was only evident when standing, disappeared on walking and was not present when the patient was seated, holding the legs outstretched against gravity. On incremental doses of clonazepam, objective measures showed no effect on hand tremor but a dose-related decrease in leg tremor amplitude (up to 80% reduction on 4 mg/day).

This study indicates that response to clonazepam is not unique to high frequency orthostatic tremor. Orthostatic tremor (defined by the behavioural situation in which it occurs rather than frequency characteristics) may be a variant of essential tremor showing a different pharmacological responsiveness to that of classical hand tremor.

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Serum vitamin E concentrations in adult-onset spinocerebellar degeneration.

Sir: Deficiency of vitamin E is now recognised as a cause of certain spinocerebellar syndromes, including those associated with abetalipoproteinaemia and other conditions in which there is chronic malabsorption of fat. More recently, vitamin E deficiency was described in an ataxic patient without evidence of generalised fat malabsorption.

The principal neurological features of vitamin E deficiency are limb and gait ataxia, areflexia and loss of proprioception and vibration sense. Patients presenting in this way are often diagnosed as having spinocerebellar degeneration for which there is no specific treatment. The possibility of occult vitamin E deficiency raises the hope of cure for some of these patients. With this question in mind, we measured vitamin E concentrations in an unselected group of adult Chinese patients with spinocerebellar degeneration.

Fourteen patients (9 male, 5 female) diagnosed as having spinocerebellar degeneration were studied. All had ataxia with long
tract signs (11 patients) or areflexia (6 patients) to suggest a spinal or peripheral nerve component to their cerebellar deficit. Their ages at the onset of symptoms ranged from 16 to 65 years. Five of them had first degree relatives suffering from similar disabilities, and none had any evidence of fat malabsorption or liver disease.

Vitamin E concentrations were estimated in non-fasting samples of serum using a fluorometric method. The mean result was 27.2 μmol/l, range 17.4–56.7 μmol/l. The reference range for our laboratory based on 300 apparently healthy individuals was 11.5–45.6 μmol/l. None of the patients therefore had a below-normal vitamin E concentration, but one had an above-normal level.

Our failure to demonstrate a deficiency of vitamin E in a group of 14 patients suggests that such deficiency is uncommon among adult-onset cases of spinocerebellar degeneration, but nevertheless worth seeking as the condition is otherwise untreatable.

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Serum Vitamin E concentrations in degenerative ataxias

Sir: Prolonged and severe vitamin E deficiency is known to cause a progressive neurological disorder comprising limb and gait ataxia, distal loss of proprioception and vibration sense, and areflexia. This usually occurs in abetalipoproteinemia or other fat malabsorptive disorders such as biliary atresia, cystic fibrosis and after extensive intestinal resection, but patients with an identical neurological syndrome and an apparently genetically determined selective deficiency of vitamin E have also been reported. Although most of the cases of selective vitamin E deficiency have developed symptoms before the age of 20 years and inheritance is assumed to be autosomal recessive, a family containing patients with onset in the sixth decade or later and possibly exhibiting X-linked inheritance has been described.

Serum vitamin E concentrations are normal in Friedreich’s ataxia, a disorder resembling the early onset neurological syndrome associated with isolated vitamin E deficiency. We have now measured serum vitamin E concentrations, using high performance liquid chromatography and fluorimetry (normal range 11.5–35.0 μmol/l), in 50 patients with a variety of degenerative ataxic disorders. None of them were known to be taking vitamin E supplements or had any clinical evidence of malabsorption.

There were 12 with early onset cerebellar ataxia with retained reflexes (median serum vitamin E concentration 22.4, range 11.0–35.0 μmol/l), 11 with other early onset ataxias (median 21.7, range 15.8–48.4 μmol/l), 4 with autosomal dominant cerebellar ataxia (median 29.6, range 13.1–46.6 μmol/l), and 23 with idiopathic late onset cerebellar ataxia (median 24.4, range 12.6–37.7 μmol/l). Seven of the cases of idiopathic late onset cerebellar ataxia, one with autosomal dominant cerebellar ataxia, and 10 of those with other early onset ataxias had depressed or absent tendon reflexes, usually combined with loss of vibration and joint position sense. Not all of these patients had electrophysiological evidence of a peripheral sensory neuropathy. Over the same period of time we have identified two patients with apparently isolated deficiency of vitamin E, both of whom had previously been diagnosed as having Friedreich’s ataxia, with ataxia developing before the age of 20 years, areflexia, marked loss of joint position sense, and undetectable serum vitamin E concentrations.

Neurologists need to know which clinical circumstances dictate that serum vitamin E concentrations should be measured in patients with progressive ataxic syndromes. It is clearly important not to overlook treatable causes of these disorders such as vitamin E deficiency, even if they can be identified in only a very small proportion of patients. The neurological consequences of severe vitamin E deficiency appear to be remarkably consistent, reflecting the pathological findings of a central-peripheral distal sensory axonopathy preferentially affecting centrally directed axons. On the basis of this and our data, we suggest that the measurement of serum vitamin E concentrations should be confined to degenerative ataxias associated with depressed or absent tendon reflexes and abnormal proprioception, regardless of whether or not peripheral sensory nerve action potentials are abnormal. This applies to patients presenting at any age, in view of the late age of onset in some deficient cases.

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