

**Essential tremor: response to primidone**  
**SIR.**—The response of the syndrome of essential tremor (syn: benign familial tremor) to propranolol is variable, and although most patients show some objective improvement, this is not related to plasma concentrations,<sup>1</sup> and clinical failures are not uncommon. O'Brien and his colleagues<sup>2</sup> recently reported good results due to primidone and its metabolite phenylethylmalonamide. We report our preliminary experience of primidone in essential tremor.

Primidone was given as Mysoline (ICI) to five patients with severe and moderately disabling essential tremor (table). Half a tablet containing 250 mg

Table

Patient	Sex	Age (yr)	Family history	Relief by alcohol	Duration (yr)
TB	M	66	—	+	12
HL	M	65	—	+	20
AB	F	61	+	+	20
FH	F	80	+	?	30
WC	M	47	+	+	6

was given for two to three days, and the dose was then gradually increased during the next week to 750–1000 mg per day in two or three doses. No drowsiness or ataxia was encountered; no patient had to reduce or withdraw the drug. Improvement was evident within a few days in all patients, and by seven to 10 days the response was stable and continuous throughout the day. The degree of response was clinically more marked than we have seen with any of the previously popular pharmacological agents—including propranolol 120–240 mg daily. Amelioration was not related to duration or age, and affected voice, head and limb tremor equally. Samples of tremor seen in writing, drawing numbers, drawing smooth wavy lines and spirals were recorded in each patient; examples are shown in the figure. One lady, totally unable to write for 10 years, sent a slightly tremulous but easily read letter after one week; holding cups of liquid without spills was reported by all the patients, whilst greater facility in manual skills ranked from crocheting to snooker.

Primidone is metabolised to phenyl-

ethylmalonamide (PEM) 50%, phenobarbitone 5% and unconjugated primidone 20%,<sup>2</sup> though earlier workers regarded phenobarbitone as its major breakdown product. O'Brien reported good results in essential tremor in 12 patients, and attributed this after careful studies (using the individual metabolic products alone) to the action of PEM. Our results confirm the prompt and clinically gratifying response which has been attained without toxicity.

The fact that the drug has been used for decades in epilepsy, often in higher doses, suggests that its side effects are already well known and that its long-term use in essential tremor should be safe, and easily monitored by plasma measurements. In this assessment, drug levels were not measured because clinical response and dose control were readily apparent. Larger studies are desirable to show if there is a therapeutic range for primidone, or for the derived phenobarbitone which correlates

with clinical efficacy, and to see if this range correlates with its known range of anticonvulsant activity. Our preliminary evidence implies that primidone is the drug of choice for essential tremor. Long-term follow-up is now needed. The preparation of pure PEM and its clinical use in this disorder should be encouraged.

References

- 1 Jefferson D, Jenner P, Marsden CD. Relationship between plasma propranolol concentration and relief of essential tremor. *J Neurol Neurosurg Psychiatry* 1979; **42**:831–7.
- 2 O'Brien MD, Upton AR, Toseland PA. Benign familial tremor treated with primidone. *Br Med J* 1981; **282**: 178–80.

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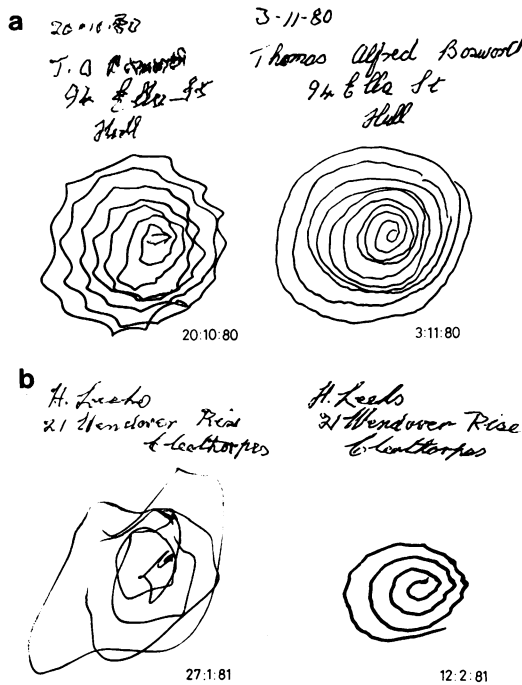


Figure Writing and spiral drawing before and during treatment with primidone.