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**Cimetidine induced postural and action tremor**

SIR,—Cimetidine, an H<sub>2</sub> receptor antagonist used in the treatment of peptic ulceration has been reported to cause a number of central nervous system side effects.<sup>1</sup> We have recently seen three patients who developed tremor on cimetidine which resolved when the drug was discontinued, but recurred on a rechallenge.

*Case 1* A 68 year old male with chronic obstructive airways disease and polycystic kidneys developed a marked coarse postural and action tremor (8-10 Hz) of the upper limbs four days after commencing cimetidine (800 mg orally daily) for treatment of upper gastrointestinal bleeding. There were no associated focal neurological signs, and on stopping the drug the clinical features resolved over three days leaving a mild residual action tremor, which the patient admitted to having had for some years. The patient was rechallenged with intravenous cimetidine (200 mg) under controlled conditions, the tremor being recorded by transducer. Within 10 minutes the tremor became exaggerated, with superimposed myoclonic jerks. The tremor resolved within five minutes after propranolol 2 mg intravenously.

*Case 2* A 72 year old female with known ischaemic heart disease was

treated for 10 days with cimetidine (1 g orally daily) and metoclopramide (total dose 70 mg) for a pyloric ulcer. She developed a marked postural and action tremor (8-10 Hz) of the upper limbs, which on clinical examination was associated with increased tone in the arms. The abnormal signs resolved within 48 hours of stopping the cimetidine and metoclopramide. A controlled rechallenge with intravenous cimetidine (200 mg) 72 hours after stopping the drug resulted in recurrence of the tremor, which was abolished by propranolol (2 mg) intravenously. Transducer recordings were again obtained.

*Case 3* A 46 year old female patient who was receiving cimetidine (1 g orally daily) for peptic ulceration developed severe tremor of all limbs. The tremor diminished when the cimetidine was discontinued by her general practitioner. A week later a clinical diagnosis by thyrotoxicosis was made (serum thyroxine 246 mmol/l) and the cimetidine was restarted. The tremor again worsened markedly, but was diminished by the addition of propranolol (40 mg twice daily) to her therapy.

An extrapyramidal syndrome has previously been reported in one patient who was receiving cimetidine,<sup>2</sup> but he was also receiving metoclopramide and dromperidol, drugs known to produce extrapyramidal effects. Two of the present cases are elderly patients in whom an underlying postural and action tremor was markedly aggravated by cimetidine. It appears that other side effects of cimetidine are more common in the elderly.<sup>1</sup> In case 3 a thyrotoxic tremor was considerably intensified by cimetidine. The increase in tone initially noted in the second patient was probably due to metoclopramide.<sup>3</sup> We have given intravenous cimetidine (200 mg) to healthy adults under controlled conditions and have not produced tremor.

The mechanism for the effect of cimetidine is obscure. On rechallenge, tremor was associated with myoclonic jerks in the first patient, but not in the other two. Myoclonic jerks have been noted in patients with cimetidine-induced confusional states.<sup>1</sup> It is not clear whether the effect of cimetidine in producing tremor is due to a central or peripheral action. The confusional state caused by cimetidine has been

attributed to H<sub>2</sub>-receptor blockade in the CNS<sup>1</sup> and the myoclonus also suggests a central effect. Propranolol is thought to act peripherally in reducing physiological tremor.<sup>4</sup> However, the effect of propranolol on cimetidine induced tremor does not necessarily indicate a peripheral origin. The abolition of the tremor by beta-adrenoceptor blockade suggests cimetidine has aggravated an underlying physiological or essential tremor.<sup>5</sup> Exacerbation of physiological or essential tremor by cimetidine suggests that histaminergic pathways are normally involved in the suppression of tremor.

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Copies of the tremor recordings are available on request.