Letters

The blind spot will be enlarged in patients with optic neuritis³ and pseudopapilloedema.⁹ However, if the eyes are unequally involved then the blind spot will be asymmetrically enlarged suggesting a process other than papilloedema.² As shown in this report and in previous studies^{1 2 5} serial determinations of blind spot size can provide a useful index of treatment response in patients with increased intracranial pressure.

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References

- 1 Davis L. The blind spot in patients with intracranial tumours. *JAMA* 1929; 42:794-7.
- 2 Chamlin H, Davidoff LM. Papilloedema. Its differential diagnosis, with special reference to minimal testing of the blind spot at two meters. *Arch Neurol Psychiat* 1952; 68:213-32.
- 3 Scott GI. Traquair's Clinical Perimetry. London: Henry Kimpton, 1957: 302-3.
- 4 Huber A. Eye signs and symptoms in brain tumors. Saint Louis: CV Mosby, 1976: 111-3.
- 5 Jefferson A, Clark J. Treatment of benign intracranial hypertension by dehydrating agents with particular reference to the measurement of the blind spot area as a means of recording improvement. *J Neurol Neurosurg Psychiatry* 1976; 39:627-39.
- 6 Armaly MF. The size and location of the normal blind spot. *Arch Ophthalmol* 1969; 81:192-201.
- 7 Brns J. The Blind Spot of Mariotte. *Acta Ophthalmol* 1939; supplement 17.
- 8 Chan AK. Visual field changes in primary open-angle glaucoma. *Int Ophthalmol Clin* 1979; 19:95-125.
- 9 Hoyt WF, Pont ME. Pseudopapilloedema: Anomalous elevation of the optic disk. *JAMA* 1962; 181: 191-6.

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Latent idiopathic torsion dystonia provoked by thyrotoxicosis

SIR,—Chorea occasionally occurs in thyrotoxicosis.¹⁻⁴ Usually it remits as the over-active thyroid is controlled, but occasionally it persists.⁵ We now describe a patient in whom another type of dyskinesia, torsion dystonia, was provoked by thyrotoxicosis.

At the age of 17 years, a Caucasian woman with no Jewish ancestry, developed spasms of her neck, twisting her chin to the right, and intermittent shaking of the right arm. Unfortunately, this typical picture of segmental dystonia was mis-diagnosed as hysteria, and she spent the next year in a mental hospital, during which time the dystonia gradually disappeared. Between 1951 and 1978 she was only aware of rare mild torticollis when under extreme stress, but she did develop mild rheumatoid arthritis in 1965, for which she had been taking prednisolone 7.5 mg daily since 1973. In December, 1978, she again developed spasms of the neck and pronounced shaking of the right arm. In addition, she had lost weight and had experienced night sweats. On examination then she had spasmodic torticollis with the chin deviated to the right and hypertrophy of the left sternomastoid, intermittent repetitive dystonic spasms of the trunk, arching of her back into excessive lordosis and pulling her body to the right, and dystonic spasms of the right arm which was extended and hyper-pronated. In addition, there was exophthalmos, lid lag and a smooth uniform goitre. The clinical diagnosis was of idiopathic segmental torsion dystonia and thyrotoxicosis, the latter being confirmed biochemically (T4=244 nmol/L, T3=5.09 nmol/L, FTI=382). Thyroid microsomal and thyroglobulin antibodies were present in high titre. The thyrotoxicosis was treated with carbimazole (10 mg thrice daily, reducing to 5 mg twice daily) but proved very difficult to control.

Indeed, she remained thyrotoxic up till April, 1980, when we saw her for the first time (by courtesy of Dr A Hopkins). Then she had severe, exhausting dystonic spasms affecting the neck, trunk and right arm, which rendered her more or less chairbound. Clinical evidence of thyrotoxicosis was again confirmed biochemically (T4=172 nmol/L, T3=3.05 nmol/L). Eventually her thyroid over-activity was brought under control by a combination of radioactive iodine and carbimazole (10 mg four times a day), and the dystonic abnormal movements gradually settled. On two occasions, however, she stopped drug therapy, with the result that she rapidly became thyrotoxic again, and the dystonic movements became dramatically worse. Now that she is euthyroid, the dystonia is very mild, with a slight tendency for torticollis and scoliosis to the right, and for the right outstretched arm to hyper-pronate.

It has been suggested that chorea in thyrotoxicosis is due to hyperthyroidism causing increased sensitivity of striatal dopamine receptors to dopamine.^{4 6} Admittedly, the chorea usually disappears as the thyrotoxicosis is controlled, suggesting a biochemical rather than a structural cause, but this hypothesis does not explain why it is such a rare occurrence in hyperthyroidism. Such a mechanism may have been responsible for the activation of dystonia in our patient, although involvement of dopaminergic mechanisms in dystonia is much less obvious than in chorea. However, we believe that some other unknown mechanism is more likely to have been responsible in our patient. For her severe dystonia did not respond to treatment with dopamine antagonists (tetraabenazine 150 mg daily; haloperidol 12 mg daily) while she remained hyperthyroid.

References

- 1 Svner JC, Fancher PS, Kemble JW. Chorea associated with hyperthyroidism. *US Armed Forces Med J* 1954; 5:61-6.
- 2 Heffron W, Eaton RP. Thyrotoxicosis presenting as choreo-athetosis. *Ann Int Med* 1970; 73:425-8.
- 3 Fidler SM, O'Rourke RA, Buchsbaum HW. Choreoathetosis as a manifestation of thyrotoxicosis (case report). *Neurology (Minneapolis)* 1971; 21:55-77.

- 4 Weiner WJ, Klawans HL. Hyperthyroid chorea. In: Vinken PJ, Bruyn GW, eds. *Handbook of Clinical Neurology*. Amsterdam: North-Holland Publishing Co, 1976; vol 27, 279-81.
- 5 Delwaide PJ, Schoenen J. Hyperthyroidism as a cause of persistent chorea. *Acta Neurol Scand* 1978; 58:309-12.
- 6 Klawans HL, Shenker DM, Weiner WJ. Observations on the dopaminergic nature of hyperthyroid chorea. In: Barbeau A, Chase TN, Paulson GW, eds. *Advances in Neurology*. New York: Raven Press, 1973; vol 1, 543-9.

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Cimetidine induced postural and action tremor

SIR,—Cimetidine, an H_2 receptor antagonist used in the treatment of peptic ulceration has been reported to cause a number of central nervous system side effects.¹ 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,² 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.¹ 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.³ 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.¹ 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_2 -receptor blockade in the CNS¹ and the myoclonus also suggests a central effect. Propranolol is thought to act peripherally in reducing physiological tremor.⁴ 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.⁵ Exacerbation of physiological or essential tremor by cimetidine suggests that histaminergic pathways are normally involved in the suppression of tremor.

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References

- 1 Schentag JJ, Cerra FB, Calleri DeGlopper E, Rose JQ, Bernard. Pharmacokinetic and clinical studies in patients with cimetidine associated mental confusion. *Lancet* 1979; i:177-181.
- 2 Barbier J-PH, Mirsch J-F. Confusion mentale chez un malade traité par la cimetidine. *Nouv Presse Med* 1977; 7:1484.
- 3 Kataria M, Traub M, Marsden CD. Extrapyramidal side-effects of metoclopramide. *Lancet* 1978; ii:1254.
- 4 Jefferson D, Marsden CD. Metoprolol in essential tremor. *Lancet* 1980; i:427.
- 5 Scopa J, Longley BP, Foster JB. Beta-adrenergic blockers in benign essential tremor. *Curr Therapeutic Res* 1973; 15:48-51.

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Copies of the tremor recordings are available on request.