mechanism of lagophthalmos in Ecstasy abuse is not known, and its occurrence is somewhat surprising as this drug is a central nervous system stimulant.

In conclusion, Ecstasy use should be considered in all young patients who have unexplained corneal epitheliopathy. We feel that the corneal erosions seen in our patients could be attributed to lagophthalmos rather than direct corneal toxicity.

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Sir,

The Site of the Autoantigen in Dysthyroid Eye Disease: A Significant Negative

There is indirect evidence to suggest that dysthyroid eye disease is an autoimmune disorder.[1] However, our understanding is hampered by the current failure to identify either a specific autoantibody or an antigen against which the autoimmune response is directed. One hypothesis has been that the autoantigen is located within the extraocular muscles as most of the clinical manifestations of the disease can be attributed to their involvement. This is supported by the enlargement of the extraocular muscles on CT scan and the demonstration by histopathology of lymphocytic infiltration of the muscles and deposition of glycosaminoglycans. However, it has also been suggested that the autoantigen resides in other tissues such as the orbital fat or the retrobulbar fibroblast.

The extraocular muscles contain several muscle fibre types one of which resembles amphibian tonic muscle fibres, whereas the skeletal musculature in mammals resembles the amphibian twitch muscle fibres. The tonic muscle fibres differ from twitch fibres on the basis of morphology,[2] innervation,[3] pharmacology[4] and electrophysiology.[5] These tonic fibres are not present in human skeletal muscles and are therefore an attractive candidate for containing the autoantigen. However, in mammals, tonic muscle fibres are not unique to the extraocular muscles but are also found in the muscles of the middle ear cavity.[6,7] It is quite conceivable that involvement of these muscles may produce only minor symptoms that could easily be overlooked, or indeed be subclinical.

We looked for subclinical involvement of the muscles of the middle ear by using the acoustic reflex as the best objective measure in 5 patients with well-established dysthyroid eye disease. No evidence for middle ear involvement was found in these patients and this strongly suggests that the tonic muscle fibres are not the site of the autoantigen.

Patients and Methods

Five patients with dysthyroid eye disease were studied (4 female, 1 male) ranging in age from 51 to 69 years (mean 61 years). The patients were recruited from the Moorfields Eye Hospital's Thyroid Eye Clinic and all had well-established dysthyroid eye disease diagnosed on the basis of the clinical features and demonstration of enlargement of the extraocular muscles on CT scan. None had a significant past history or family history of otological or facial nerve disorder. None had a history of noise exposure, serious head injury or exposure to ototoxic agents. The duration of clinical dysthyroid eye disease ranged from 1 to 33 years (mean 9 years). At the time of the study these patients were clinically and biochemically euthyroid.

Clinical examination of the ears and facial nerve function was performed, including dewaxing of the external auditory canals and tuning fork tests using a 512 Hz (C2) fork. Pneumatic otoscopy was performed using an otoscope with a halogen light source. Pure tone audiometry was performed on a Kamplex AC30 audiometer in accordance with the BSA recommended procedures for frequencies: 0.25, 0.5, 1, 2, 4 and 8 kHz. Bone conduction and appropriate masking were performed as required.[8–10] Admittance measurements and acoustic reflex thresholds (ARTs) were established using a GSI 33 middle

Table I. Audiometric findings in cases of dysthyroid eye disease

Case no.	Pure tone average (dBHL)		Middle ear compliance (ml)		Ipsilateral acoustic reflex threshold (dBHL)		Contralateral acoustic reflex threshold (dBHL)	
	Right	Left	Right	Left	Right	Left	Right	Left
1	4	5	0.7	1.4	90	95	105	95
2	10	12	0.4	0.4	80	90	85	85
3	32	28	0.7	0.6	75	80	75	80
4	5	7	0.6	0.7	75	85	90	75
5	0	0	0.7	0.6	90	95	99	100

ear analyser. Tympanometry was performed at a probe tone frequency of 226 Hz at 85 dB sound pressure level sweeping from +200 decapascals (dPa) to −400 dPa. ARTs were determined ipsilaterally and contralaterally for stimulating frequencies 0.5, 1, 2 and 4 kHz.[11]

Results

All patients had normal tympanic membranes, facial movements and Rinne tuning fork tests. Although the Weber tuning fork test inexplicably lateralised in 1 patient, this is a not uncommon finding in otherwise normal subjects.

The audiometric results are summarised in Table I. All patients exhibited normal pure tone thresholds for their age (pure tone average shown for 0.5, 1 and 2 Hz) and normal compliance. Middle ear pressures and both contralateral and ipsilateral acoustic reflex thresholds were likewise normal. The thresholds at 1 kHz for the auditory reflex are illustrated in Table I. Corresponding thresholds at 0.5, 2 and 4 kHz were also within the normal range.

Discussion

Dysthyroid eye disease is presumed to be a tissue-specific autoimmune disorder but the antigen has not been identified. Many of the clinical manifestations can be accounted for by the effects on the extraocular muscles, and the extraocular muscles do contain a fibre type that is almost unique in the mammalian musculature and most closely resembles the tonic muscle fibres of amphibians. If they are the antigen, then it would be expected that other sites that contain tonic fibres would also be involved. The only other site that we are aware of where such fibres are found is the muscles of the middle ear cavity. The failure to find involvement of the middle ear in patients with established dysthyroid eye disease argues against the extraocular muscles being the site of the autoantigen.

There is other work that also leads to this conclusion. In histological studies, although the inflammation seems centred on the extraocular muscles, the fibres appear histologically intact with no evidence of active destruction.[12] The conclusion that the extraocular muscle fibres do not contain the autoantigen is further reinforced by normal electromyographic studies in most patients with the disease.[13] It would also explain the failure of other workers to find an autoantibody directed against extraocular muscle fibres.[14–18]

Abnormalities have been documented in other orbital tissues and particularly the fibroblast.[19] It is possible that the extraocular and/or orbital fibroblasts contain the putative autoantigen and that they respond to immune attack by the formation and deposition of glycosaminoglycans. This would have a clear parallel with pretibial myxoedema.

Our work, together with the other studies referred to above, is further evidence against the extraocular muscle being the site of the autoantigen.

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Sir,

Blepharospasm and Fuchs' Endothelial Dystrophy

We would like to report what appears to be an association between bilateral corneal decompensation (secondary to Fuchs' endothelial dystrophy) and severe blepharospasm. We have found this in 4 patients. This association has not previously been reported to our knowledge.

The 4 female patients were aged 52, 50, 49 and 54 years at the time of diagnosis of their blepharospasm; 2 were non-identical twins. In all patients the dystonia progressed to involve the lower facial muscles and efforts at treatment medically with tetrabenzine and clonazepam were unhelpful.

These patients were referred to an ophthalmologist when they developed symptoms of reduced vision. A diagnosis of Fuchs' endothelial dystrophy was made in all patients associated with early cataract and normal intraocular pressure. The time to diagnosis from the onset of the blepharospasm was a 22, 20, 16 and 12 years (mean 17.5 years) respectively. All patients developed bilateral corneal decompensation within 6 years of seeing the ophthalmologist and underwent corneal grafting. Histological examination confirmed the diagnosis of Fuchs' endothelial dystrophy.

To test the hypothesis that continued severe blepharospasm might be directly related to the endothelial changes, 10 patients who had suffered blepharospasm for at least 10 years (mean 12 years) and who were attending the botulinum toxin clinic underwent endothelial photographs. Endothelial photographs were also taken of uncomplicated age/sex-matched pre-operative cataract cases as a control. However, comparison of the endothelial morphology and cell count using a grid and counting technique revealed no significant difference between the groups.

Comment

Essential blepharospasm is an involuntary repetitive closure of the eyelids. It is usually bilateral and progressive, with half the patients having other involuntary movements.[1] Approximately 10% of affected patients have been reported to have a family history of some type of dystonia.[2] There have been reports of dystonias which appeared to be dominantly inherited.[3]

Fuchs' corneal endothelial dystrophy is a bilateral condition; women are affected more severely and more frequently than men. It may be inherited as an autosomal dominant trait with incomplete penetrance[4] but there is no other evidence that the dystrophy is primary. The corneal endothelium transports water from the corneal stroma into the anterior chamber. This produces a state of relative corneal dehydration and maintains its clarity. The fluid transport depends upon aerobic mechanisms and the required oxygen is thought to diffuse from the anterior chamber rather than from the tear film.[5] However, corneal hypoxia induced by exposing the anterior corneal surface to nitrogen or placing a thick contact lens on the eye has been shown to cause the stroma to swell.[6] Upon restoration of air to its anterior surface the cornea thins to a degree consistent with the restoration of endothelial pump action. Evaporation from the tear film with a resultant increase in its osmolality also draws water from the cornea.[7]

It has been reported that chronic corneal hypoxia may lead to permanent changes in corneal structure and function.[6] It was possible that in the cases presented, the prolonged lid closure associated with blepharospasm may have reduced the oxygen available to the anterior surface of the cornea as well as reducing tear evaporation, leading to chronic hypoxia and endothelial damage. However, this hypothesis was not substantiated in the small series studied, which revealed no significant difference in the number or morphology of endothelial cells in those with severe blepharospasm compared with normals. That the endothelial cell counts were the same in the two groups also mitigates against the theory that there might be direct structural damage to the endothelium due to corneal flexing as a consequence of the blepharospasm.

It has been reported that where there is low endothelial cell density there is marked corneal swelling in response to hypoxia and on restoration of oxygen a slow recovery occurs.[8] These patients did not show an earlier age of onset or faster rate of progression of the corneal decompensation than is usual in Fuchs' endothelial dystrophy.

The observation of 4 cases with both conditions, and particularly the 2 non-identical twins, raises the possibility of genetic linkage. Both conditions have been reported to be inherited as autosomal dominant pedigrees in some cases,[3,4] although there was no previous family history that indicated prior cases and examination of the children was normal.

A toxic drug effect from treatment of the dystonia was also considered, but this complication has not been reported before with these medications despite wide usage.

We thought it important to report the co-incidence of Fuchs' endothelial dystrophy and blepharospasm, but from the evidence of a small series it seems likely to have been simply fortuitous. Moreover, it could not be shown that even severe blepharospasm had any compromising effect on the endothelial cells, because the corneal endothelial failure seemed to progress rapidly to bilateral corneal decompensation at the same rate as in other patients with Fuchs' endothelial dystrophy.

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