LETTERS TO THE JOURNAL

Sir,

Methylenedioxyamphetamine ('Ecstasy') Associated Keratopathy

3,4-Methylenedioxyamphetamine ('Ecstasy') is a dangerous 'designer drug' of abuse. It is a methoxylated amphetamine related to both hallucinogens and stimulants. The drug is known to affect synaptic serotonin and noradrenaline release, though the precise mode of action is unknown. There are no reports of ophthalmic complications of ingestion of this drug to our knowledge, and we report three such cases.

Case Reports

Case 1. A 31-year-old woman attended ophthalmic casualty with a 1 day history of bilateral ocular pain and blurred vision associated with diffuse punctate corneal epithelial erosions affecting almost the entire surface of both corneas (particularly the centre, but sparing the upper limbus) together with a 1 mm diameter right corneal epithelial infiltrate. Her acuity was 6/36 in each eye at presentation. The infiltrate was scraped and was sterile on culture. It settled rapidly on topical chloramphenicol 0.5% q.d.s. and atropine 1% b.d. and acuity improved to 6/9 right and 6/6 left. She was not a contact lens wearer and did not know the cause of her keratopathy. She is a registered drug addict and is on regular prescribed oral methadone. She denied any alcohol intake but on direct questioning she admitted to ingesting one tablet of Ecstasy at a party 2 days prior to presentation. She had taken the tablet at 10 p.m. and remained awake until 4 a.m. She did not admit to taking crack cocaine or any other prescribed medications or illicit drugs.

Case 2. An 18-year-old man attended casualty with a 1 day history of bilateral painful blurring of vision associated with fine bilateral interpalpebral punctate corneal erosions. He saw 6/9 right and 6/6 left. Occ chloramphenicol 1% stat was prescribed for both eyes. He does not wear contact lenses and admitted to having taken one tablet of Ecstasy 36 hours previously. He had ingested the tablet at 9 p.m. and remained awake until 10 a.m. He did not admit to having taken alcohol, crack cocaine or any other prescribed medications or illicit drugs.

Case 3. A 19-year-old man attended ophthalmic casualty with a 12 hour history of painful watery photophobic left eye having left his gas-permeable contact lenses in overnight. His acuity was 6/12 right and 6/18 left. He had fixed dilated pupils measuring 8 mm, a 2.2 mm diameter central macroerosion of the left cornea and central punctate corneal erosions affecting the right eye. On direct questioning he admitted that he had inserted his contact lenses at 10 p.m. the previous evening and had then ingested three tablets of Ecstasy. He had remained awake throughout the night and then removed his contact lenses at 3 p.m. He had been awake continuously for 36 hours at the time of examination. He did not admit to taking alcohol, crack cocaine or any other prescribed medications or illicit drugs. Occ chloramphenicol 1% stat (both eyes) and double padding of his left eye were prescribed and his symptoms resolved rapidly.

Discussion

These three patients presented with otherwise unexplained corneal epitheliopathy following ingestion of Ecstasy. Two of the patients (cases 1 and 3) had taken this drug on previous occasions.

There is relatively little formal information on the psychological, behavioural and neurotoxic effects of this drug in humans,[1] though there are several case reports of fatalities from hyperthermia and cardiorespiratory collapse.[2,3] Liester *et al.*[1] have divided the adverse side effects of this compound into amphetamine effects (e.g. tachycardia, dry mouth, palpitations, nausea and insomnia), impaired judgement and gait, panic attacks and death.

It is interesting to note that similar corneal complications have been reported following the use of crack cocaine. Corneal epithelial defects following the use of crack cocaine were first described by McHenry *et al.*[4] These epithelial defects may lead to frank corneal ulceration and infectious keratitis.[5] Sachs *et al.*[5] have noted that crack cocaine smoke may have a direct toxic effect on the corneal epithelium and also may lead to damage because of possible corneal anaesthesia. None of these mechanisms attributed to crack cocaine corneal injury are applicable to patients who take Ecstasy alone.

The corneal changes seen in our cases do not readily fall into the known categories of amphetamine toxicity or toxic crack fumes. The distribution of corneal epithelial changes would suggest corneal exposure (lagophthalmos) as the likely cause. Alcohol and other central nervous system depressants are known to cause symptomatic lagophthalmos and are thought to interfere with normal blinking, lid closure and eye position during sleep.[6] The

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.

D. O'Neill, FRCS, FRCOphth, MRCPI, DO
J. K. Dart, MA, DM, FRCS

Moorfields Eye Hospital,
City Road,
London EC1V 2PD, UK

References

1. Liester MB, Grob CS, Bravo GL, Walsh RN. Phenomenology and sequelae of 3,4-methlenedioxyamphetamine use. J Nervous Mental Dis 1992;180:345–52.
2. Chadwick IS, Curry PD, Linsley A, Freemont AJ, Doran B. Ecstasy, 3,4-methlenedioxyamphetamine (MDMA), a fatality associated with coagulopathy and hyperthermia. J R Soc Med 1991;84:371.
3. Campkin NT, Davies UM. Another death from Ecstasy. J R Soc Med 1992;85:61.
4. McHenry JG, Zeiter JH, Madion MP, Cowden JW. Corneal epithelial defects after smoking crack cocaine. Am J Ophthalmol 1989;108:732.
5. Sachs R, Zagelbaum BM, Hersh PS. Corneal complications associated with the use of crack cocaine. Ophthalmology 1993;100: 187–91.
6. Lyons CJ, McNab AA. Symptomatic nocturnal lagophthalmos. Aust NZ J Ophthalmol 1990;18:393–6.

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