a small residual foveal haemorrhage. After this visit she defaulted from follow-up.

Comment

Ocular manifestations in meningitis are thought to occur in over 70% of children,[1] and fundus involvement in around 5% of cases.[2] These fundal complications include papilloedema,[1,2] optic atrophy,[1,2] temporal disc pallor[1,2] and chorioretinitis in both tuberculous[1–3] and cryptococcal meningitis,[4] and panuveitis and endophthalmitis in cryptococcal meningitis.[4]

As far as we are aware intraocular haemorrhage has not been described in any form of meningitis – conceivably a clotting disorder could have caused the haemorrhage and this is well known in meningococcal meningitis,[5] but clotting studies were normal throughout the patient's illness.

Intraocular haemorrhage is a well-recognised complication of subarachnoid haemorrhage;[6] it is thought to be caused by the transmission of intracranial pressure along the optic nerve with subsequent nerve sheath dilation and rupture of dural and bridging vessels. Retinal venous hypertension brought on by obstruction of the central retinal vein may be the source of the haemorrhage.[7]

It seems conceivable that our patient could have had a rise in intracranial pressure at some stage in her illness and this could have precipitated a retinal venous haemorrhage. Although the cerebrospinal fluid pressure is often not taken in the acute situation, the presence of drowsiness can indicate raised intracranial pressure.

Whatever the underlying cause for the haemorrhage, resolution was spontaneous (up to the time of default) and it would appear that the initial management of these situations should be conservative.

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Sir,
Maculopathy Associated with Diazepam

There is a well-known affinity between diazepam and mammalian retina,[1,2] but there have been no reports of associations between the drug and retinal degenerations. We present such a case, and discuss the evidence suggesting that this may be more than a chance association.

Case Report

A 40-year-old male Caucasian was referred by his optician after asymptomatic macular abnormalities were found on routine examination. He had no ocular history and no family history of ocular disease. He had a long history of anxiety complicated by excessive alcohol intake, and had been taking up to 30 mg daily of diazepam for the previous 7 years. In addition he had received short courses of tricyclic antidepressants, monoamine oxidase inhibitors, fluoxetine and propranolol. Other benzodiazepines such as temazepam had also been used in the past.

The patient was emmetropic and saw 6/9 in the right eye and 6/6 in the left. Both fundi showed macular atrophic changes with scattered hyperpigmentation (Fig. 1). Fluorescein angiography confirmed retinal pigment epithelial degenerative change (Fig. 2).

On further examination 3 months later there was no change. The patient did not attend for electro-oculography (EOG) and electro-retinography (ERG) and has evaded follow-up despite our efforts since.

Discussion

Diazepam has been commonly prescribed to treat anxiety, insomnia, epilepsy and muscle spasms over the last 25 years. In recent years long-term therapy has been discouraged due to well-publicised central side-effects including tolerance and dependence, and difficulties in drug withdrawal.[3] Doses of 6–15 mg
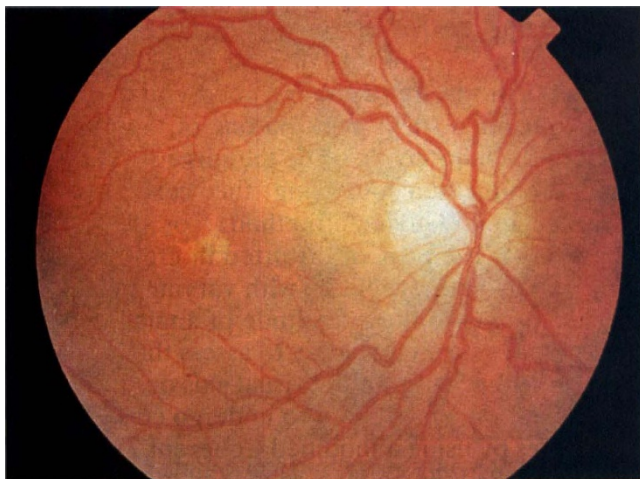
Fig. 1. *Right fundus on presentation.*

daily are commonly prescribed, although higher doses are occasionally used as tolerance develops. The therapeutic action of benzodiazepines is primarily due to their modulation of gamma-aminobutyric acid (GABA) receptors,[4] which are present in the brain and eye in similar concentrations.[5]

GABA is the main inhibitory neurotransmitter in the central nervous system. There are probably three subclasses of receptor, only one of which (GABA A) is modulated by benzodiazepines.[6] In mammalian retinae amacrine cells release GABA and specific high-affinity binding sites are localised to the inner plexiform layer, but non-specific binding also occurs in the retinal pigment epithelium, the ciliary body and throughout the retina.[2]

Robbins and Ikeda[1] found no acute or chronic effect of diazepam on cat or rat retinal function as assessed by ERG, but Jaffe[7] found acute attenuation of the ERG in human volunteers after diazepam administration. The EOG potential has also been shown to be reduced in humans after a single dose of 20 mg diazepam.[8]

Various side-effects of diazepam on the eye have been described in small numbers. They are listed in
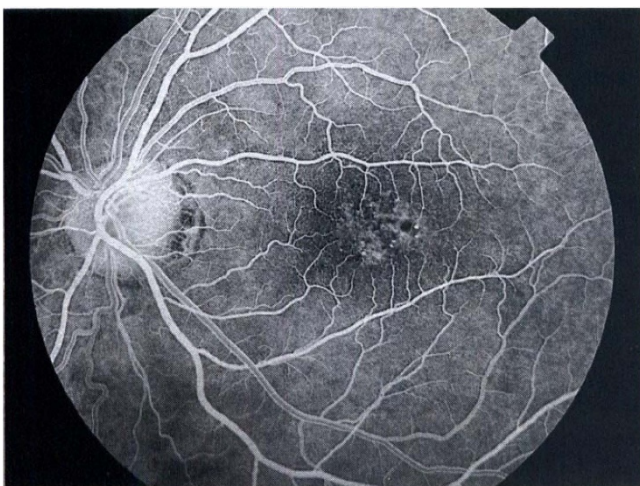
Table I. Ophthalmological effects of benzodiazepines

Effect	Mechanism
Decreased eye movements/ tracking	GABA agonist
Allergic conjunctivitis	Unknown
Angle closure glaucoma	Anticholinergic/pupil sphincter relaxation
Visual field defect	?Central/retinal GABA modulation

Table I.[9] The only reported case of diazepam-induced alteration of retinal function is a well-supported case of reversible visual field loss in a patient receiving 100 mg of drug daily.[10]

Diazepam has no known effect on vascular flow, and any long-term effect on the choroid or retinal pigment epithelium is not easy to explain in terms of the location of the high-affinity GABA receptors in the inner plexiform layer. However, the effect upon the EOG does show some evidence for diazepam modulation at the level of the outer retina, and there are non-specific binding sites at this level.

This patient had no family history, but could still demonstrate an unusual form of an inherited disease such as pattern dystrophy or cone dystrophy. Benign concentric annular macular dystrophy causes progressive perifoveal retinal pigment epithelial atrophy without initial electrophysiological changes.[11] There are, however, good reasons to suggest that this is a drug-induced effect: benzodiazepines do bind to both outer and inner retinal layers and have effects upon the EOG, ERG and receptive visual field. Further reports of retinal abnormalities in patients taking these drugs (particularly at high doses) would be encouraged.

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Fig. 2. *Left eye: mid-venous phase fluorescein angiogram.*

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Sir,
Ensuring Graft Centration using a Modified YAG Laser

Optimal results following penetrating keratoplasty depend on accurate centration of the graft as well as radially positioned sutures of the correct tension. Graft eccentricity is known to cause astigmatism[1,2] and a clear graft can have poor visual results due to this complication.[3] A graft which is optically centred correctly and whose border is nearer to the limbus in one meridian may be at a higher risk of rejection. In keratoconus a similarly centred graft whose border has not completely cleared an inferiorly placed cone can result in unexpected astigmatism due to varying wound thicknesses.[4] Notwithstanding these possible reasons for placing an optical graft eccentrically, the common practice is to aim for accurate centration on the visual axis. Surgical techniques for localising the graft have traditionally involved intraoperative methods, often with the patient under general anaesthetic. The imprint of the trephine can be inspected for concentricity with the pupil,[5,6] but it can be difficult to be sure the surgeon is not looking obliquely at the pupil centre instead of straight down the visual axis. It has been suggested that miotics may make this task easier[6] and often these would be used immediately pre-operatively to protect the lens during the operation, but dilation or constriction of the pupil has been found to shift its centre.[7] The anatomical centre of the recipient cornea can be marked by measuring with calipers[8] and this may be the only method if the cornea is severely opacified.

Methods used by radial keratotomy surgeons to

ascertain the centre of the optical zone with the operating microscope are less applicable to graft patients as they require either a good visual acuity in order to fixate a small mark on one of the objective lenses of the microscope while the surgeon marks the corneal epithelium overlying the centre of the entrance pupil (Guyton's method),[9] or the corneal light reflex is used (often distorted in graft patients) using one or both eyepieces with varying degrees of error according to the magnitude of angle lambda.[7]

We conducted a pilot study to assess the feasibility of marking the centre of the visual axis on the cornea of three keratoconics about to undergo corneal graft procedures by using a modified Coherent 7970 YAG laser. We asked the patients to look between the two red He–Ne aiming beams of the laser (8° above and below the YAG axis) and focused them in the mid-stroma enabling the YAG energy to be delivered to the visual axis on the cornea. To help patient fixation and to prevent the patients having to gaze straight at the He–Ne beams we positioned a small flashing green light-emitting diode (LED) between the two aiming beams as seen by the patient (Fig. 1). This was attached by a thin cable to a battery unit. It was mounted behind the laser housing, at the front of the microscope unit, and can be fitted without loss of warranty in a matter of minutes simply with a screwdriver. Its installation is simplified by the existence of a suitable hole between the two objective lenses of the microscope, which is fastened to the laser housing using one screw (Fig. 2).

The patients were set up on the chin rest in the normal way but with the other eye occluded. The aiming beams were aligned approximately in the centre of the miosed pupil but focused in the cornea. The patients were then asked to fixate on the green flashing light while confirming the red aiming beams were equidistant above and below. The YAG laser was then fired resulting in an intra-stromal gas
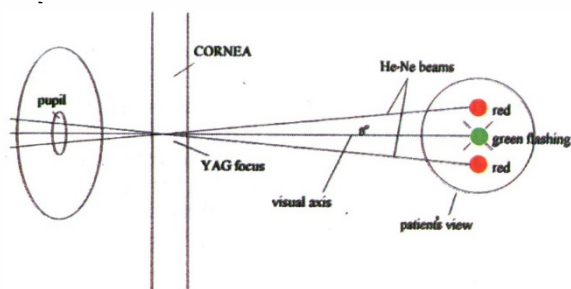

Fig. 1. *The aiming beams lie 8° above and below the YAG axis and converge at its focus. They are set up to focus on the mid-stroma and pass through the miosed pupil; then the patient is asked to fixate on the flashing green LED.*

Fig. 2. *The microscope optics come away from the main laser body by loosening a screw. The fixation light is fitted in the microscope mounting plate between the objective lenses.*