Sir,

Response to Dr Wishart (Non-steroidal drug-induced glaucoma)

We appreciate the thoughtful comments made by Dr Wishart[1] and his interest in our review article.[2] There is no way to compare non-medication-induced angle closure from other factors, nor are we suggesting that it is a more common event. The important issue is that physicians need to be aware of the potential of certain drugs to provoke an angle-closure attack in high-risk patients. Gonioscopy helps to identify high-risk patients, especially the hyperopic middle-aged or older patient, and would help physicians in advising their patients of the relative risk. Most cases of pharmacologically induced angle closure have reportedly been due to a pupillary block mechanism, with fewer cases being secondary to plateau iris configuration and choroidal effusions.[3,4] Therefore, a prophylactic laser peripheral iridotomy would be expected to be protective. The decision as to whether that would be appropriate given the risks of angle-closure glaucoma is weighed against the risks of the laser procedure. Dr Wishart noted the prevalence of a narrow angle in the Caucasian population to be relatively low. We suggest that it would be important to identify this population by gonioscopy so that appropriate counseling could be offered. The prevalence of narrow angles in other ethnic groups, especially Asians, is significantly higher.[5]

The reference for the statement 'at least one third of acute closed angle glaucoma cases are related to over-the-counter or prescription drugs' was the third reference[4] of our manuscript, but had been cited in error.

The patients studied by Mapstone[6] had experienced an acute attack in one of their eyes, and their contralateral eye that had had no sign of glaucoma or had been cases of intermittent angle-closure glaucoma underwent a tropicamide challenge test. In fact, not all the studied eyes had glaucoma but had occludable angle. The point that the risk of tropicamide causing angle closure is 0 is a curious comment, as this point certainly is not substantiated by any large trial in a large high-risk population. Provocative testing is known to be of limited predictive value. Although it is agreed that even in narrow angles dilation may not precipitate angle closure in every case, the obligation of physicians is to (1) recognize which patients may be at risk, (2) advise the patients of a potential risk with pharmacological dilation, and (3) offer a preventive treatment like prophylactic laser iridotomy with risks and benefits reviewed when deemed appropriate.

Conflict of interest

The authors declare no conflict of interest.

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MR Razeghinejad[1,2], MJ Pro[1] and LJ Katz[1]
[1]Glaucoma Service, Wills Eye Institute, Thomas Jefferson University, Philadelphia, PA, USA
[2]Department of Ophthalmology, Shiraz University of Medical Sciences, Shiraz, Iran
E-mail: razeghinejad@yahoo.com

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Sir,

Potential damage to a potential space

It was interesting to read the article by Gupta *et al*[1] reporting the use of trans-scleral vision blue (TSVB). As the authors state, this is an off-label use and as such there should be good evidence to support its use or a robust audit to determine its efficacy. They reported that 'there was no evidence of complications as a result of TSVB injection'; how did the authors look for such complications? Fourier domain optical coherence tomography (OCT) may be used to evaluate the photoreceptor inner–outer segment junction that has been shown to be disrupted when exposed to subretinal VB.[2] Similarly, microperimetry and fundus autofluorescence may be useful.

The inner retina has evolved to be naturally isolated from direct contact with contents of the vitreous and blood. When this selective permeability is disrupted, as it occurs in many pathological situations, the presence of relatively 'harmless' endogenous fluids may result in damage. There should therefore be strong reasons before iatrogenically disrupting this balance, as the RPE and photoreceptors may be insulted either directly, by exposure to toxic agents, or indirectly, via non-iso-osmolar solutions. The authors cite Veckeneer *et al*[3] stating 'At 0.06% Trypan blue (TB) was concluded to be harmless'. In these experiments, however, the dye injection was intravitreal and should not be extrapolated to confirm safety if placed in the subretinal space. A further *in vitro* model tested the toxicity of 0.15% TB (higher than used here) in RPE cells and reported its safety.[4] Subsequent *in vivo* experiments with subretinal 0.15% TB injections in rabbits showed significant photoreceptor and RPE damage.[2] Even the injection of an iso-osmolar balanced salt solution has been shown to cause mild photoreceptor outer-segment damage.[2]

One important, and perhaps overlooked, finding of this study may be the increased occurrence of occult breaks around areas of prior retinal cryopexy. This could be used to strengthen the argument favouring laser retinopexy over cryopexy, but more importantly

highlights that this is an area where we ought to be extra vigilant in our search for breaks when performing repeat surgery.

Conflict of interest
The author declares no conflict of interest.

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K Khan

Department of Ophthalmology, Leeds Institute of Molecular Medicine, St James' University Hospital, Leeds, UK
E-mail: medknk@leeds.ac.uk

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Sir,

Dye toxicity in the context of recurrent retinal detachment repair

We thank Dr Khan[1] for his comments regarding our paper.[2] In the context of retinal detachments (RD) where the break is not clinically detectable, the issue is balancing the risk of inevitable persistent RD and vision loss, against the use of a technique that will allow the break to be identified while causing minimal complications. There is no standard accepted technique at this time. Although Fourier domain OCT can show attenuation, alteration, and disruption of the junction line between photoreceptor outer segment/inner segment (OS/IS), however, the correlation of these findings with postoperative vision remains inconsistent and most reports continue to include examples of exceptions to statistical trends.[3]

The decision to use dye at our centre was made after the data on Trypan blue (at a higher concentration than used in our series) injection was available.[4] The use of this dye was later reported in >45 patients.[5] Before adopting the use of the dye at our centre, the senior author used either silicone oil or encirclement. Both techniques were associated with their own complications; the latter was only effective in 60% of cases in this group of patients and often associated with pain.

Penha *et al*'s[6] investigation was in the context of macular holes. Toxicity is more relevant in the macular area and the dyes were shown to cause RPE atrophy in the areas that the subretinal bleb was created. Trypan blue caused the least amount of toxicity of the dyes investigated. In the context of identifying clinically undetectable breaks that are most likely to be peripheral, and possibly associated with atrophic retinal areas that have had previous cryotherapy, the risk of further peripheral RPE atrophy caused by dye toxicity needs to be balanced against the risk of persistent RD and visual loss if the break is not found. Regardless of the use of dye, the RD itself may cause disruption to the microanatomy (OS/IS junction).[7,8]

Finally, with respect to the occurrence of retinal breaks near to areas of cryopexy, we simply chose to report our findings rather than attempt to draw any conclusions, as the number of cases were thankfully small.

Conflict of interest
The authors declare no conflict of interest.

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D Gupta and RL Burton

Department of Ophthalmology, Norfolk and Norwich University Hospital, Colney Lane, Norwich, UK
E-mail: dgupta_01@yahoo.com

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