

## CORRESPONDENCE

### Fundal white dots: observations from a murine model of congenital ocular toxoplasmosis

EDITOR,—In the *BJO* Ben Ezra and Forrester have reviewed extensively current knowledge concerning the phenomenon of multiple evanescent white dot syndrome (MEWDS), a specific clinical entity which is characterised by the presence of evanescent or permanent, small, discrete subretinal lesions, which occur in the absence of vitreous inflammation.<sup>1</sup>

Multiple pale lesions<sup>2,3</sup> (Fig 1) can be

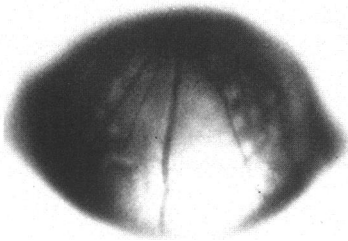


Figure 1 Peripheral fundus showing a number of foci of retinal disturbance.

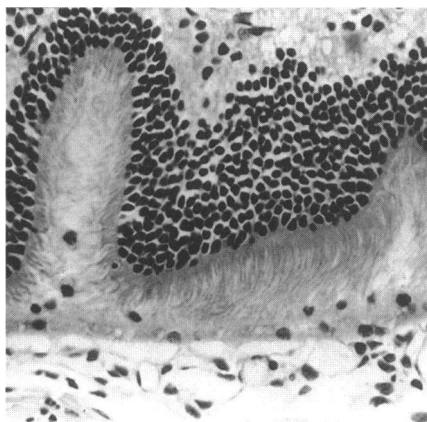


Figure 2 Inflammatory cells among the photoreceptor outer segments are associated with disruption to the architecture of the outer nuclear layer giving it an undulating appearance.

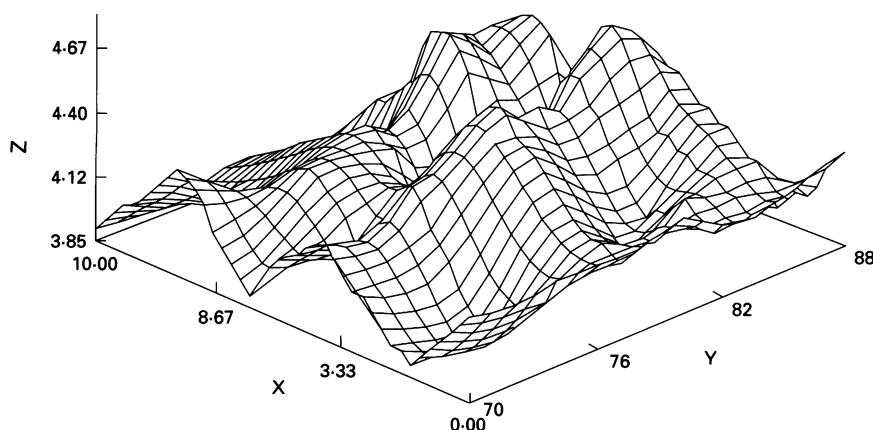


Figure 3 Three dimensional image demonstrates dome-shaped appearance of the lesions.

observed in the outer retina of a small proportion of mice with experimentally induced congenital ocular toxoplasmosis.<sup>4</sup> These focal lesions, which closely resemble MEWDS in humans, were clearly seen in the peripheral retina using indirect microscopy, and imparted an orange hue to the underlying choroid. The lesions were observed in the eyes of approximately 16% of congenitally infected mice and occurred either unilaterally or bilaterally. They were only observed from 3 weeks postpartum.

Histopathological examination of these refractive disturbances<sup>3,5</sup> within the otherwise transparent murine retina revealed that they consisted of focal elevations of the photoreceptor layer (Fig 2). Clusters of inflammatory cells in the form of lymphocytes and macrophages were a consistent feature and were located between the photoreceptor and pigment epithelial layers of the disorganised retina. Immunocytochemical labelling consistently failed to reveal *Toxoplasma* antigen within or in apposition to these lesions.<sup>6</sup>

Three dimensional reconstructions (Fig 3) of these lesions using serial sections of resin embedded tissue and standard SAS GRAPH routines, revealed that they were consistently dome-shaped, and did not result from artefactual folds in the tissue consequent upon processing or cutting of the tissue.

It is our contention that the focal cellular infiltrates are likely to impair the intrinsic processing mechanisms for removal of photoreceptor elements with the result that focal elevations of the photoreceptors appear in the retina; these are then perceived clinically, under direct illumination, as small discrete deep retinal lesions. They were evanescent in some eyes in which progression to atrophy of the photoreceptor layer had taken place in association with retinal vasculitis. This led us to hypothesise that there may be an autoimmune component associated with the pathogenesis of the ocular toxoplasmosis in the mouse model.<sup>7</sup>

Ben Ezra and Forrester suggest that extravasated foci of leucocytes will render the white dot lesions pale relative to the surrounding unaffected tissue when the fundus is illuminated with white light. Based on our own observations with the mouse model of ocular toxoplasmosis, we would concur with this notion. We contend further, however, that an additional contributor to the clinically observed white dot syndrome may be architectural modification to the overlying deep retina into dome-shaped configurations. This would result in refractive anomalies as well as reflectance of some of the incident light impinging on the retina. Such optical effects

would also impart to the lesions a paler coloration relative to the surrounding non-affected areas.

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- 4 Hay J, Hutchison WM, Lee WR, Siim JC. Cataract in mice congenitally infected with *Toxoplasma gondii*. *Ann Trop Med Parasitol* 1981; 75: 455-7.
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### Reply

EDITOR,—Hay and Dutton refer to 'multiple pale lesions' in the model of congenital ocular toxoplasmosis in mice and believe that they are similar to the 'white dots' observed in humans in the various conditions we reviewed. We believe that they are confusing atrophic retinal patches and/or diffractive aberrations in the mouse model of congenital ocular toxoplasmosis with the evanescent (choroidal - retinal pigment epithelium) white dots we have described in our paper. We, therefore, would not concur with their assumption that the patches they observe are comparable with the white dots observed in humans.

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### Natural outcomes of stage 1, 2, 3, and 4 idiopathic macular holes

EDITOR,—In order to evaluate the results of surgical intervention in the treatment of macular holes it is essential that we understand the natural history and visual prognosis of all four stages of macular holes. The paper by Hikichi *et al* in the *BJO*<sup>1</sup> was heralded in the accompanying editorial as providing just such an insight into the natural history of idiopathic macular holes. However, I would like to highlight some striking similarities between their data on stage 2 macular holes presented in this study and those reported by the same authors in an article entitled 'The natural history of stage 2 macular holes', published in the *American Journal of Ophthalmology*<sup>2</sup> (Table 1).

The authors may suggest that publication of such similar data is justified as this study is the first to document the natural history of all four stages of macular holes in a single article. However, the data on stage 3 and 4 holes do little more than echo the authors' findings in



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