# EDITORIAL

## THE VITREORETINAL INTERFACE: SCIENCE AND SERENDIPITY

The interface between the neural retina and the virtually acellular vitreous cortex provides a focus for a wide range of pathological interactions. The network of heterotypic collagen fibrils confers on the vitreous gel a corporate integrity and mobility, especially after vitreous detachment, which can lead to neuroretinal disruption at points of abnormal vitreoretinal adhesion or, in the case of giant tears, at the posterior border of the vitreous base. In the first of five related reviews in this issue, Paul Bishop provides an update on the biochemistry and ultrastructure of these vitreous proteins – including types II, IX and V/XI collagens. Meanwhile, at least two classes of molecular genetic abnormality in the major collagen fibrils of the vitreous have been shown to underlie the anomalous gel development in Stickler's arthro-ophthalmopathy, as described in this issue by Martin Snead. Defective production of the type II collagen homotrimer through various premature termination codons is said to result in a retrolental vitreous remnant which allows biomicroscopic differentiation of these patients from others with defects such as amino acid substitutions in the alpha 1 (XI) chain of type V/XI collagen at the core of the fibrils. These observations have yet to be independently confirmed, and the search goes on for explanations for the phenotypic heterogeneity within Stickler's families, not least congenital myopia and giant tear formation in childhood contrasting with complex retinal detachments from multiple posterior breaks in older family members.

The pathophysiology of non-vascularised or vascular cell outgrowths onto the neuroretinal surface are reviewed in this issue by research teams headed by Ian Grierson and Mike Boulton. Grierson emphasises the fundamental distinction between glial repair (i.e. gliosis with minimal if any contraction) and the contractile, fibrous consequences of fibroblastic or pigment epithelial cell responses to cytokines and bioactive glycoproteins as in proliferative vitreoretinopathy (PVR). Boulton then considers, in relation to proliferative diabetic retinopathy, the principles of growth factor involvement in pathological processes and repair. Target cell responses to growth factors can be extremely variable depending on their concentration and the context of (or combination with) the scores of other peptides potentially involved, as well as on regulation of target cell receptors. Ophthalmologists are familiar with what might be clinical examples of the paradoxical consequences that can arise, e.g. scatter photocoagulation of ischaemic peripheral retina may result in *regression* of epiretinal neovascularisation but *induction* of non-vascularised fibrocellular membranes and macular pucker.

These scientific issues are no more enigmatic than in the pathogenesis and management of idiopathic macular holes. Even in these days of monochromatic interrogation and, indeed, surgical exploration and extraction of the neuroretinal surface, one is reminded of Vogt's declaration (reported by Hruby[1]) that observations in the posterior vitreous may be 'illusory rather than real'. Macular holes are sometimes regarded as part of a spectrum of premacular traction, including macular pucker, there being a presumption[2] of a role for prefoveal gel contraction in macular hole formation. Why such etherial tangential traction should result not in folding of the retina but in 'foveal dehiscence' is unclear, though the appearance is reminiscent of the everted margins of certain large peripheral retinal breaks (often erroneously attributed to PVR) and of the rolled-over edges of outer leaf breaks in acquired retinoschisis. Speculations on the pathophysiology of macular holes have had to be reviewed in the light of the outcome of surgery for full-thickness macular holes (i.e. vitrectomy and internal tamponade), which was initiated as a 'pragmatic, clinical approach towards an otherwise untreatable condition'.[3] Kelly and Wendel's attempts to flatten the detached rim of retina around a macular hole and thereby to improve vision resulted not only in 'closure' of the hole (i.e. apposition of the edges of the break to the pigment epithelium) but, at least in some early cases, an

 

entirely unexpected improvement in biomicroscopic and psychophysical parameters.[4] This was inconsistent with previous assumptions that there had been a substantial loss of foveal neuroretina (i.e. into an operculum) during hole formation.[2] There is also some limited histological evidence[5,6] of 'centripetal replacement of the fovea' following successful surgery[2] and a role for intraretinal gliosis without chorioretinal adhesion (i.e. 'patching without glueing'[7] or 'closure by healing', rather than 'closure and sealing').

Zden Gregor in this issue describes the surgical approaches being adopted to perfect the healing of macular holes, including the use of macular marinades such as preparations of growth factors[8] or other cytokine sources such as serum and platelets.[9,10] These new health technologies have a questionable scientific rationale since they were predicated on experimental models of 'biological glue for retinotomy' which resulted in fibrocellular chorioretinal adhesion and epiretinal membranes, not reparative intraretinal gliosis.[11,12] Thus, these adjunctive therapies remain essentially empirical, and have yet to be shown through clinical trials to add benefit to scrupulous epimacular dissection (which might itself simply represent another means of inducing glial repair[13]) without, it is hoped, aberrant scarring and late reopening of the hole.[14] Since breakdown of the blood–retinal barrier has been implicated in PVR, however, caution is certainly required in extending the use of adjunctive additives from idiopathic holes to traumatic and myopic macular holes associated with extensive retinal detachment and peripheral breaks.

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*References*


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