

## MINI REVIEW

## Adhesives in retinal detachment surgery

Methods of break sealing have not changed significantly since Gonin devised the operation of ignipuncture using scleral cautery, as all current techniques rely on the production of a thermally induced inflammatory lesion which heals to form a chorioretinal scar. The treated break has to be closed against the retinal pigment epithelium while healing is taking place, which in simple detachments is usually achieved by scleral indentation. In complicated cases where vitrectomy has been performed and in selected simple detachments an internal tamponading agent is required to close the retinal break while the chorioretinal scar develops. Internal tamponade with gas and air can be complicated by cataract formation, raised intraocular pressure, or secondary glaucoma. Silicone oil causes cataract, glaucoma, and keratopathy in a considerable proportion of cases, and most develop refractive errors and emulsification. Early removal of silicone oil helps to reduce the incidence of some of these complications and makes them easier to manage, but retinal redetachment occurs in 12-30% of eyes. In addition, cryotherapy has been implicated in the pathogenesis of proliferative vitreoretinopathy, as it induces breakdown of the blood-retinal barrier, causes a localised inflammatory response, and disperses viable retinal pigment epithelial cells into the vitreous cavity.

Several adhesives have been tried as a novel, non-inflammatory means of creating chorioretinal adhesion for selected complicated detachments. Their main advantage is that break sealing would occur immediately, making internal tamponade largely unnecessary. The adhesives that have been evaluated include cyanoacrylates, fibrin, mussell glue, and other synthetic and biological compounds. Some of these adhesives have already found a place in the management of certain anterior segment conditions.

The cyanoacrylates are a group of adhesives formed by the condensation of cyanoacetates and formaldehyde, which rapidly polymerise on contact with anions. During polymerisation heat is produced, and during hydrolytic degradation formaldehyde is released. Brooks McCuen is currently championing the use of cyanoacrylates in retinopathy, and he uses N-butylcyanoacrylate (Histoacryl), which has been shown to be less toxic than methylcyanoacrylate. Minute drops of the adhesive are applied to the edge of flattened retinal breaks after vitrectomy, fluid/air exchange, and drying of the retinal surface. The adhesive is mixed with iophendylate, which slows polymerisation, and is delivered with a specially designed applicator which prevents the adhesive from polymerising within the delivery system. In preliminary animal work Histoacryl produced strong, immediate, and permanent adhesion between the retina and retinal pigment epithelium,<sup>1</sup> but localised retinal necrosis developed round the drop of adhesive. Affected retina either developed full thickness retinal holes or became atrophic.<sup>2</sup> These findings were more pronounced in silicone oil filled eyes,<sup>3</sup> which could be due either to an insulating effect or to localisation of toxic products.

So far 34 patients have been treated with Histoacryl, with good surgical results.<sup>4,5</sup> It appears that the human retina is less susceptible to cyanoacrylate toxicity than the rabbit retina, though two eyes developed periadhesive retinal holes. McCuen currently advocates the use of cyanoacrylate retinopathy for the management of complicated retinal detachments

that have been refractory to other forms of treatment and to avoid the complications of internal tamponade with silicone oil.

Fibrin, made from either autologous plasma, human or autologous fibrinogen, and bovine thrombin, has also been used experimentally and clinically. In experimental animal models fibrin has been shown to be non-toxic, but it produces only temporary adhesion because the fibrin clot readily lyses despite the addition of aprotinin, a proteolytic enzyme that delays fibrinolysis. Fibrin retinopathy has also been associated with the formation of epiretinal membranes when used in the rabbit. Coleman has treated seven patients with macular holes and giant retinal tears, and he applied the adhesive to the edge of the break after vitrectomy with peroperative retinal flattening and fluid-air exchange. The retina became reattached in three of the four eyes with macular holes, but none of the giant retinal tears remained flat postoperatively. No complications that could be attributable to the fibrin were noted after surgery.<sup>6</sup>

Other adhesives that have been evaluated for retinopathy in an experimental setting are mussell protein, transforming growth factor beta (TGF- $\beta$ ), acetate polymers, and polysiloxanes. The latter are adhesives used in dentistry. The acetate polymer looks promising, as it gives good adhesion between the retinal pigment epithelium and retina and is not toxic.<sup>7</sup> The polysiloxane adhesive has the advantage that it can be delivered in an aqueous environment, but it causes a localised granulomatous tissue reaction.<sup>8</sup> Mussell glue has also undergone preliminary evaluation in an animal model. The foot of the mussell bivalve attaches itself to underlying substrates via a byssus thread, using a powerful two-component proteinaceous adhesion. Natural, extracted adhesive and protein manufactured by bioengineering techniques are both available, though they have not yet passed FDA regulations. Preliminary studies show that this adhesive may prove of value in retinopathy, as it is not toxic nor does it stimulate an inflammatory reaction when injected into the vitreous cavity.<sup>9</sup> TGF- $\beta$  has been delivered to retinal breaks in a hyaluronic acid vehicle, where it stimulated a localised wound healing response with sealing of retinal breaks.<sup>10</sup> Although breaks were sealed with TGF- $\beta$ , as with cryotherapy, a time factor is involved, and internal tamponade would still be necessary.

Despite considerable research the ideal adhesive remains elusive as those evaluated to date are either toxic, difficult to deliver, provide only transient adhesion, depend on a cellular wound healing response, or stimulate an inflammatory reaction with epiretinal membrane formation. The ideal adhesive would be readily available, easy to prepare, store, and sterilise and also be easy to apply to the retinal-RPE surface. Some of the problems of delivery would be avoided if a one-component adhesive were available that had a polymerisation time that could be manipulated. The adhesive would have to provide permanent adhesion or stimulate a purely localised wound healing response, be non-toxic and non-inflammatory. If a suitable adhesive could be found, the management of selected complicated detachments would be simplified and the complications related to cryotherapy and internal tamponade avoided.

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