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Internal Limiting Membrane Peeling in Vitreo-retinal Surgery

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Abstract. Peeling the internal limiting membrane of the retina has become a very common procedure performed by vitreo-retinal surgeons. The combination of new microsurgical instrumentation with the availability of different dyes to stain this thin and transparent membrane has facilitated the performance of internal limiting membrane peeling, reducing the time and trauma associated with this maneuver. Internal limiting membrane peeling has been used to treat a variety of retinal pathologies, including full-thickness macular hole, epiretinal membrane, macular edema, vitreomacular traction syndrome, and Terson syndrome, among others. Although it appears that peeling the internal limiting membrane in these retinal conditions may be associated with better anatomical and visual outcomes following surgery, further evidence through randomized controlled clinical trials is still needed to guide the vitreo-retinal surgeon on the appropriate use of this surgical maneuver. (**Surv Ophthalmol 53**:368–396, 2008. © 2008 Elsevier Inc. All rights reserved.)

Key words. epiretinal membrane • full-thickness macular hole • ILM • indocyanine green • infracyanine green • internal limiting membrane • macular edema • macular hole • trypan blue • vitreo-retinal surgery

Introduction

ANATOMY OF THE INTERNAL LIMITING MEMBRANE

The internal limiting membrane (ILM) represents the structural boundary between the retina and the vitreous. It is a periodic acid schiff (PAS)-positive basement membrane. It has a smooth inner (vitreal) surface and an irregular retinal surface, in close apposition with the plasma membrane of the Müller cells. The close association of the ILM and the Müller cells suggests that the ILM derives from these cells.[65] The ILM is thickest posteriorly, in the parafoveal and peripapillary regions, and measures an average of 2.5 μm in thickness.[66]

FUNCTION OF THE INTERNAL LIMITING MEMBRANE

In a study to investigate the role of the ILM in the survival of ganglion cells (GCs) in the embryonic chick and mouse embryo, it was observed that most

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GCs underwent apoptotic cell death when the ILM was removed at the embryonic day 5.[110] Reconstitution of the ILM rescued most of the GCs from cell death. GC death in vivo was always accompanied by the retraction of radial cell (neuroepithelial cells and Müller glia cells) processes, and GCs were rescued by keeping radial cell retraction to a minimum.[110] This suggested that the ILM was involved in GCs survival by anchoring the radial cells end feet to the vitreal surface of the retina, bringing GCs and end feet of radial cells in contact with each other. As the connection to the radial cell end feet was lost, GCs died. GCs survived when the ILM was removed slightly later, at the embryonic day 7. By embryonic day 7, the radial cells no longer need the ILM to extend their processes throughout the retina, providing further evidence to support the above hypothesis. In the aged human eye, the removal of the ILM has no obvious detrimental effects found to date, suggesting that the ILM may have its main function during early embryogenesis.[110]

Given the difficulties encountered to investigate the healing process that occurs following ILM peeling in humans, this phenomenon has been studied in non-human primates, and it was found that up to 12 months following peeling of the ILM no regeneration of this membrane was observed.[272] However, healing of the ILM-debrided area occurred in the form of stretching and flattening of neighbouring Müller cell processes in addition to reactive gliosis over the nerve fibres in the denuded area.[272]

Surgical Techniques

HISTORIC REVIEW

The ILM received virtually no clinical attention until vitrectomy for removal of epimacular proliferation became a routine surgical procedure in the 1980s, when ILM fragments were often identified during routine histological evaluation of surgical specimens.[193] In 1990, Morris and colleagues presented at the Annual Meeting of the American Academy of Ophthalmology a series of cases in which intentional ILM removal was performed in patients with Terson syndrome and sub-ILM macular hemorrhages. In these cases the surgeon removed both the blood and the detached ILM. After an average follow-up of 32 months, 83% of eyes had a visual acuity of 20/25 or better without clinically visible ILM reproliferation. Based on this experience, these authors suggested in 1994 that ILM removal was to be considered in all forms of tractional maculopathy.[266] There is now an increasing interest in peeling the ILM in many vitreoretinal diseases, and this is the subject of this review.

METHODS OF PEELING THE INTERNAL LIMITING MEMBRANE

Technique of Peeling

Prior to ILM removal a standard pars plana vitrectomy (PPV), including detachment and removal of the posterior hyaloid, is performed. Complete removal of the posterior hyaloid during PPV is important to eliminate any possible scaffolding for cellular proliferation and subsequent retinal traction.[298] Several surgical techniques, which have been summarized herein, have been described to induce a posterior vitreous detachment (PVD) intraoperatively.

Thus, Han and associates[111] proposed two maneuvers to detach the posterior hyaloid: 1) to use an extrusion suction needle applied close to the optic disk, with a suction control of up to 150 mmHg, to engage, elevate, and detach the posterior hyaloid or 2) to incise and elevate the posterior hyaloid face near the optic disk by using a membrane pick or microvitreoretinal blade (MVR).

Mein and colleages[251] designed a canulated extrusion needle which could detect any residual posterior hyaloid and remove it with suction. Vander and Kleiner[368] described the use of bipolar endodiathermy to retract the posterior hyaloid nasal to the disc. By using this method a hole was also created in the posterior hyaloid through which a spatula, a retractor, or even the diathermy instrument itself could be then introduced and use to lift the posterior hyaloid and to complete the PVD.

Peyman and colleagues[298] reported a new 10-0 nylon adjustable tip brush for brushing the posterior hyaloid circumferentially in the peripapillary area. Complete or partial exposure of the tip from its sleeve could modify the stiffness of the brush. By brushing the posterior hyaloid microholes could be created, which would allow fluid to dissect the posterior hyaloid face from the retinal surface. Peyman and associates[297] also described the use of triamcinolone acetonide to facilitate the visualization of the transparent posterior hyaloid and to assist on its removal during PPV.

Pharmacologic vitreolysis has also been used to achieve a complete PVD. Asami and co-workers[12] reported their experience with intravitreal injection of autologous plasmin in 10 cases of diabetic macular edema (DME). The authors achieved a spontaneous PVD in 20%, induced actively a PVD by using 100 mm Hg vacuum in 50% of cases, and by using 200 mm Hg vacuum in the remaining 30% of cases. In the control group (n = 10) where no plasmin was used only 10% showed a spontaneous PVD, whereas in the remaining cases