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Clinicopathological changes at the vitreoretinal junction: posterior vitreous detachment

MP Snead[1], DRJ Snead[2], S James[2] and AJ Richards[3]

Abstract

Separation of the vitreous and posterior hyaloid membrane (PHM) or posterior vitreous detachment (PVD) typically occurs between the ages of 45 and 65 years in the general population, but may occur earlier in myopic or otherwise predisposed individuals. Age-related synergetic changes occurring within the cortical and central gel must be distinguished from the PHM, which envelopes it.

This study reports on the correlation between 'true' PVD seen clinically by the physician using dynamic examination, high-power slit-lamp biomicroscopy, and oblique illumination with some of its histological, immunohistochemical, and ultrastructural features post-mortem. The presence of the Weiss ring does not necessarily indicate total clean separation of PHM, nor does its absence confirm that the PHM remains attached, since it may be destroyed during the process of separation.

Immediately prior to PVD with the vitreous gel attached, the PHM must, by definition, form part of the inner limiting membrane. The detached PHM frequently exhibits basement membrane (BM) and its indigenous laminocytes stain focally for GFAP and type IV collagen. The PHM is distinct from and much thicker than the BM of Müller cells alone and the factors that initiate or limit separation of the PHM require greater study, particularly the role of laminocyte proliferation and migration.
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Keywords: vitreous; retinal detachment; PVD; ILM

Introduction

The relationship between the vitreous body and retina has been the focus of much research for over a hundred years. Despite such prolonged investigation, there is still much that is not understood, particularly

(a) The changes preceding and initiating uncomplicated (or 'physiological') separation of the posterior hyaloid membrane (PHM) from the retina and,
(b) The pathological variations of this process that influence so many of the vitreoretinal disorders dealt with today and thereby their management.

The attached vitreous and inner limiting membrane

The junction between the attached vitreous and retina has been extensively studied for over a century. Retzius[1] described a membranous structure coining the term membrana limitans retinae interna and suggested the terminations of Müller cells as a contributory component. This concept was later clarified by Wolff and Pedler,[2,3] who observed that although the Müller cells inserted into the inner limiting membrane (ILM) of the retina, it was in itself a separate and distinct extracellular structure. This latter notion was confirmed by Heergard and Matsumoto *et al*,[4–6] who demonstrated that the ILM was separate from the plasma membrane of the Müller cells.

Although more recent research has benefited from the vastly improved image resolution afforded by electron microscopy (EM), it must be remembered that the structure with all its topographical variations visualised as the 'ILM' on light microscopy, is a composite of the 0.1 μ

[1]Vitreoretinal Service, University of Cambridge Addenbrooke's NHS Trust, Cambridge, UK

[2]Department of Pathology, University Hospital of Coventry and Warkwickshire NHS Trust, Coventry, UK

[3]Department of Pathology, University of Cambridge, Cambridge, UK

Correspondence: MP Snead, Vitreoretinal Service, Box 41, Addenbrooke's NHS Trust, Hills Road, Cambridge, Cambridgeshire CB2 2QQ, UK
Tel: +012 232 167 01; Fax: +012 232 179 68.
E-mail mps34@cam.ac.uk

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basement membrane (BM) demonstrated on EM[7] and the 3–10 μ smooth glass-like structure visualised by light microscopy (either in the laboratory or more commonly under the operating surgical microscope in theatre) (Figure 1).

Symptoms of posterior vitreous detachment

Separation of the vitreous and PHM or posterior vitreous detachment (PVD) typically occurs between the ages of

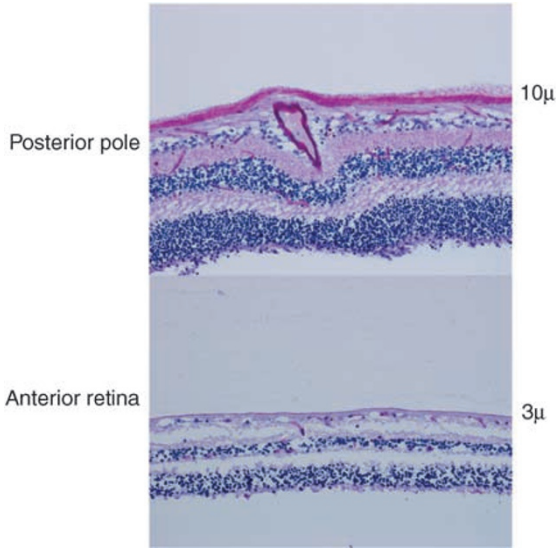

Figure 1 The inner limiting membrane (ILM) visualised on light microscopy. Note the topographical variations in ILM thickness between anterior and posterior retina (H&E $\times$200).

Table 1 Symptoms of posterior vitreous detachment

45–65 years
Sudden onset (new) floaters
Arc of golden or white light
Temporal field
Best seen in dark
Usually single
Induced by saccades
May precede separation of PHM by 24–48 h
Floaters subside (but persist)
Flashing light resolves 4–12 weeks

Abbreviation: PHM, posterior hyaloid membrane.

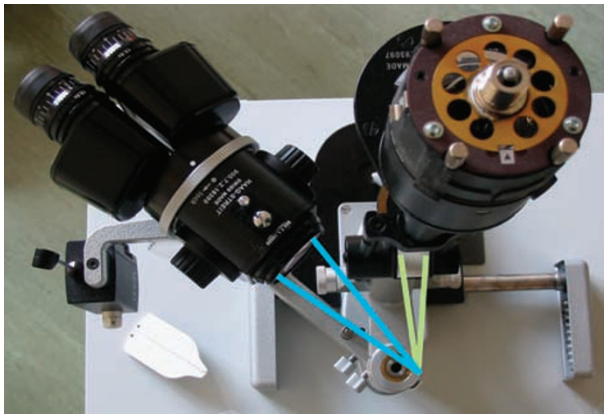

Figure 3 Examination of the vitreous architecture and PHM demands 'off' axis illumination with or without a condensing lens. The integrity and relationships of the PHM will be lost with coaxial illumination. Photograph courtesy of Dr PAR Meyer.

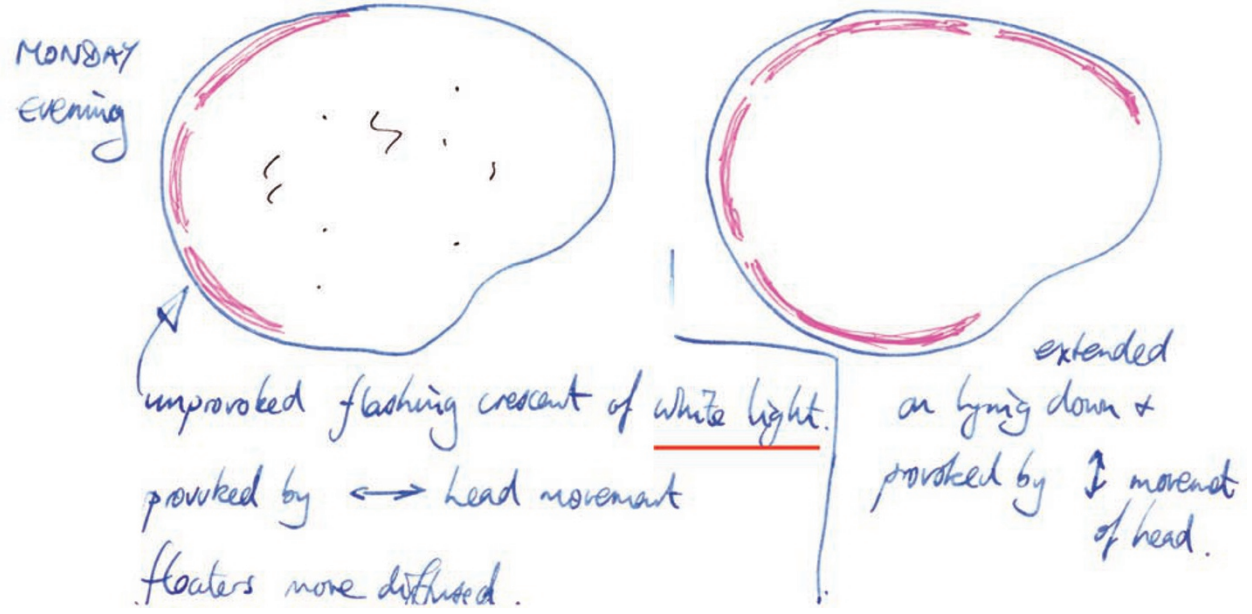

Figure 2 Clinical features of the light associated with posterior vitreous detachment as described by a patient. Note the white light, temporal distribution, and exacerbation or induction by movement.

45–65 years in the general population, but may occur earlier in myopic individuals. Even so, PVD is rare before the age of 30 years unless the patient has some other underlying predisposing factor such as previous penetrating trauma or uveitis. Vitreous separation may go unnoticed by the patient, but in those individuals who are symptomatic, separation of the vitreous body and PHM is associated with a sudden onset (new) floaters and an arc of golden or white light in the temporal field of vision. The light associated with PVD has certain typical and distinctive pathognomonic features. It is usually best seen in the dark or with dim background illumination and may be induced by eye movement (Figure 2). On occasion, the temporal white light may actually precede separation of the PHM by 24–48 h. In most patients, the flashing light resolves after 4–12 weeks and the visual floaters subside as the shadows cast by the PHM opacities move off axis and defocus from the retina (Table 1).

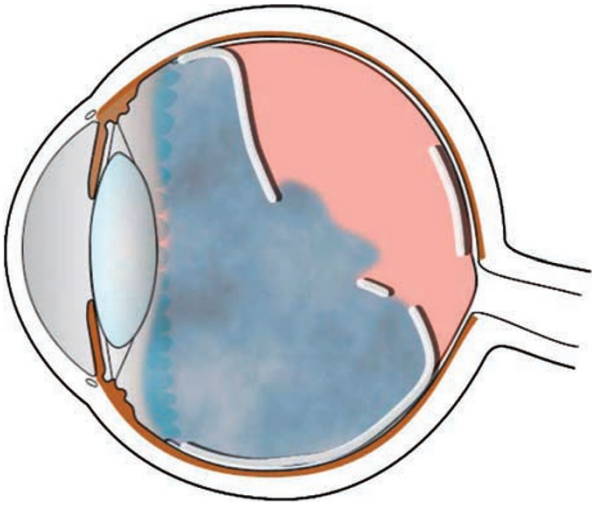

Figure 4 Schematic representation of a PVD with Weiss ring but with an adjacent 'rhexis' and residue of PHM on the retinal surface. This is a relatively common scenario in clinical practice, but without significant secondary contracture, patients remain oblivious of their asymptomatic cellophane maculopathy.

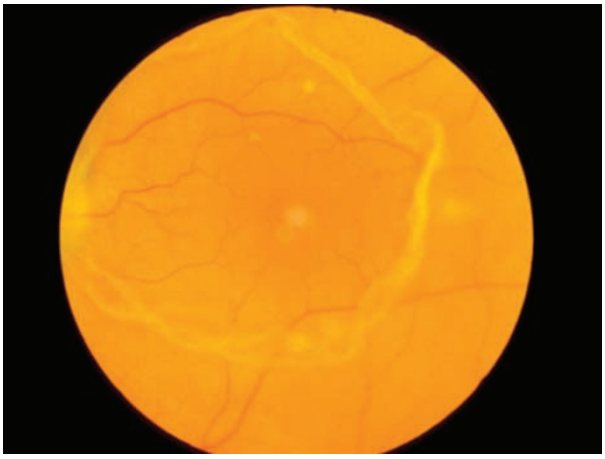

Figure 5 Fundus photograph showing incomplete separation of the PHM, with residue remaining over the macula. Note scrolled edges.

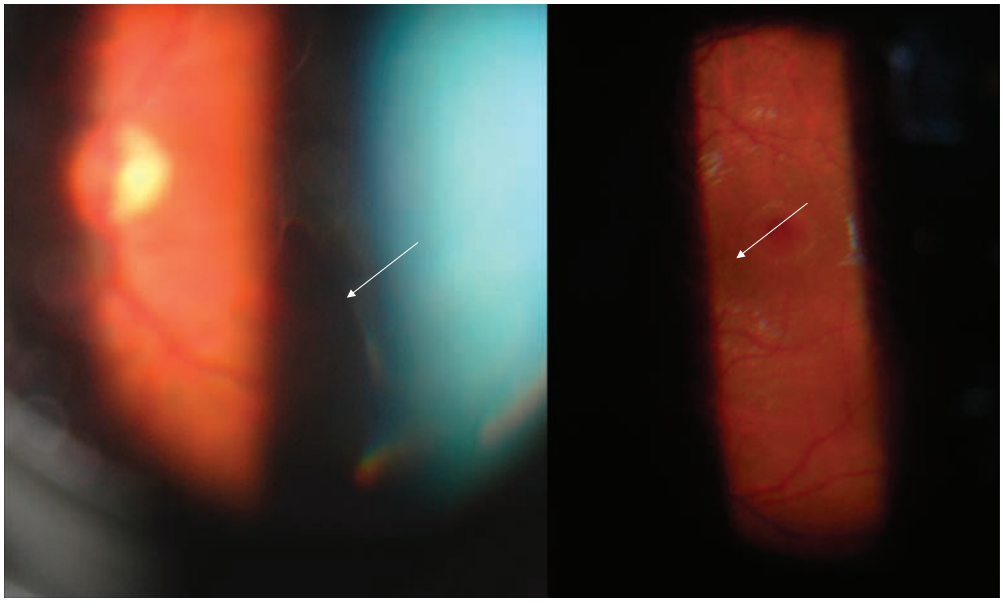

Figure 6 Slit-lamp photograph: PVD and stage 4 macular hole. (Left) Note the rhexis-like defect (arrow) in detached PHM, which is relatively shortened and under tension. (Right) Residual PHM remains at macula (arrow).

Signs of PVD

In a similar vein to the transparent cornea and anterior chamber, the glass-like clarity of the vitreous means that examination of its architecture and relationships demand off axis illumination with dark field, specular biomicroscopy (Figure 3). Dynamic examination to shake out the folds in the collapsed PHM allow inspection of its continuity and relationship to the retina. Coaxial illumination might afford the observer an image of the Weiss ring against the red reflex, but little or nothing of the vitreous architecture and integrity of the PHM. The presence or otherwise of a Weiss ring alone is insufficient for diagnosis of PVD, as it may be destroyed or distorted during the process of separation or more commonly, the Weiss ring separates leaving an adjacent 'rhexis' of PHM on the retinal (and particular macular) surface (Figures 4–6).

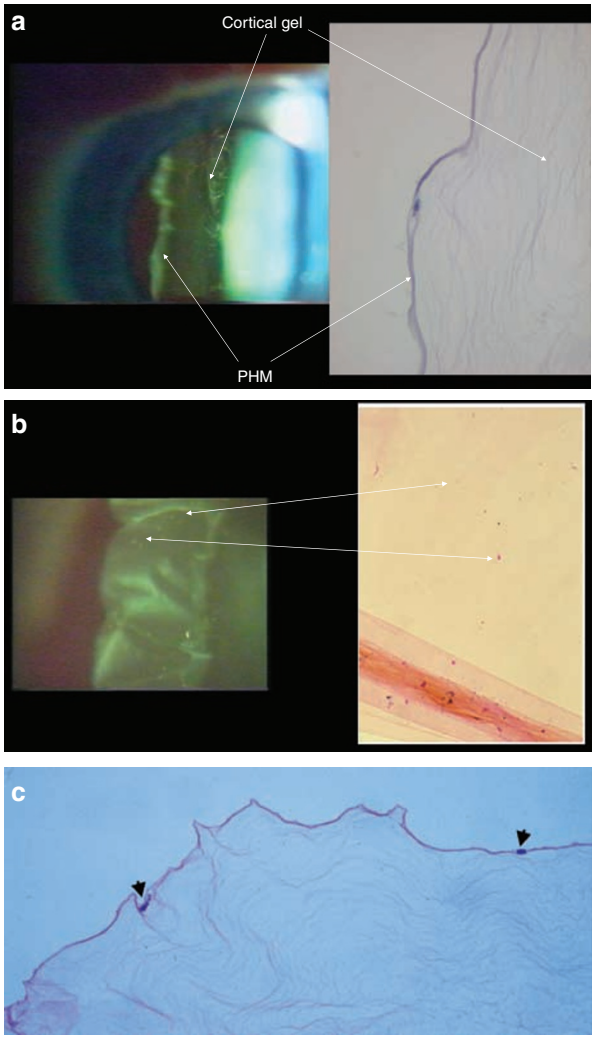

Figure 7 (a) Slit-lamp and light microscopy images of detached PHM. Note the characteristic glossy, crinkled appearance of the PHM studded with laminocytes. Laminocytes are more densely populated at the posterior pole (b) and they diminish in density more anteriorly (c). Reproduced with permission from Snead *et al Eye* 2002; **16**: 447–453.

Clinicopathological correlates

When the vitreous has separated from the retina, the detached PHM can be examined under high power using the slit-lamp microscope and oblique illumination. These techniques have been used to study the clinical correlation between the 'true' PVD observed clinically by the physician and its histological correlate visualised post-mortem.[8,9] It is important not to mistake the age-related synergetic changes occurring within the cortical and central gel with the distinctive structure of the PHM which envelopes it. The cortical vitreous forms a loose, fluffy indistinct smudge of variable thickness, in contrast to the shiny crinkled surface of the enveloping PHM. If the gel is very collapsed, the PHM can be visualised on slit-lamp directly in the anterior vitreous cavity, but if the separation is at an early stage, the PHM is shortened or the gel structure more robust, then a 90D or similar condensing lens will be required to examine the vitreous cavity more posteriorly. In either event, it is important to maintain an angle of separation between observer and illumination source (Figure 3). Closer inspection of the PHM at high magnification reveals that it is studded with its indigenous population of laminocytes, which can also be studied on light microscopy (Figure 7). Even in patients with uncomplicated PVD and without associated vitreoretinal pathology, there is a wide variation in thickness and transparency of the PHM. Occasional areas of focal thickening and reduplication

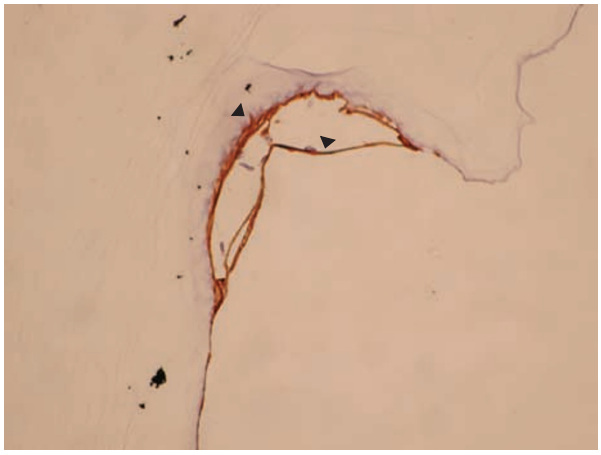

Figure 8 Detached posterior hyaloid membrane stained for type IV collagen. Note convolution and contracture of PHM together with duplication, thickening, and schisis (arrowheads) ($\times$ 400). Reproduced with permission from Snead *et al Eye* 2002; **16**: 447–453.

Figure 9 Detached posterior hyaloid membrane (PHM) stained for glial fibrillary acid protein. Note the focal convolution and contracture of PHM ($\times 200$).

(Figure 8) as well as obvious areas of contracture and shortening, probably accounting for the crinkled slit-lamp appearance and hypothetically for induction of PVD itself, can be seen (Figure 9).

Electron microscopy

The high (98%) water content of the vitreous body makes it highly susceptible to artifactual change and shrinkage during processing and dehydration for studies using EM. Nevertheless, using either transmission or scanning techniques, the distinct differences between the PHM and cortical vitreous are readily discernable (Figure 10a and b).

Conclusion

This article reports the clinical symptoms and signs of PVD and separation of the PHM, together with illustrations of some of its histological, immunohistochemical, and ultrastructural features. It follows that immediately prior to PVD the PHM must, by definition, form part of what we observe pre-PVD as the ILM. The term posterior hyaloid face, which has recently been popularised, should be abandoned in favour of the definitive structural membrane recognised and reported by Hruby, Straatsma, and Zimmerman,[10,11] and also by others. The PHM frequently exhibits BM and its laminocytes stain focally for GFAP and type IV collagen, but it is distinct from and much thicker than the BM of Müller cells alone. Ocular BMs appear to demonstrate unique structural characteristics distinguishing them from BMs elsewhere—they are thicker, have a different antigenic profile, and appear to demonstrate an age-related increase that might imply active production.

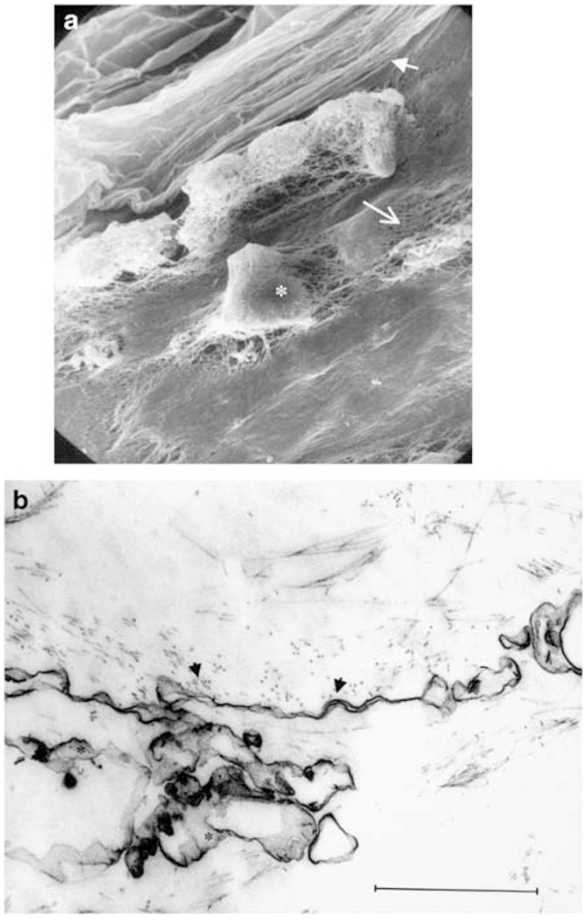

Figure 10 (a) SEM detached PHM. PHM (solid arrow). Cortical gel (open arrow), laminocyte (asterisk). Reproduced with permission from Snead *et al* Eye 2002; **16**: 447–453. (b) TEM detached PHM. Showing extensive convoluted PHM. In some areas (asterisk) the membrane is shown in tangential section. Cortical collagen fibres (arrows) can be seen to be more heavily associated with one side of the membrane but are present throughout the gel. Scale bar = 1 μm. Reproduced with permission from Snead *et al Eye* 2002; **16**: 447–453.

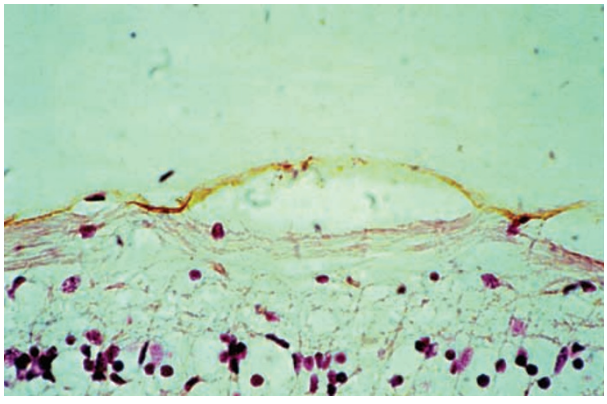

Figure 11 Attached posterior hyaloid membrane: 80-year-old patient, high myopia, syneresis but no clinical separation of the PHM. Stain for type IV collagen ($\times 400$). Reproduced with permission from Snead *et al Eye* 2002; **16**: 447–453.

If this hypothesis is correct, then it raises the further question as to whether they reduplicate as suggested in a variety of pathological vitreomaculopathies.[12]

The relationship if any, between syneresis and separation of PHM remains poorly understood. Many patients with advanced synergetic change and large multiple lacunae within the body of the vitreous gel do not exhibit 'PVD' as defined by separation of the PHM clinically or histologically (Figure 11). In contrast, the PHM, which characterises PVD, can still separate many years after vitrectomy and the removal of all cortical and central gel. The presence of the Weiss ring does not necessarily indicate total clean separation of PHM, nor does its absence sustain the notion that the PHM remains attached, as it may be destroyed during the process of separation. In some situations associated with, for example, Horseshoe tear formation or vitreomacular traction syndrome,[12] PVD may be a violent intraocular event associated with cellular proliferation and surface tension. However, what initiates or limits separation of the PHM, or enhances adherence requires much greater study, and particularly the role of laminocyte proliferation and migration.

Acknowledgements

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