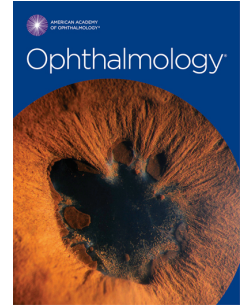


Journal Pre-proof



Idiopathic Epiretinal Membrane and Vitreomacular Traction Preferred Practice Pattern®

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Idiopathic Epiretinal Membrane and Vitreomacular Traction Preferred Practice Pattern®

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Preferred Practice Pattern® guidelines are developed by the Academy's H. Dunbar Hoskins Jr., MD Center for Quality Eye Care without any external financial support. Authors and reviewers of the guidelines are volunteers and do not receive any financial compensation for their contributions to the documents. The guidelines are externally reviewed by experts and stakeholders before publication.

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RETINA/VITREOUS PREFERRED PRACTICE PATTERN® DEVELOPMENT PROCESS AND PARTICIPANTS

The Retina/Vitreous Preferred Practice Pattern® Panel members wrote the Idiopathic Epiretinal Membrane and Vitreomacular Traction Preferred Practice Pattern® (PPP) guidelines. The PPP Panel members discussed and reviewed successive drafts of the document, meeting in person twice and conducting other review by e-mail discussion, to develop a consensus over the final version of the document.

Retina/Vitreous Preferred Practice Pattern Panel 2018–2019

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We thank our partners, the Cochrane Eyes and Vision US Satellite (CEV@US), for identifying reliable systematic reviews that we cite and discuss in support of the PPP recommendations.

The Preferred Practice Patterns Committee members reviewed and discussed the document during a meeting in June 2019. The document was edited in response to the discussion and comments.

Preferred Practice Patterns Committee 2019

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The Idiopathic Epiretinal Membrane and Vitreomacular Traction PPP was then sent for review to additional internal and external groups and individuals in July 2019. All those returning comments were required to provide disclosure of relevant relationships with industry to have their comments considered (indicated with an asterisk below). Members of the Retina/Vitreous Preferred Practice Pattern Panel reviewed and discussed these comments and determined revisions to the document.

FINANCIAL DISCLOSURES

In compliance with the Council of Medical Specialty Societies' Code for Interactions with Companies (available at www.cmss.org/codeforinteractions.aspx), relevant relationships with industry are listed. The Academy has Relationship with Industry Procedures to comply with the Code (available at <http://one.aao.org/CE/PracticeGuidelines/PPP.aspx>). A majority (100%) of the members of the Retina/Vitreous Preferred Practice Pattern Panel 2018–2019 had no financial relationship to disclose.

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The disclosures of relevant relationships to industry of other reviewers of the document from January to October 2019 are available online at www.aao.org/ppp.

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OBJECTIVES OF PREFERRED PRACTICE PATTERN® GUIDELINES

As a service to its members and the public, the American Academy of Ophthalmology has developed a series of Preferred Practice Pattern® guidelines that **identify characteristics and components of quality eye care**. Appendix 1 describes the core criteria of quality eye care.

The Preferred Practice Pattern® guidelines are based on the best available scientific data as interpreted by panels of knowledgeable health professionals. In some instances, such as when results of carefully conducted clinical trials are available, the data are particularly persuasive and provide clear guidance. In other instances, the panels have to rely on their collective judgment and evaluation of available evidence.

These documents provide guidance for the pattern of practice, not for the care of a particular individual. While they should generally meet the needs of most patients, they cannot possibly best meet the needs of all patients. Adherence to these PPPs will not ensure a successful outcome in every situation. These practice patterns should not be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the best results. It may be necessary to approach different patients' needs in different ways. The physician must make the ultimate judgment about the propriety of the care of a particular patient in light of all of the circumstances presented by that patient. The American Academy of Ophthalmology is available to assist members in resolving ethical dilemmas that arise in the course of ophthalmic practice.

Preferred Practice Pattern® guidelines are not medical standards to be adhered to in all individual situations. The Academy specifically disclaims any and all liability for injury or other damages of any kind, from negligence or otherwise, for any and all claims that may arise out of the use of any recommendations or other information contained herein.

References to certain drugs, instruments, and other products are made for illustrative purposes only and are not intended to constitute an endorsement of such. Such material may include information on applications that are not considered community standard, that reflect indications not included in approved US Food and Drug Administration (FDA) labeling, or that are approved for use only in restricted research settings. The FDA has stated that it is the responsibility of the physician to determine the FDA status of each drug or device he or she wishes to use, and to use them with appropriate patient consent in compliance with applicable law.

Innovation in medicine is essential to ensure the future health of the American public, and the Academy encourages the development of new diagnostic and therapeutic methods that will improve eye care. It is essential to recognize that true medical excellence is achieved only when the patients' needs are the foremost consideration.

All Preferred Practice Pattern® guidelines are reviewed by their parent panel annually or earlier if developments warrant and updated accordingly. To ensure that all PPPs are current, each is valid for 5 years from the approved by date unless superseded by a revision. Preferred Practice Pattern guidelines are funded by the Academy without commercial support. Authors and reviewers of PPPs are volunteers and do not receive any financial compensation for their contributions to the documents. The PPPs are externally reviewed by experts and stakeholders, including consumer representatives, before publication. The PPPs are developed in compliance with the Council of Medical Specialty Societies' Code for Interactions with Companies. The Academy has Relationship with Industry Procedures (available at www.aao.org/about-preferred-practice-patterns) to comply with the Code.

Appendix 2 contains the International Statistical Classification of Diseases and Related Health Problems (ICD) codes for the disease entities that this PPP covers. The intended users of the Diabetic Retinopathy PPP are ophthalmologists.

METHODS AND KEY TO RATINGS

Preferred Practice Pattern® guidelines should be clinically relevant and specific enough to provide useful information to practitioners. Where evidence exists to support a recommendation for care, the recommendation should be given an explicit rating that shows the strength of evidence. To accomplish these aims, methods from the Scottish Intercollegiate Guideline Network¹ (SIGN) and the Grading of Recommendations Assessment, Development and Evaluation² (GRADE) group are used. GRADE is a systematic approach to grading the strength of the total body of evidence that is available to support recommendations on a specific clinical management issue. Organizations that have adopted GRADE include SIGN, the World Health Organization, the Agency for Healthcare Research and Policy, and the American College of Physicians.³

- ◆ All studies used to form a recommendation for care are graded for strength of evidence individually, and that grade is listed with the study citation.
- ◆ To rate individual studies, a scale based on SIGN¹ is used. The definitions and levels of evidence to rate individual studies are as follows:

I++	High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias
I+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
I-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
II++	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
II+	Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
II-	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
III	Nonanalytic studies (e.g., case reports, case series)

- ◆ Recommendations for care are formed based on the body of the evidence. The body of evidence quality ratings are defined by GRADE² as follows:

Good quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Insufficient quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate Any estimate of effect is very uncertain

- ◆ Key recommendations for care are defined by GRADE² as follows:

Strong recommendation	Used when the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not
Discretionary recommendation	Used when the trade-offs are less certain—either because of low-quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced

- ◆ The Highlighted Findings and Recommendations for Care section lists points determined by the PPP Panel to be of particular importance to vision and quality of life outcomes.
- ◆ All recommendations for care in this PPP were rated using the system described above. Ratings are embedded throughout the PPP main text in italics. Literature searches to update the PPP were undertaken in April 2018 and June 2019 in PubMed and the Cochrane Library. Complete details of the literature searches are available online at www.aao.org/ppp.

HIGHLIGHTED FINDINGS AND RECOMMENDATIONS FOR CARE

1 _____
2 Risk factors for epithelial membrane (ERM) include increasing age, other retinal pathologies (e.g., posterior
3 vitreous detachment [PVD]), uveitis, retinal breaks, retinal vein occlusions, diabetic retinopathy^{4,5}, and ocular
4 inflammatory diseases).

5 _____
6 The majority of ERMs will remain relatively stable and do not require therapy. In patients who have areas of
7 vitreomacular traction (VMT) of 1500 μm or less, the incidence of spontaneous release of traction from the
8 macula occurs in approximately 30% to 40% of eyes over a follow-up of 1 to 2 years.

9 _____
10 Spectral-domain optical coherence tomography (SD-OCT) is a highly sensitive and routine methodology
11 used to diagnose and characterize ERM, VMT, and associated retinal changes.

12 _____
13 Vitrectomy surgery is often indicated in affected patients who have a decrease in visual acuity,
14 metamorphopsia, double vision, or difficulty using their eyes together. Vitrectomy for ERM or VMT usually
15 leads to improvement of the metamorphopsia and visual acuity. On average, approximately 80% of patients
16 with ERM or VMT will improve by at least 2 lines of visual acuity following vitrectomy surgery.

INTRODUCTION

1 DISEASE DEFINITION

2 Epiretinal membranes (ERMs) are sheet-like structures that develop on the inner surface of the
3 neurosensory retina. Vitreomacular adhesion (VMA) is an attachment of the posterior cortical vitreous
4 to the macula without resultant traction. Vitreomacular traction (VMT) occurs when the posterior
5 cortical vitreous partially separates from the retina yet some areas of adhesion remain that exert
6 tractional forces on the neurosensory retina. Thickening, distortion, intraretinal cystoid changes,
7 macular hole, and even subretinal fluid in the macula can result from the VMT.⁶ The macular changes
8 that result from either ERM or VMT lead to similar symptoms: reduced visual acuity,
9 metamorphopsia, difficulty using both eyes together, and even diplopia.

10 PATIENT POPULATION

11 The patient population is predominately adults.

12 CLINICAL OBJECTIVES

- 13 ♦ Describe the pathogenesis of ERM and VMT
- 14 ♦ Recognize symptoms and signs of ERM and VMT
- 15 ♦ Describe the natural history without treatment
- 16 ♦ Propose a treatment strategy
- 17 ♦ Educate the patient about treatment options
- 18 ♦ Optimize visual function and/or relief of symptoms

19

BACKGROUND

20 Epiretinal membranes consist of fibrocellular proliferation on the surface of the neurosensory retina, with or
21 without wrinkling of the retina. They comprise reactive cellular elements, vitreous structures, and fibrotic
22 components.¹ Idiopathic ERMs do not have a clearly identifiable cause.⁴

23 Secondary ERMs may occur after retinal breaks or detachments, or following intraocular surgery, trauma, or
24 retinal laser or cryotherapy treatment.¹ An ERM is likely due to reactive wound healing and is associated with
25 a proliferation of either reactive retinal pigment epithelial (RPE) cells and/or retinal glial cells. Epiretinal
26 membranes are also common in eyes with retinal vascular disease^{5,7} (e.g., diabetic retinopathy and venous
27 occlusions) and/or inflammation. A systematic review from 2016 which included over 49,000 subjects found
28 that ERMs are relatively common among aged population the meta-analysis showed that only greater age and
29 female gender significantly conferred a higher risk of ERM.⁸

30 The vitreous is most firmly attached at the vitreous base, the optic nerve head, and the macula.^{9,10} A posterior
31 vitreous detachment (PVD) evolves and progresses over years.⁶ Initially, the posterior vitreous will partially

1 detach yet will remain attached within the macular region. Eventually, a complete detachment occurs when
2 the vitreous detaches from the macula and finally from the optic nerve head. When the vitreous detaches from
3 the nerve head, the patient may see the acute onset of floaters or even flashes or photopsia. Combined, these
4 represent the classic symptoms for the onset of an acute PVD. On fundus examination, a Weiss ring
5 represents the glial remnant from the attachment at the optic nerve on the posterior cortical vitreous and is
6 typically seen on the posterior vitreous face anterior to the optic nerve.

7 During the evolution of a PVD, vitreous may remain adherent to the macula. Vitreomacular adhesion, the
8 attachment of the posterior cortical vitreous to the neurosensory retina, may represent the normal evolution of
9 a PVD. Vitreomacular traction occurs when the perimacular vitreous continues to separate from the posterior
10 retina yet remains adherent to a region or area near the center of the macula.^{6,10} The pathologic mechanism
11 responsible for such an abnormal adhesion within the macula that leads to VMT is unclear. The combination
12 of attachment at the macula with surrounding vitreous separation creates traction and may lead to thickening,
13 distortion, intraretinal cystoid changes and even subretinal fluid or tractional detachment at the macula.⁶
14 Epiretinal membranes can also lead to macular traction and similar visual symptoms. Both ERM and VMT
15 may lead to loss in visual acuity, metamorphopsia, difficulty in using both eyes together, even diplopia.

16 The most common type of ERM appears as a thin, translucent, cellophane-like membrane on the surface of
17 the retina.^{9,11} An ERM may not lead to tractional changes, and the underlying neurosensory retina may often
18 appear normal. Epiretinal membranes can contract, however, leading to folds in the retina, distortion of the
19 inner and even the outer macula, traction on retinal vessels, and even displacement of the macula, or ectopia.
20 The normal foveal depression is often absent or distorted, and the macula may develop cystoid spaces,
21 lamellar macular hole, or even a full-thickness hole.

22 Epiretinal membranes that have a thicker, white, fibrotic appearance that obscures the underlying retina, are
23 more likely to become symptomatic and displace the macula than the thinner, more translucent ERMs.^{4,12}

24 The macular changes in VMT are often similar to the changes of the retina that result from an ERM. In VMT,
25 raised edges of adherent vitreous may be seen in a peripapillary distribution around the optic nerve head and
26 is referred to as vitreopapillary traction. This condition can be confused with optic nerve disorders such as
27 papilledema.¹³ There is some suspicion that vitreopapillary traction might be associated with decreased vision
28 and even ischemic optic neuropathy in some cases.¹⁴ Further studies are required to verify this.

29 INCIDENCE AND PREVALENCE

30 Epiretinal membrane and VMT are relatively common retinal conditions. Higher prevalence of both
31 conditions is associated with older age.⁴ Vitreomacular traction is less common than ERM and affects
32 an estimated 0.4% to 2.0% in a population of U.S. adults over the age of 63.¹⁵ The prevalence of
33 ERMs is based on several population-based studies conducted in various ethnic groups worldwide
34 over the past 20 years. It is estimated to occur in approximately 30 million adults in the United States
35 43 to 86 years old.¹⁶ Epiretinal membranes may be bilateral in up to 20% to 35% of cases.^{7,17-19}
36 Prevalence rates⁴ range from a low of 2.2% and 3.4% in the Beijing Eye Study²⁰ and in the Handan

1 Eye Study in rural China, respectively,⁷ to moderate (7% and 8.9%) in two Australian populations,^{17,21}
2 to a high of 18.8% and even 28.9% among Latinos in Los Angeles²² and in a multi-ethnic study
3 conducted in six communities in the United States (Multi-Ethnic Study of Atherosclerosis [MESA]).¹⁹
4 The presence or absence of ERM in most studies was based on the use of nonmydriatic retinal
5 photography.¹⁶⁻²⁴ More recently, at the 20-year follow-up examinations of the Beaver Dam Eye Study
6 population (mean age of 74.1 years), spectral-domain optical coherence tomography (SD-OCT) was
7 used and documented a higher prevalence of 34.1%.¹⁵ In eyes with no macular pathology on clinical
8 exam prior to cataract surgery, prevalence of ERM with routine SD-OCT ranged from 2.2% to
9 11.0%.^{25,26}

10 In most populations studied, cellophane maculopathy (the early asymptomatic form of ERM) occurred
11 more frequently than thicker or more opaque preretinal macular fibrosis (a term used for symptomatic
12 ERM).^{7,18,19,22} The prevalence of cellophane maculopathy varied from 1.8% and 2.2% in urban and
13 rural China^{7,20} to as high as 16.3% among Los Angeles Latinos²² and 25.1% in MESA.¹⁹ Diabetes and
14 hypercholesterolemia are associated with higher rates of cellophane maculopathy.¹⁹ Preretinal macular
15 fibrosis prevalence was more consistent across studies, with rates ranging from 0.7% in rural China⁷
16 to 3.5% among Asian Indians,²³ 3.8% in MESA,¹⁹ and 3.9% in Melbourne, Australia.²¹ There are
17 several reasons that might explain the variable prevalence results from different studies, including the
18 sensitivity of the specific testing or imaging modality used, differences in classification of ERM, and
19 differences in the populations (e.g., age, ethnicity, lifestyle).

20 RISK FACTORS

21 Increasing age was consistently identified as a risk factor for ERM in all studies.⁴ Prevalence varies
22 by ethnicity, but patterns are not consistent across studies. For example, in the United States, MESA
23 data suggest that the prevalence of any ERM was highest in persons of Chinese ancestry (39.0%),
24 intermediate in Hispanics (29.3%) and whites (27.5%), and lowest in blacks (26.2%),¹⁹ whereas the
25 data from China suggested that the ERM prevalence rates were much lower (2.2% and 3.4%).^{7,20}
26 Epiretinal membrane occurs more frequently in persons with retinal pathology (e.g., uveitis and other
27 ocular inflammatory diseases,²⁷ retinal breaks,²⁸ retinal vein occlusions,^{15,16,19} proliferative diabetic
28 retinopathy^{4,15}) and following cataract surgery.^{4,15} It may be associated with impaired visual acuity or
29 visual field loss,^{15,20} particularly for those eyes with more severe ERMs.²² A number of other more
30 speculative risk factors have been suggested but have not been confirmed. These include gender,⁴
31 myopia,²⁹ hyperopia,³⁰ smoking,^{7,21} higher education,⁴ diabetes,⁴ hypercholesterolemia,⁴ narrow
32 retinal arteriolar diameter,⁴ body mass index,²¹ and stroke.²¹

33 PATHOGENESIS OF EPIRETINAL MEMBRANE AND VITREOMACULAR TRACTION

34 Epiretinal Membrane

35 A longstanding hypothesis was that ERMs develop when a PVD results in microbreaks of the
36 internal limiting membrane (ILM) that, in turn, allow for the migration of retinal glial or

1 possibly RPE cells onto the anterior retinal surface, where they proliferate.^{11,31} The hypothesis
2 was supported when RPE cells, fibrous astrocytes, astrocytes, and fibrocytes were observed in
3 ERMs of eyes that had no apparent retinal breaks, laser or cryopexy, or eye surgery.³² An
4 alternative hypothesis gaining acceptance is that ILM breaks are not necessary for ERMs to
5 develop, and an ERM may originate from cells in the cortical vitreous remnants on the ILM that
6 are activated into myofibroblasts resulting in membrane formation and contraction.^{4,10,33}
7 Epiretinal membranes have also been observed in eyes without an obvious PVD.³⁴ In eyes with
8 a PVD, vitreous remnants have been documented on the surface of the retina.^{10,35} Even the
9 presence of a Weiss ring does not always indicate that there has been a complete separation of
10 the posterior hyaloid membrane from the entire posterior retinal surface.³⁶

11 Laminocytes, vitreous cells from the posterior hyaloid membrane (hyalocytes), have been
12 shown to represent a major cellular component of idiopathic ERMs.³⁷ Hyalocytes, however, are
13 not native to the vitreous but originate from bone-marrow-derived cells and are continuously
14 renewed.³⁸ Extracellular matrix material has also been consistently detected in specimens of
15 ERMs from eye bank eyes or from surgically removed membranes.^{4,32,37} Retinal glial cells,
16 hyalocytes, their transdifferentiation into fibroblasts and myofibroblasts, along with the
17 development of extracellular matrix and fibrosis, together lead to ERM formation.⁴ In summary,
18 these and other studies show that the formation of an ERM includes some combination of
19 vitreous collagen, several different potential cellular origins, differentiation of these cells, and
20 the formation of new collagen and an extracellular matrix material. The constitution of ERMs
21 varies and, therefore, ERMs are likely have a variety of possible origins and causes.

22 Vitreomacular Traction

23 As mentioned, the process of a PVD may be a prolonged one, and portions of the posterior
24 cortical face may remain adherent to the macula and lead to tractional changes. Investigators
25 have broadly separated VMT, based on OCT, into small and large areas of adherence. A
26 localized vitreomacular attachment of about 500 μm causes elevation, traction, and subsequent
27 intraretinal cystoid spaces in the foveal neurosensory retina. A broad attachment measuring
28 about 1500 μm (approximately 1 disc diameter) can cause more elevation of the macula, even
29 to the point of a macular retinal detachment, yet this configuration is less likely to have
30 intraretinal cystoid spaces.^{35,39} Of course, there is a continuum of areas of attachment from
31 pinpoint to over 1500 μm in diameter. The vitreous attachment may release spontaneously over
32 time, especially in eyes with more focal areas of adherence.⁴⁰

33 Epiretinal membranes often contain native vitreous collagen on histopathology specimens and
34 may evolve between the neurosensory retina and a vitreous attachment.³⁹ Because they adhere
35 tightly to the ILM, ERMs may play a role in VMT by binding the remaining attachment of the
36 vitreous to the macula.^{39,41,42}

37

CARE PROCESS

1 PATIENT OUTCOME CRITERIA

2 Patient outcome criteria include the following:

- 3 ◆ Prevent vision loss and functional impairment
- 4 ◆ Optimize visual function
- 5 ◆ Minimize symptoms (e.g., metamorphopsia, diplopia)
- 6 ◆ Maintain or improve quality of life

7 DIAGNOSIS

8 HISTORY

9 Many people with ERM have stable vision with few symptoms, whereas others are more
10 symptomatic and have progressive loss of visual function. Patients are often especially bothered
11 by metamorphopsia or diplopia and may experience difficulties in reading, driving, or even being
12 able to use their eyes together.⁴³⁻⁴⁶ Commonly, patients report that they close one eye while
13 reading in order to eliminate the distortion from the affected eye.

14 Patients with VMT have similar symptoms of impaired visual function and metamorphopsia that
15 may be acute or chronic depending on the severity of the traction and the resulting distortion or
16 detachment of the macula. Frequently, the visual acuity of patients with either VMT or ERM
17 does not change dramatically during short-term follow-up.^{12,47,48}

18 Examination

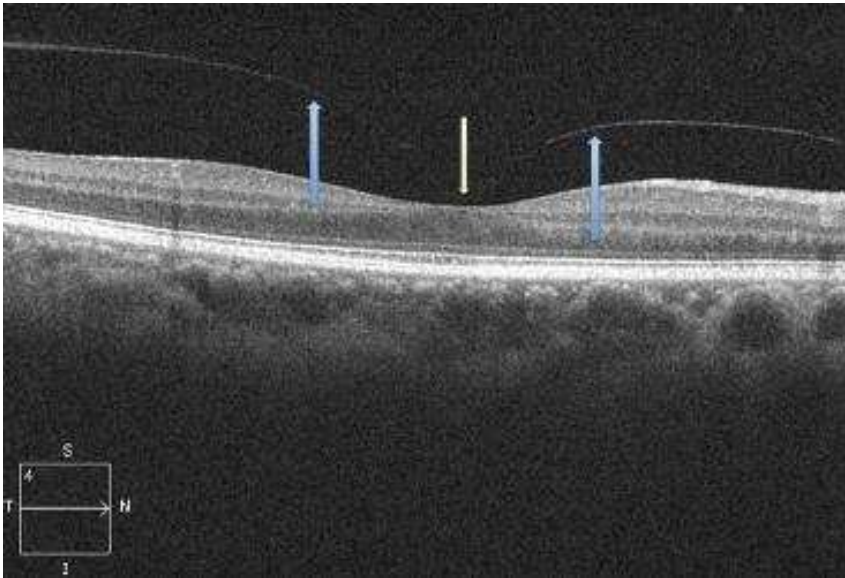
19 Examination includes the following elements:

- 20 ◆ Slit-lamp biomicroscopy of:
 - 21 ◆ The macula and vitreoretinal interface
 - 22 ◆ The optic disc to rule out an optic pit or advanced cupping
- 23 ◆ An indirect peripheral retinal examination
- 24 ◆ Amsler grid test and/or Watzke-Allen test

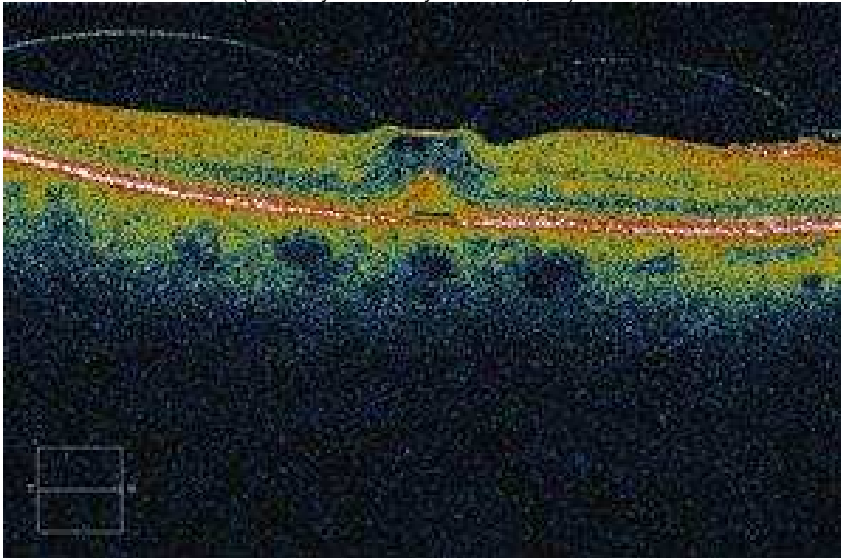
25 Diagnostic Tests

26 Optical coherence tomography is a highly sensitive and routine method used to diagnose
27 and characterize VMA (see Figure 1), ERM, VMT (see Figure 2), and the associated retinal
28 changes.^{6,26,39,40,47,49-52} Comparing the OCT images in the abnormal eye with images of a
29 normal eye (see Figure 3) is a very helpful educational tool to help patients better
30 understand their eye problem. An ERM on OCT appears as a hyper-reflective and
31 sometimes irregular layer on the inner surface of the retina (see Figure 4), usually adherent

1 across the surface of the retina. It frequently attached by pegs emanating from the inner
 2 retinal surface with intervening hyporeflective spaces of ERM separation that gives a
 3 corrugated appearance in cross section. Optical coherence tomography commonly
 4 demonstrates that the traction from the ERM leads to elevation of the normal foveal
 5 depression. The inner retina is typically thrown into folds, with thickening of the macula
 6 and associated cystoid spaces in various retinal layers.⁵³ Using OCT imaging, lamellar
 7 macular holes (see Figure 5) may have variable degrees of inner-retinal tissue loss, often
 8 with well-delineated edges that are affected by tractional elements from the ERM.⁵⁴⁻⁵⁷



9
 10 **FIGURE 1.** Vitreomacular adhesion. The posterior vitreous face (blue arrows) is separated from the neurosensory
 11 retina and a foveal attachment (white arrow) or VMA remains. Note that there is no secondary retinal pathology
 12 from this attachment site. (Courtesy of Timothy W. Olsen, MD)



13
 14 **FIGURE 2.** Vitreomacular traction. (Copyright © 2015 American Academy of Ophthalmology)
 15

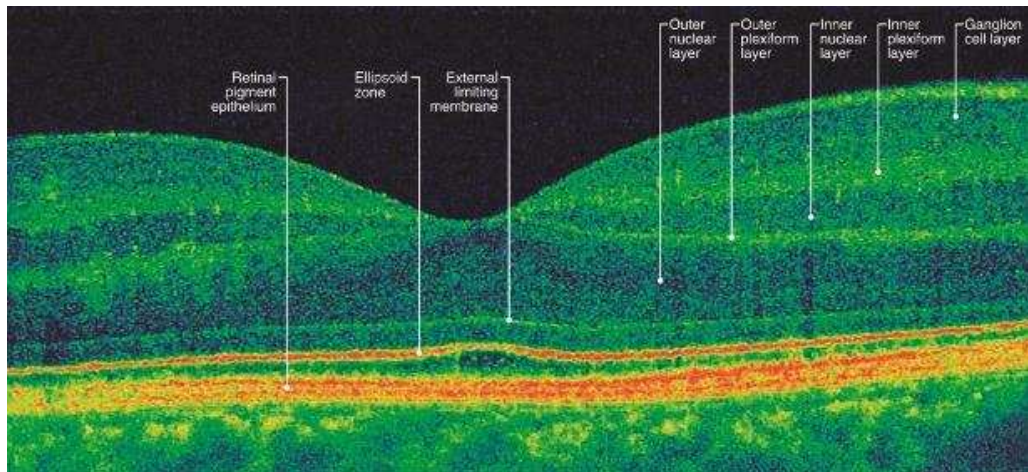


FIGURE 3. Normal retina. The various layers of the retina are easily visualized using spectral-domain optical coherence tomography through the fovea. (Copyright © 2015 American Academy of Ophthalmology®)

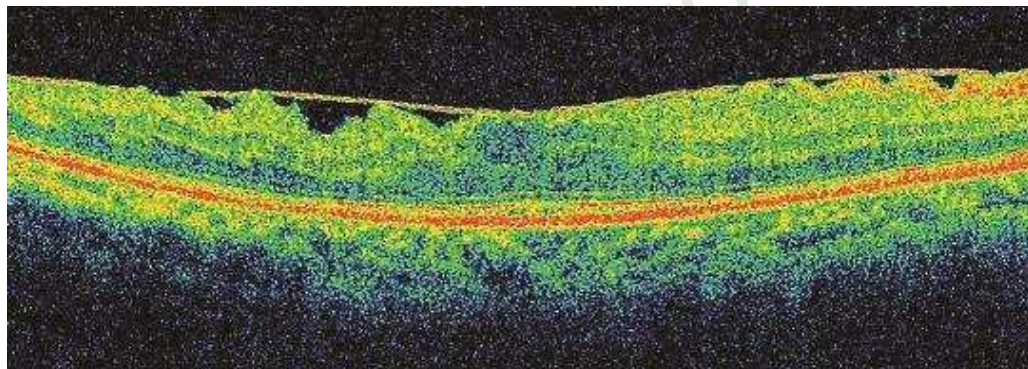


FIGURE 4. Epiretinal membrane. Optical coherence tomography reveals a fine, moderately reflective membrane variably attached to the inner retinal surface. There is associated retinal edema. (Copyright © 2015 American Academy of Ophthalmology®)

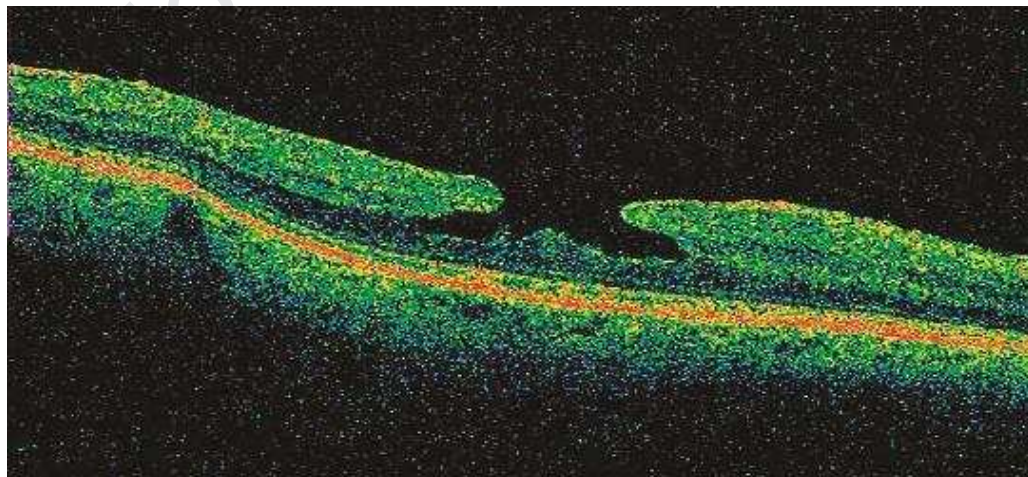


FIGURE 5. Lamellar hole. Optical coherence tomography demonstrates an intraretinal split, with separation of the inner and outer foveal retinal layers and the absence of a full-thickness foveal defect. (Copyright © 2015 American Academy of Ophthalmology®)

1 The OCT findings of VMT are similar, except that the posterior hyaloid remains partially attached
2 to the macula and is separated in the perimacular region.^{58,59} Cystoid spaces may be present in the
3 entire macular region in VMT. Presumably, these changes are due to anterior-posterior vitreous
4 traction associated with VMT as opposed to a more tangential traction from an ERM. The extent of
5 the VMT varies from a small focal adhesion to a large, broad adhesion that extends over the entire
6 macula.^{40,60} Both ERM and VMT often occur together; thus, the features are commonly combined.³⁹
7 In 60 eyes with ERM, the vitreous was noted to be adherent to the macula in 57%.⁶¹ Similarly,
8 13/20 eyes (65%) with VMT were noted to also have an ERM.⁶²

Journal Pre-proof

1 Ancillary Tests

2 A fluorescein angiogram or optical coherence tomography angiography (OCTA)^{63,64} may
3 be helpful to evaluate ERMs and/or VMT.⁶⁵ The fluorescein angiogram and OCTA may be
4 useful to detect other retinal pathologies that can be associated with ERMs, such as a
5 branch retinal vein occlusion, diabetic retinopathy, macular telangiectasia, choroidal
6 neovascularization, and other inflammatory conditions. The fluorescein angiogram may be
7 relatively normal in eyes with early ERM. As ERM contraction increases, the macular
8 vessels may become tortuous near the epicenter of traction or straightened around the
9 epicenter of traction. Some retinal vessels, especially the capillaries that are under
10 tractional forces, may demonstrate a leakage pattern, best detected by comparing the early
11 stages of the angiogram with the later stages. The dye may pool in cystoid spaces,
12 especially in the recirculation phase. However, the staining and leakage in the fovea is
13 usually not as uniformly circular as typically seen in pseudophakic cystoid macular edema
14 (which is often accompanied by a hyperfluorescent optic nerve in the later phase of the
15 angiogram). Retinal vascular changes, such as capillary dropout, telangiectasia, collateral
16 vessels, and microaneurysm formation that are more widespread, suggest diabetic
17 retinopathy or central vein occlusion.

18 MANAGEMENT

19 Nonsurgical

20 Patients should be informed that the majority of ERMs will remain relatively stable and do not
21 require therapy.¹² Patients should also be reassured that there is a very successful surgical
22 procedure that could address worsening symptoms or decreasing visual acuity. Furthermore,
23 patients should be encouraged to periodically test their central vision monocularly in order to
24 detect changes that may occur over time, such as increasing metamorphopsia and/or
25 development of a small, central scotoma. Educating patients about the signs and symptoms of
26 progression and regular monocular Amsler grid testing are both important. Although the visual
27 acuity rarely improves spontaneously, it may worsen.

28 Observation without Treatment

29 Using fundus photography, a population-based study of 3654 persons showed that only 29% of
30 ERMs progressed over 5 years; 26% regressed, and 39% remained approximately the same.
31 Only 20% of eyes with cellophane maculopathy progressed over the same time period.¹² A
32 clinic-based study of 34 eyes with ERM and lamellar macular holes showed that the vision did
33 not change over a mean follow-up of 18 months, although two eyes progressed to a full-
34 thickness macular hole.⁴⁷ A prospective study of 47 eyes with ERM found that the visual acuity
35 and clinical appearance did not change over a mean of 38 months.⁴⁸ A study using SD-OCT
36 images found that the ERM separated from the retina in only 16 of 1091 (1.5%) eyes with a pre-
37 existing PVD but in 21/157 (13.6%) of eyes that did not have an apparent PVD over a mean

1 follow-up of 33 months.⁶⁶ The separation of the ERM led to improved visual acuity in both
2 groups.

3 In eyes with VMT of 1500 μm or less, patients often have stable visual acuity, and the
4 incidence of spontaneous release of traction from the macula occurs in 23% to 47% of eyes
5 over a follow-up of 1 to 2 years.^{40,52,59,60,67-69} Usually the release of traction results in an
6 improvement in visual acuity and less severe symptoms, assuming no full-thickness macular
7 hole is created. An earlier study, however, found that the visual acuity in 34 of 53 eyes (64%)
8 with VMT decreased 2 Snellen lines or more over 60 months of follow-up.⁶⁹ However, 43/53
9 (81%) of the eyes reported in this study had cystoid macular spaces detected at baseline. Thus,
10 eyes with cystoid spaces at baseline may represent a cohort of patients with a more guarded
11 prognosis.⁷⁰

12 Surgery

13 Vitreopharmacolysis – Ocriplasmin

14 Ocriplasmin is a recombinant proteolytic enzyme that was approved by the FDA for
15 intravitreal injection for the treatment of symptomatic VMA (VMT) in 2012.⁷¹ The phase
16 III ocriplasmin studies did not evaluate the use of ocriplasmin in people specifically with
17 ERM; however, a small number of subjects with ERM and VMT was included in the study.
18 The ERM/VMT in this combination group released in 8.7% subjects receiving the drug
19 compared with 1.5% in the placebo group.⁷¹ Given this small and uncertain effect,
20 intravitreal ocriplasmin is not an effective treatment of the ERM.^{72,73}

21 The inclusion criteria in the phase III studies of ocriplasmin included all eyes with vitreous
22 traction on the macula, including a subset of eyes with stage 2 macular holes. Overall, 27%
23 of eyes in the ocriplasmin group reached the primary end point (resolution of VMA),
24 compared with 10% of placebo-injected eyes ($P<0.001$). A subgroup analysis of multiple
25 covariates in the study suggested that resolution of the VMA may be achieved more often
26 in younger patients (<65 years), eyes without an ERM, eyes with a full-thickness macular
27 hole and associated VMA, phakic eyes, and eyes with a focal VMA of 1500 μm or less.⁷⁴ A
28 Cochrane review of 932 eyes in four studies concluded that although ocriplasmin is useful
29 in the treatment of symptomatic VMA, up to 20% of eyes treated with ocriplasmin will still
30 require additional treatment with pars plana vitrectomy within 6 months.⁷⁵ (*I+, Good*
31 *quality, Strong recommendation*) There were more ocular adverse events in eyes in the
32 ocriplasmin group than in the control treatment group (sham or placebo injection). Some of
33 these adverse events, particularly vitreous floaters and photopsia, are known to be
34 associated with PVD.⁷⁵ If considering treatment with ocriplasmin, the treating physician
35 should compare the treatment with observation, injecting a gas bubble into the vitreous, or
36 vitrectomy surgery. The discussion should include the relevant risks versus benefits for
37 each of these options.

1 Complications of Ocriplasmin

2 A review of the adverse effects in the two phase III ocriplasmin studies was performed; it
3 included 465 eyes treated with ocriplasmin and 187 eyes treated with placebo. During the
4 first week after injection, the ocriplasmin group had about a 10% risk of developing
5 vitreous floaters and photopsia, eye pain, and a combination of either blurred vision or
6 decreased vision. Most of these early symptoms resolved.⁷⁶

7 The greatest concern about potential toxicity was with acute severe vision loss,
8 electroretinographic abnormalities, dyschromatopsia, and disruption of the photoreceptor
9 layers. A review of the two phase III trials reported that only 10 subjects had
10 electroretinography changes, eight of whom had resolution of the measured dysfunction.
11 Sixteen subjects reported dyschromatopsia and these symptoms resolved in 14. Follow-up
12 was not possible in the other two subjects, since one subject died and the other did not
13 return for further evaluation.⁷⁶ The FDA concluded that the most severe complications,
14 which include dyschromatopsia, electroretinographic changes, and visual field changes, are
15 rare and usually reversible.⁷⁷ Nevertheless, the use of ocriplasmin is controversial and its
16 use has not been widely accepted.⁷⁸⁻⁸¹

17 In a Macula Society survey study, members reported retrospective visual acuity, clinical
18 and OCT data on outcomes of ocriplasmin usage for symptomatic VMA in 208 subjects.
19 These authors found that visual acuity decreased 2 or more lines in 35 eyes (18%)
20 (compared with 0.6% in the MIVI-TRUST studies) and by 3 or more lines in 27 eyes
21 (14%) at the final visit. Complications included photopsias (15%), dimness of vision
22 (14%), decreased color vision (10%), macular hole development (5% [similar to MIVI-
23 TRUST]), macular retinal pigment epithelium atrophy (2.7%), retinal detachment (1.9%)
24 and retinal tear (1.4% [higher than in MIVI-TRUST]).⁸¹

25 An analysis of postmarketing data found a lower rate of adverse events than were reported
26 from the trials.⁸² The authors hypothesized that the lower rates in the postmarketing survey
27 may have been due to a reluctance to report adverse events by the treating physician.

28 Clinicians should give careful consideration to all options when considering the use of
29 ocriplasmin.⁸³ The use of ocriplasmin for the management of idiopathic macular hole or
30 VMA associated macular hole is presented in the Idiopathic Macular Hole PPP.⁸⁴

31 Known side effects of ocriplasmin include⁷⁷⁻⁸²:

- 32 ◆ Decreased visual acuity
- 33 ◆ Retinal tears
- 34 ◆ Floaters
- 35 ◆ Blue-yellow vision, dyschromatopsia, or dark vision
- 36 ◆ Photopsias
- 37 ◆ Disruption of the photoreceptor layers
- 38 ◆ Visual field abnormalities
- 39 ◆ Electroretinography changes

- 1 ◆ Weakening of zonular fibers and possible lens subluxation

2 Gas Injection for Vitreomacular Traction

3 The injection of intravitreal gas has been reported to also induce release of VMT within 1
4 month in 40% of study eyes in a relatively small cohort of 15 eyes.⁸⁵ A cohort of 30 eyes
5 showed a slightly higher rate of release of 73% within 1 month.⁸⁶ Another, smaller study (9
6 eyes) used SF6 gas and had similar results (56% within 1 month).⁸⁷ In another study of 56
7 eyes, the rate of release of VMT using 0.3 ml pure C3F8 was 85.7% and the rate of closure
8 of small holes was 60%.⁸⁸ Overall, this technique is worthy of addressing in randomized
9 clinical trials. In the absence of evidence from such trials, clinicians need to use their
10 judgment and counsel patients closely on the available limited evidence.

11 Vitreotomy Surgery

12 The decision to intervene surgically in patients with ERM/VMT usually depends on the
13 severity of the patient's symptoms, especially the impact on their activities of daily living.
14 Patients should be asked how much they are bothered and/or impaired by their visual
15 dysfunction; asking about impairments of reading or driving ability is usually very
16 important. Patients should also specifically be questioned about distortional changes.
17 Vitreotomy surgery for ERM/VMT is elective rather than urgent. Earlier surgical
18 intervention for ERM may result in better long-term visual acuity recovery than delayed
19 surgery, yet the time frame of the delay is considered in months rather than in days.⁸⁹ With
20 regards to VMT, patients do not typically improve without vitrectomy surgery when the
21 area of VMT is broad (>1500 µm), when there is an accompanying pathologic detachment
22 of the macula, or when the presenting visual acuity is poor.³⁹ Overall, the recommendation
23 to observe or perform surgery is mainly based on patients' discomfort with their vision,
24 along with their understanding of the associated risks (e.g., cataract). Appropriate
25 intervention should be made with careful informed consent and a discussion of the risk-
26 benefit ratio of surgery.

27 *Preoperative Discussion for Vitrectomy*

28 The preoperative discussion should include the risks (e.g., cataract, retinal tears, retinal
29 detachment, endophthalmitis, vision loss due to retinal damage) versus the benefits of
30 vitrectomy surgery. Discussion should also cover the following aspects of vitrectomy
31 surgery:

- 32 ◆ The risk of cataract progression following pars plana vitrectomy in phakic eyes is high.
33 Such progression occurs at variable rates and may be age-dependent.
- 34 ◆ If a cataract is present, cataract surgery may be deferred, recommended prior to
35 vitrectomy surgery, or done at the same time as vitrectomy surgery.
- 36 ◆ The type of anesthesia used is typically local monitored anesthesia. General anesthesia
37 may also be used, especially for anxious or claustrophobic patients.
- 38 ◆ Usually the visual acuity and symptoms of distortion will improve but not necessarily
39 resolve completely. In some cases, visual acuity may decrease and not recover.

- 1 ◆ Risk of epiretinal membrane recurrence.
- 2 ◆ There is a risk of increase or decrease in postoperative intraocular pressure especially in
- 3 patients with glaucoma.
- 4 ◆ The surgeon is also responsible for planning postoperative care and for communicating
- 5 care instructions.^{72,73}

6 **Technique**

7 Epiretinal membranes and VMT are often present in the same eye. During surgery, both
8 the VMT and ERM must be removed from the retina surface in order to release the
9 traction on the macula.³⁹ Furthermore, some suggest that removal of the ILM around the
10 macula releases the traction even more completely and reduces the rate of recurrence.⁹⁰
11 One potential explanation for the reduced rate of recurrence in eyes that undergo ERM
12 and ILM removal could be related to residual glial and fibrotic elements seen on the
13 retinal surface of the ILM on histopathology after ERM removal in 80% of specimens
14 in one study.⁹⁰

15 Surgical removal of ERM/VMT is usually performed using a 23-, 25-, or, a 27-gauge
16 vitrectomy system combined with local, monitored anesthesia care. The core vitreous is
17 removed, and the surgeon induces a detachment of the posterior hyaloid from the optic
18 nerve and macula. The off-label use of Indocyanine green dye, trypan blue, or
19 triamcinolone may be used during surgery to highlight the ILM and remaining vitreous,
20 respectively. The posterior hyaloid is commonly separated from the retinal surface
21 using aspiration, an illuminated pick, or forceps. The peripheral vitreous is shaved,
22 particularly near the cannulas, to minimize the risk of iatrogenic retinal breaks during
23 instrument exchanges. The vitreous is separated from the retinal surface, extending at
24 least anteriorly to the equator, and removed. Next, the ERM and frequently the ILM are
25 removed with intraocular forceps, often under specialized viewing systems to enhance
26 visualization of the macula. Typically, a forceps, microvitreoretinal blade, diamond-
27 dusted silicone tip, loop, or a needle may be used to elevate an edge of either the ERM,
28 ILM, or both together, which is then peeled and removed with a forceps.⁷² Regardless
29 of the technique, the surgical objectives are to gently free the macula of tractional
30 elements.

31 Histopathology of the peeled membrane demonstrates variable amounts of ILM.
32 However, often there are patches of ERM and large areas of ILM left on the retinal
33 surface after the initial peel. These remnants can be difficult to visualize. Many
34 surgeons choose to use agents such as indocyanine green dye, brilliant blue dye, trypan
35 blue, or off-label triamcinolone to help visualize the ILM and facilitate the peel. The
36 safety of these dyes remains somewhat controversial, yet many surgeons agree that very
37 low concentrations of dyes appear safe and may minimize trauma to the retina because
38 the ILM is more easily visualized. Minimizing excessive intraoperative exposure of the
39 macula to light is important. An ERM typically is thicker and has a shaggy or irregular

1 configuration, whereas the ILM is thin, homogenous, and scrolls following removal
2 from the retinal surface.

3 Once the ERM, ILM, or VMT has been removed, the retina can be examined for retinal
4 breaks or detachment. A small intraocular air bubble may be used to help seal
5 nonsutured sclerotomies. When a surgeon suspects a full thickness or deep lamellar
6 hole, a more complete fluid-gas exchange using a nonexpansile or minimally expansile
7 concentration of C3F8 or SF6 gas is performed.

8 ***Removal of the Internal Limiting Membrane***

9 Table 1 lists 10 studies that compare the results of removing the ERM alone with
10 removing both the ERM and ILM. Five of the studies found that peeling the ILM with
11 the ERM led to a lower incidence of recurrent ERM. Two studies showed no difference
12 between peeling or not peeling the ILM. Of note, ILM peeling can be associated with
13 loss of inner retinal tissue, although the functional impact of this finding is unclear. A
14 systematic review of 13 studies found no difference in visual acuity outcomes between
15 the two groups but greater anatomical success with ILM peeling.⁹¹ (*I+*, *Good quality*,
16 *Discretionary recommendation*) One study did report that the ILM not peeling group
17 experienced greater and faster recovery of retinal sensitivity than the ILM peeling
18 group.⁹²

TABLE 1 RESULTS OF NO ILM PEEL VS. ILM PEEL IN ERM AND VMT

Study	Study Design	No. of Eyes with ERM	Follow-up (mos)	Results	ERM Removal with or without ILM Peel Was Not Favored	Removal of Both ILM and ERM Was Favored	ERM without ILM Removal Favored
Park et al, 2003 ⁹³	Case Series	44	At least 3	24 eyes no ILM peel (Group A); 20 eyes with ILM peel (Group B). Average increase in logMAR was 0.33 in Group A and 0.41 in Group B. Recurrence rate of ERM was 21% in Group A and 0% in Group B.		●	
Bovey et al, 2004 ⁹⁴	Case Series	71	Range 6-59, mean 21.7	ERMs peeled with no attempt to peel ILM but ERM then studied by histopathology. 55 of 71 eyes had long segments of ILM and 16 did not: the 55, which had ILM, had 3 lines of vision gain compared to 1 line in non-ILM group; recurrence rate of ERM was 9% in ILM group and 56% in non-ILM group.		●	
Koestinger and Bovey, 2005 ⁹⁵	Case Series	75	Mean, 20	ERM removed in only 55 eyes and ILM also peeled in 20 eyes using ICG to stain. No difference in VA between groups.	●		
Kwok et al, 2005 ⁹⁶	Case Series	42	Mean, 32.8	Mean, 32.8 17 ERMs removed with no ILM peel, and in 25 eyes both ERM and ILM were peeled. Postop VA was logMAR 0.65 in the non-ILM peel group and 0.46 in the peel group. ERM recurred in 3/17 non-ILM peel group and 0/25 of ILM peel group.		●	
Shimada et al, 2009 ⁹⁷	Case Series	246	12	104 eyes ERM removed only; 142 eyes ERM and ILM removed. Recurrence rate of ERM was 17/104 (16.3%) in ERM-only group and 0/142 eyes in ERM/ILM group. Postop VA did not differ between the groups.		●	
Fang et al, 2017 ⁹¹	Systematic Review	359	At least 3	Systematic review of 13 studies; no difference in BVCA at 12 mos (primary outcome) between ERM/ILM group vs ERM-only group, but there was significantly increased CMT in the ILM peeling group	●		
Oh et al, 2013 ⁹⁸	Case Series	43	12	23 eyes ERM only; 20 eyes ERM and ILM peeled. ILM peel group was not favored at 3 mos. No difference between two groups at 12 months for VA, central retinal thickness, and mfERG.	●		

Sandali et al, 2013 ⁹⁹	Case Series	440	At least 12	174 eyes had no ILM peel; 266 eyes had ILM peel. VA improvement postop was the same between two groups; VA same with dye-assisted ILM peel compared with none. Recurrence rate of ERM was in 8.6% in non-ILM peel group and 2.6% in ILM peel group.	●
Ripandelli et al, 2015 ⁹²	Randomized Controlled Trial	60	12	ILM removed in 30 eyes, ERM only in 30 eyes. Microperimetry showed statistically significantly greater and faster recovery in ERM-only group.	●
Tranos et al, 2017 ¹⁰⁰	Randomized Controlled Trial	102	12	ILM removed in 50 eyes, ERM only (no ILM) in 52 eyes. No difference in BCVA or OCT thickness.	●

BCVA = best-corrected visual acuity; ERM = epiretinal membrane; ICG = indocyanine green; ILM = internal limiting membrane; mfERG = multifocal electroretinography; OCT = optical coherence tomography; postop = postoperative; VA = visual acuity; VMT = vitreomacular traction

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Outcome

Vitrectomy surgery is often indicated in patients who are affected by a decrease in visual acuity, metamorphopsia, double vision, or difficulty using their eyes together. Table 2 lists results for ERM and VMT following vitrectomy. On average, the visual acuity improves by 2 lines or more after surgery. The visual results are highly variable, however; although some patients experience large visual acuity gains, it is important to note that, overall, 10% to 20% of patients will have unchanged or worse vision following surgery. Although results are variable, scores on the NEI Vision Function Questionnaire-25, on average, improve postoperatively.¹⁰¹ Most metamorphopsia improves and may normalize. Thus, even in the absence of visual acuity gain, some patients are pleased with the relief from some or all of the metamorphopsia.

A study of 43 eyes showed that preoperative OCT evidence of intact inner photoreceptor and ellipsoid zone, also referred to as the inner segment/outer segment junction, was associated with better visual acuity after a vitrectomy for ERM.¹⁰² A similar study showed that the integrity of the ellipsoid zone and the cone outer segment tips line (also known as the interdigitation zone) was also correlated with better visual acuity.¹⁰³ The outer retina, the ellipsoid zone, and the photoreceptors' outer segment length may improve or even normalize after vitrectomy, and each feature is correlated with improved visual acuity.^{102,104} In another study of 101 eyes using time-domain OCT, the presence of photoreceptor disruption was found to be a predictor of poor visual outcome after surgery.³

TABLE 2 RESULTS OF VITRECTOMY FOR EPIRETINAL MEMBRANE AND VITREOMACULAR TRACTION

Study	No. of Patients	Follow-up (mos)	Results
ERM Diagnosis			
Koerner and Garweg, 1999 ⁶¹	60	Mean 24.7	73% improved vision; 61% 20/50 or better; 57% final VA better than preop
Wong et al, 2005 ¹⁰⁵	125	10.3	VA improved by a mean of 0.31 log units or 3 lines of vision; 16% had unchanged acuity postop
Ghazi-Nouri et al, 2006 ¹⁰¹	20	4	No postop gain in mean VA; 40% gained 2 lines or more; metamorphopsia decreased significantly ($P=0.02$); VFQ-25 improved significantly ($P=0.03$)
Arndt et al, 2007 ⁴⁴	85	12	56% of patients had metamorphopsia preop and 13% postop
Bouwens et al, 2008 ¹⁰⁶	107	Results at 12	Mean postop VA gained 2 lines; 83% had less metamorphopsia
Okamoto et al, 2009 ¹⁰⁷	28	3	LogMAR improved from 0.49 preop to 0.24 postop; 11 (39%) had no change in logMAR; VFQ-25 scores significantly improved
Matsuoka et al, 2012 ¹⁰⁸	26	12	LogMAR VA 0.41 preop, 0.17 at 3 mos, 0.10 at 12 mos; metamorphopsia score (baseline, 3, and 12 mos was 202, 137 and 108 respectively); VFQ-25 scores significantly better at 3 and 12 mos
Garcia-Fernandez et al, 2013 ¹⁰⁹	88	12	82% had better vision but 10% worse postop
Dawson et al, 2014 ¹¹⁰	237	6	Mean preop 20/120; mean postop 20/40
VMT Diagnosis			
Koerner and Garweg, 1999 ⁶¹	50	Mean 10	73% improved vision; 66% 20/50 or better; 60% final VA better than preop
Witkin et al, 2010 ⁶²	20	28.6	Mean VA preop was 20/122 and postop was 20/68
Jackson et al, 2013 ¹¹¹	Meta-analysis 259 eyes from 17 articles	Variable; range 6-35	Mean preop logMAR 0.67; mean postop 0.42; 33% gained 2 or more lines; 21% of eyes had same or decreased VA postop

ERM = epiretinal membrane; logMAR = logarithm of the minimum angle of resolution; mos = months; postop = postoperative; preop = preoperative; VA = visual acuity; VFQ-25 = National Eye Institute Visual Function Questionnaire; VMT = vitreomacular traction

Complications

The majority of phakic patients develop a progressive nuclear cataract following vitrectomy for ERM.¹¹²⁻¹¹⁶

Retinal breaks and detachments are less common with current vitrectomy surgery, likely due to smaller-gauge instruments, cannulated sclerotomies, improved visualization of the retinal periphery, and management of the peripheral vitreous, including treatment of retinal breaks and or localized detachments. There may also be less vitreous incarceration leading to retinal traction with smaller-gauge sclerotomies. Retinal breaks have been reported to occur in approximately 1% of cases (8/548) during vitrectomies performed using a 23-gauge cannula system.¹¹⁷ Another study also found that retinal detachments occur in 1% (2/166) of consecutive 23-gauge vitrectomies.¹¹⁸ A third study reported that in a total of 349 eyes retinal detachments occurred in 1% of eyes undergoing a 23-gauge vitrectomy and in 3.5% of eyes undergoing 20-gauge vitrectomy.¹¹⁹ Endophthalmitis has been reported in less than 0.05% of vitrectomies.¹²⁰⁻¹²² Macular hole formation is also a potential complication of vitrectomy surgery for ERM and VMT.¹²³

Follow-up Evaluation after Surgery

Patients who have surgery should be examined on postoperative day 1 and again 1 to 2 weeks following surgery or sooner, depending on the development of new symptoms or new findings during early postoperative examination. The primary reasons for an earlier follow-up visit or more frequent follow-up visits are high or low intraocular pressure, a wound leak, pain, worsening vision, or other concern of a retinal complication.

Components of the follow-up examination should include the following:

- ◆ Interval history, including new symptoms
- ◆ Measurement of intraocular pressure
- ◆ Slit-lamp biomicroscopy of the anterior segment, including the wound sites and central retina, if possible
- ◆ Indirect binocular ophthalmoscopy of the peripheral retina
- ◆ Counseling on the use of postoperative medications
- ◆ Counseling on the signs and symptoms of retinal detachment
- ◆ Precautions about intraocular gas, if it has been used

PROVIDER AND SETTING

Diagnosis and management of ERM, VMT, or VMA require special expertise, surgical skills, and specialized equipment to detect alterations in the retina in order to select, perform, implement, and monitor appropriate management or treatment. Referral to an ophthalmologist who has expertise or

1 experience in managing this condition is recommended. The performance of diagnostic procedures is
2 often delegated to appropriately trained and supervised personnel. However, the interpretation of the
3 results of the diagnostic procedures, as well as the medical and surgical management of ERM,
4 requires the medical training, clinical and surgical judgment, and experience of an ophthalmologist
5 who is also trained in vitreoretinal surgery and disease.

6 COUNSELING AND REFERRAL

7 Patients should be informed to notify their ophthalmologist promptly if they have symptoms such as
8 an increase in floaters, a loss of visual field, metamorphopsia, or a decrease in visual acuity.¹²⁴⁻¹²⁶
9 Because vision rehabilitation (as described in the Vision Rehabilitation PPP) helps restore some
10 functional ability, patients with functionally limiting postoperative visual impairment should be
11 referred for vision rehabilitation and social services.¹²⁷⁻¹²⁹ Such a referral is particularly important
12 when there is a residual central or paracentral scotoma. More information on vision rehabilitation,
13 including materials for patients, is available at www.aaopt.org/smart-sight-low-vision.

14 SOCIOECONOMIC CONSIDERATIONS

15 A cost-utility analysis of ERM surgery in the better-seeing eye compared with observation resulted in
16 a mean gain of 0.755 discounted quality-adjusted life years (QALYs) (3% annual rate) per patient
17 treated. This model resulted in \$4,680 per QALY for this procedure. When sensitivity analysis was
18 performed, utility values ranged from \$6,245 to \$3,746/QALY gained, and medical costs varied from
19 \$3,510 to \$5,850/QALY gained.¹³⁰ Epiretinal membrane surgery in the worse-seeing eye compared
20 with observation resulted in a mean gain of 0.27 discounted QALYs per patient treated. The \$/QALY
21 was \$16,146, with a range of \$12,110 to \$20,183 based on sensitivity analyses. Utility values ranged
22 from \$12,916 to \$21,520/QALY.

23 A study compared the costs of surgery versus using ocriplasmin for the treatment of VMT based on
24 data from multiple surgical papers and the MIVI-TRUST study.⁷¹ When pars plana vitrectomy was
25 selected as the primary procedure, the overall imputed cost ranged from \$5,802 to \$7,931. The cost per
26 line was \$2,368 to \$3,237, the cost per line-year saved was \$163 to \$233, and the cost per QALY was
27 \$5,444 to \$7,442. If intravitreal injection of ocriplasmin was the primary procedure, the overall
28 imputed cost was \$8,767 to \$10,977. The cost per line ranged from \$3,549 to \$4,456, the cost per line-
29 year saved was \$245 to \$307, and the cost per QALY was between \$8,159 and \$10,244. If intravitreal
30 saline injection was used as a primary procedure, the overall imputed cost was \$5,828 to \$8,098. The
31 cost per line was \$2,374 to \$3,299, the cost per line-year saved was \$164 to \$227, and the cost per
32 QALY was \$5,458 to \$7,583. The conclusion was that vitrectomy surgery was more cost-effective
33 than ocriplasmin for the primary treatment of VMT.¹³¹ Overall, the results of these calculations
34 suggest that ERM surgery is a very cost-effective procedure when compared with other interventions
35 across medical subspecialties.

APPENDIX 1. QUALITY OF OPHTHALMIC CARE CORE CRITERIA

*Providing quality care
is the physician's foremost ethical obligation, and is
the basis of public trust in physicians.
AMA Board of Trustees, 1986*

Quality ophthalmic care is provided in a manner and with the skill that is consistent with the best interests of the patient. The discussion that follows characterizes the core elements of such care.

The ophthalmologist is first and foremost a physician. As such, the ophthalmologist demonstrates compassion and concern for the individual, and utilizes the science and art of medicine to help alleviate patient fear and suffering. The ophthalmologist strives to develop and maintain clinical skills at the highest feasible level, consistent with the needs of patients, through training and continuing education. The ophthalmologist evaluates those skills and medical knowledge in relation to the needs of the patient and responds accordingly. The ophthalmologist also ensures that needy patients receive necessary care directly or through referral to appropriate persons and facilities that will provide such care, and he or she supports activities that promote health and prevent disease and disability.

The ophthalmologist recognizes that disease places patients in a disadvantaged, dependent state. The ophthalmologist respects the dignity and integrity of his or her patients, and does not exploit their vulnerability.

Quality ophthalmic care has the following optimal attributes, among others.

- ◆ The essence of quality care is a meaningful partnership relationship between patient and physician. The ophthalmologist strives to communicate effectively with his or her patients, listening carefully to their needs and concerns. In turn, the ophthalmologist educates his or her patients about the nature and prognosis of their condition and about proper and appropriate therapeutic modalities. This is to ensure their meaningful participation (appropriate to their unique physical, intellectual and emotional state) in decisions affecting their management and care, to improve their motivation and compliance with the agreed plan of treatment, and to help alleviate their fears and concerns.
- ◆ The ophthalmologist uses his or her best judgment in choosing and timing appropriate diagnostic and therapeutic modalities as well as the frequency of evaluation and follow-up, with due regard to the urgency and nature of the patient's condition and unique needs and desires.
- ◆ The ophthalmologist carries out only those procedures for which he or she is adequately trained, experienced and competent, or, when necessary, is assisted by someone who is, depending on the urgency of the problem and availability and accessibility of alternative providers.
- ◆ Patients are assured access to, and continuity of, needed and appropriate ophthalmic care, which can be described as follows.
 - ◆ The ophthalmologist treats patients with due regard to timeliness, appropriateness, and his or her own ability to provide such care.
 - ◆ The operating ophthalmologist makes adequate provision for appropriate pre- and postoperative patient care.
 - ◆ When the ophthalmologist is unavailable for his or her patient, he or she provides appropriate alternate ophthalmic care, with adequate mechanisms for informing patients of the existence of such care and procedures for obtaining it.
 - ◆ The ophthalmologist refers patients to other ophthalmologists and eye care providers based on the timeliness and appropriateness of such referral, the patient's needs, the competence and qualifications of the person to whom the referral is made, and access and availability.

- ◆ The ophthalmologist seeks appropriate consultation with due regard to the nature of the ocular or other medical or surgical problem. Consultants are suggested for their skill, competence, and accessibility. They receive as complete and accurate an accounting of the problem as necessary to provide efficient and effective advice or intervention, and in turn respond in an adequate and timely manner.
- ◆ The ophthalmologist maintains complete and accurate medical records.
- ◆ On appropriate request, the ophthalmologist provides a full and accurate rendering of the patient's records in his or her possession.
- ◆ The ophthalmologist reviews the results of consultations and laboratory tests in a timely and effective manner and takes appropriate actions.
- ◆ The ophthalmologist and those who assist in providing care identify themselves and their profession.
- ◆ For patients whose conditions fail to respond to treatment and for whom further treatment is unavailable, the ophthalmologist provides proper professional support, counseling, rehabilitative and social services, and referral as appropriate and accessible.
- ◆ Prior to therapeutic or invasive diagnostic procedures, the ophthalmologist becomes appropriately conversant with the patient's condition by collecting pertinent historical information and performing relevant preoperative examinations. Additionally, he or she enables the patient to reach a fully informed decision by providing an accurate and truthful explanation of the diagnosis; the nature, purpose, risks, benefits, and probability of success of the proposed treatment and of alternative treatment; and the risks and benefits of no treatment.
- ◆ The ophthalmologist adopts new technology (e.g., drugs, devices, surgical techniques) in judicious fashion, appropriate to the cost and potential benefit relative to existing alternatives and to its demonstrated safety and efficacy.
- ◆ The ophthalmologist enhances the quality of care he or she provides by periodically reviewing and assessing his or her personal performance in relation to established standards, and by revising or altering his or her practices and techniques appropriately.
- ◆ The ophthalmologist improves ophthalmic care by communicating to colleagues, through appropriate professional channels, knowledge gained through clinical research and practice. This includes alerting colleagues of instances of unusual or unexpected rates of complications and problems related to new drugs, devices or procedures.
- ◆ The ophthalmologist provides care in suitably staffed and equipped facilities adequate to deal with potential ocular and systemic complications requiring immediate attention.
- ◆ The ophthalmologist also provides ophthalmic care in a manner that is cost effective without unacceptably compromising accepted standards of quality.

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APPENDIX 2. INTERNATIONAL STATISTICAL CLASSIFICATION OF DISEASES AND RELATED HEALTH PROBLEMS (ICD) CODES

Epiretinal membrane and vitreomacular traction, which include entities with the following ICD-9 and ICD-10 classifications:

	ICD-9 CM	ICD-10 CM
Epiretinal membrane	362.56	H35.371 H35.372 H35.373
Vitreomacular traction, adhesion	379.27	H43.821 H43.822 H43.823

ICD = International Classification of Diseases; CM = Clinical Modification used in the United States

Additional information for ICD-10 codes:

- For bilateral sites, the final character of the codes in the ICD-10 CM indicates laterality. If no bilateral code is provided and the condition is bilateral, separate codes for both the left and right side should be assigned. Unspecified codes should be used only when there is no other code option available.
- When the diagnosis code specifies laterality, regardless of which digit it is found in (i.e., 4th digit, 5th digit, or 6th digit):
 - Right is always 1
 - Left is always 2
 - Bilateral is always 3

LITERATURE SEARCHES FOR THIS PPP

Literature searches of the PubMed and Cochrane databases were conducted in April 2018; the search strategies are provided at www.aao.org/ppp. Specific limited update searches were conducted after June 2019.

(epiretinal membrane/pathology[majr] OR epiretinal membrane/physiology[majr] OR epiretinal membrane/physiopathology[majr])

(epiretinal membrane/surgery[mh] OR epiretinal membrane/therapy[mh] OR epiretinal membrane/drug therapy[mh])

epiretinal membrane/diagnosis[MeSH Major Topic]

RELATED ACADEMY MATERIALS

Basic and Clinical Science Course

Retina and Vitreous (Section 12, 2019–2020)

Focal Points

Epiretinal Membrane (2009)

Ophthalmic Technology Assessment –

Published in *Ophthalmology*, which is distributed free to Academy members; links to full text available at www.aao.org/ota.

Laser Scanning and Imaging for Macular Disease OTA (2007)

Surgical Management of Macular Holes (2001; reviewed for currency 2012)

Patient Education

Face-Down Recovery After Retinal Surgery Brochure (2014)

Retina Informed Consent Video Collection (2013)

Preferred Practice Pattern® Guidelines – Free download available at www.aao.org/ppp.

Comprehensive Adult Medical Eye Evaluation (2015)

To order any of these products, except for the free materials, please contact the Academy's Customer Service at 866.561.8558 (U.S. only) or 415.561.8540 or www.aao.org/store.

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