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Evaluation and Management of Macular Holes

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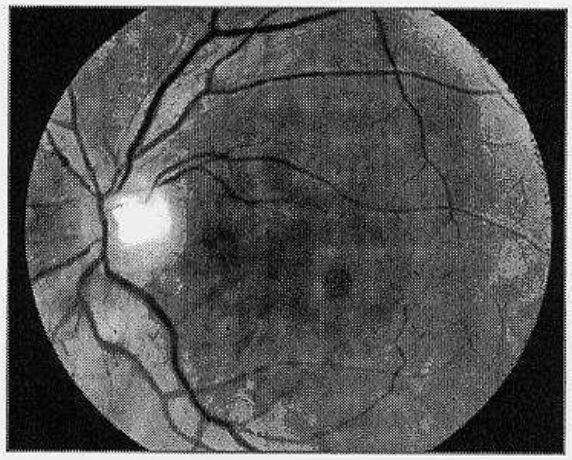

LEO LIFELONG EDUCATION FOR THE OPHTHALMOLOGIST

AMERICAN ACADEMY OF OPHTHALMOLOGY
The Eye M.D. Association

Evaluation and Management of Macular Holes

Cover: Figure 6. The clinical appearance of a macular hole demonstrates a full-thickness defect in the foveal region.

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Learning Objectives

Upon completion of this module, the reader should be able to:

- Describe the histopathology and pathogenesis of macular holes
- Explain the epidemiology and signs and symptoms of macular holes
- Summarize the treatment options for macular holes

Key Words: epiretinal membrane, fovea, internal limiting membrane, macular hole, Müller cell, pars plana vitrectomy, vitreous

Introduction

Macular holes are round defects that involve the fovea and result in visual loss. Idiopathic macular holes are by far the most common type, although they may also occur in the settings of nonsurgical trauma (including lightning injury), surgical trauma, pathologic myopia, and retinal vascular diseases. Advances in vitreous surgery and further understanding of the pathogenesis of macular hole formation over the past 30 years have culminated in treatments and success rates that would have been unthinkable just 12 years ago. This module will address evaluation and management of macular holes, an important and treatable cause of visual loss.

Epidemiology and Natural History

Macular holes affect as many as 100,000 people in the United States, and this number is expected to increase as the population ages. They occur twice as often in women as they do in men, generally in the seventh and eighth decades (mean age is 65 years). While macular holes most frequently have an idiopathic origin, trauma is responsible for up to 9% of cases. Macular hole was the cause of visual impairment in 1.9% of "visually impaired" eyes—that is, eyes with visual acuities of less than 20/40 but greater than 20/200—in the Baltimore Eye Survey.

Macular holes are not associated with medical disease or abnormal refractive errors. The natural history of full-thickness macular holes is not favorable. Once progression to full-thickness hole formation occurs, significant visual loss can be expected without surgery. Long-term followup of patients with macular holes who did not undergo surgery demonstrates progression in hole size and stage. Over an average followup of 4.5 years in the Eye Disease Case Control Study (EDCCS), 45% of eyes with idiopathic macular holes experienced a visual loss of at least two Snellen lines, with 28% experiencing a loss of three lines. Furthermore, one third of these macular holes increased in size during this period. Eight percent actually showed spontaneous regression or resolution of the macular hole, occurring only after at least a 6-year duration; however, only one third of these were associated with an improvement in vision. Visual loss generally stabilizes at 20/200 to 20/400, with development of retinal pigment epithelial atrophy surrounding the hole, resulting in a bull's-eye macular appearance.

In the EDCCS, the incidence of idiopathic macular hole formation in the opposite eye was 4.6% at 3 or fewer years, 6.5% at 4 to 5 years, and 7.1% at 6 or more years of followup. The incidence is expected to be nearly 0% in fellow eyes in which a pre-existing posterior vitreous detachment is present.

Idiopathic macular holes are only rarely associated with detachment of the macula or a more extensive rhegmatogenous retinal detachment. This more extensive retinal detachment may occur in highly myopic eyes, especially if a large posterior staphyloma exists. Retinal detachments due to a macular hole are rare and occur predominately in highly myopic eyes and in the setting of trauma.

Microscopic Anatomy of the Macula

The macula is defined histologically as having two or more layers of nuclei in the ganglion cell layer, whose cell bodies make up the nerve fiber layer. The internal limiting membrane forms the innermost layer of the retina, the outer boundary of the vitreous cortex, and the inner boundary of the nerve fiber layer. It consists of collagen fibrils, proteoglycans, the plasma membrane of the Müller (glial) cells, and possibly the basement membranes of other glial cells of the retina. The neurons of the retina are divided into three layers: the outer nuclear photoreceptor cell layer, the inner nuclear intermediate neurons (bipolar, amacrine, and horizontal), and the ganglion cell layer. The synapses are located in the outer and inner plexiform layers. In the fovea, the nerve fiber, ganglion cell, and inner plexiform layers are absent, resulting in a thickness that is

about half the thickness (100 μm) of the remainder of the macula. In the foveola, the photoreceptor layer is almost entirely composed of cones, whose radiating axons make up the outer plexiform layer in the fovea. Foveal photoreceptor axons traverse parallel to the surface of the retina and do not synapse until they have passed about 100 μm from the center of the fovea.

An inverted cone–shaped zone of specialized Müller cells, called the *Müller cell cone*, constitutes the floor of the fovea. The Müller cell cone is the primary structural support for the fovea, serving as a plug to bind together the receptor cells in the foveola. Without this glial plug, the retinal cone photoreceptors, with their thin layer of radiating nerve fibers, are highly susceptible to disruption. The vitreous cortex is adherent to the retina around the optic nerve, the retinal vessels, and at the Müller cell cone.

Pathogenesis

There is significant evidence that idiopathic macular hole formation begins with contraction of the prefoveolar vitreous cortex that is adherent to the internal limiting membrane of the Müller cell cone. In some patients, tangential, circumferential, anteroposterior contraction of the posterior vitreous cortex ultimately causes avulsion of an operculum, which consists of the internal limiting membrane, Müller cell cone, superficial inner-cone fibers (Henle's layer), and cone nuclei.

Vitreous traction on the Müller cell cone initiates the process of full-thickness macular hole formation. This begins with foveal pseudocyst formation, which may be followed by dehiscence of the pseudocyst and the Müller cell cone, thereby causing a full-thickness macular hole. The foveal center is a potential weak point because of the lack of Müller cell–photoreceptor zonular attachments in this area (see Figure 1). In some patients, especially those with chronic cases, contracture of the internal limiting membrane may also play a role in the formation and/or persistence of the macular hole.

The pathogenesis of *traumatic* macular holes is unknown. The role of vitreous traction remains questionable; nearly all studies of traumatic macular holes have found that the posterior vitreous face attached at surgery. Tangential traction may play an important role, however. Because significant visual improvement usually occurs with surgery, it is unlikely that true retinal necrosis occurs at the fovea during the formation of a traumatic macular hole.

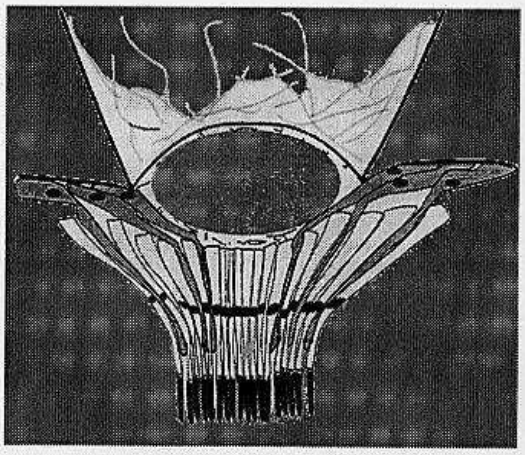

Figure 1. Vitreous traction leading to foveal pseudocyst formation. The Müller cells (gray) in the foveal region form an inverted cone. With continued vitreous traction, a macular hole could ensue. The lack of zonular attachments in the foveal center creates a potential weak point. (Reprinted with permission from Spaide RF. Closure of an outer lamellar macular hole by vitrectomy: hypothesis for one mechanism of macular hole formation. *Retina*. 2000;20:589.)

Classification of Macular Hole Stages

Gass has proposed a four-stage system of identifying idiopathic macular holes. The stages have been confirmed by optical coherence tomography studies (see Figure 2).

Stage 1. Stage 1 lesions—actually foveal pseudocysts, not full-thickness holes—have a yellow spot (stage 1a) or ring (stage 1b) centered at the fovea. They occur following perifoveal posterior vitreous cortex detachment from the retina (see Figure 3). Tangential, circumferential, anteroposterior contraction of the vitreous cortex at the foveal edges causes a split at the Müller cell cone and the resultant ophthalmoscopic appearance of the yellow spot or ring. Mild visual symptoms occur, with metamorphopsia and visual loss to 20/40. Foveal pseudocysts may be the first step in full-thickness macular hole formation, but they may also evolve into a sharply circumscribed, partial-thickness lamellar hole, may persist unchanged for months, or may resolve completely upon detachment of the posterior vitreous cortex. In approximately 50% of patients, the vitreofoveal attachment spontaneously separates, usually accompanied by restoration of the

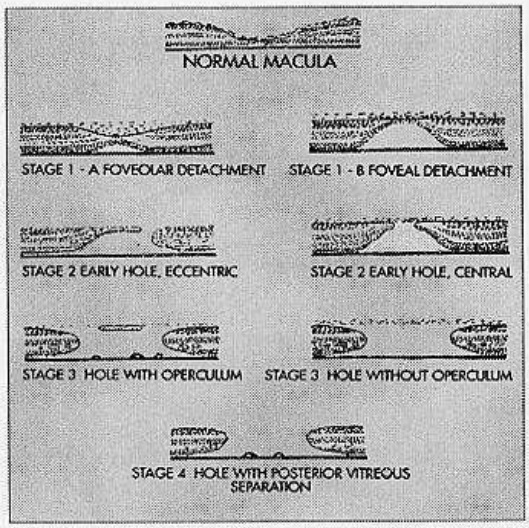

Figure 2. Gass's classification system for macular holes. (From Johnson RN, Gass JD. *Ophthalmology*. Idiopathic macular holes: observation, stages of formation, and implications of surgical intervention. 1988;95:919. Reprinted with permission from Elsevier Science.)

normal foveal depression and improvement in visual acuity. A condensation of detached vitreous cortex ("pseudo-operculum") can often be seen in such patients.

If continued contraction of attached, condensed, prefoveolar vitreous cortex and reactive glial elements takes place, posterior expansion of the cyst and eccentric opening of its roof will occur, constituting a stage 2 lesion.

Stage 2. Stage 2 macular holes are eccentric or oval full-thickness defects and are less than 400 µm in diameter (see Figure 4). Visual acuity drops further, usually to between 20/50 and 20/80. Stage 2 macular holes enlarge to stage 3 holes upon partial vitreomacular separation. This progression occurred in 74% of patients with stage 2 holes over 12 months of followup in the Vitrectomy for Macular Hole Study Group.

Stage 3. Stage 3 holes are similar to eccentric stage 2 holes but are round and have a diameter greater than 400 µm. Foveal edema and a surrounding cuff of subretinal fluid (surrounding a neurosensory retinal detachment) are seen in stage 3 holes. An operculum may be seen overlying the defect. Further vision loss (20/100 to 20/400) occurs at this stage.

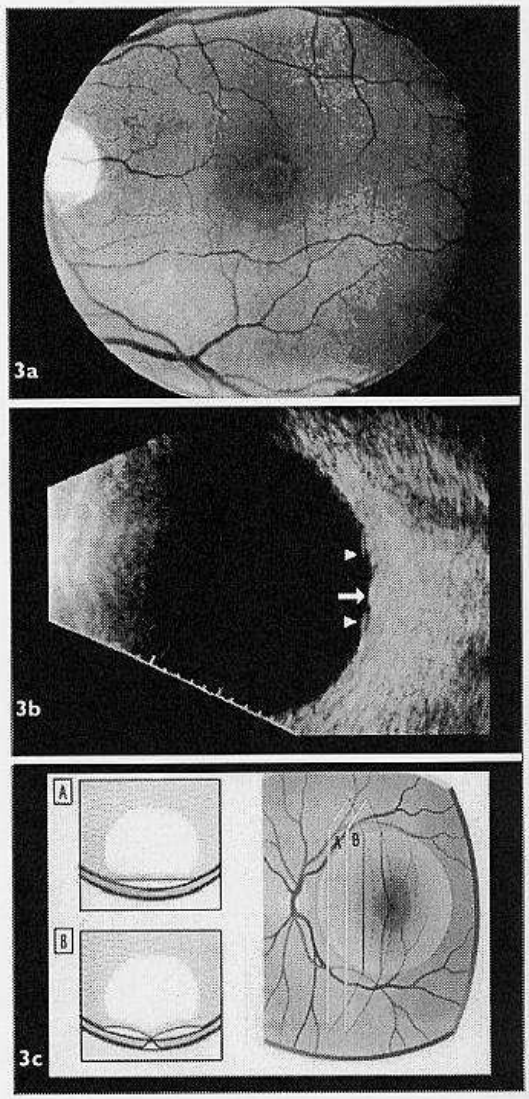

Figure 3. Stage 1 macular hole. 3a: Fundus photograph. 3b: Vertical macular section shows vitreous adherence at foveola (arrow) and pericentral vitreous separation (arrowheads). 3c: Three-dimensional illustration of perifoveal vitreous cortex detachment (inset A) with persistent vitreous foveolar adherence (inset B) with foveal detachment. The clear area in the vitreous in A and B is the premacular liquified vitreous pocket. (Reprinted with permission from Johnson MW, Van Newkirk MR, Meyer KA. Perifoveal vitreous detachment is the primary pathogenic event in idiopathic macular hole formation. *Arch Ophthalmol*. 2001;119:215-222. Copyrighted 2001, American Medical Association.)

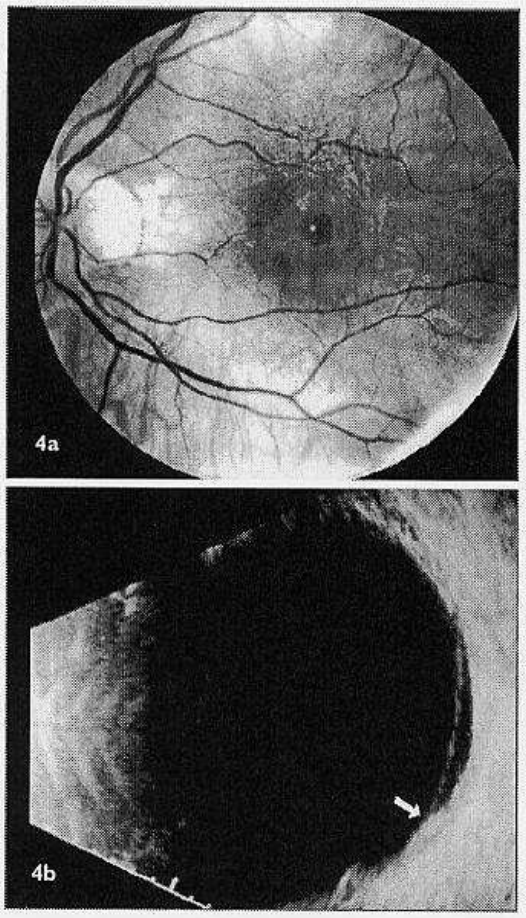

Figure 4. Stage 2 macular hole. **4a:** Fundus photograph. **4b:** Longitudinal B-scan ultrasound shows vitreous adherence at the macular hole associated with a shallow vitreous detachment to the equator. (Reprinted with permission from Johnson MW, Van Newkirk MR, Meyer KA. Perifoveal vitreous detachment is the primary pathogenic event in idiopathic macular hole formation. *Arch Ophthalmol.* 2001;119:215-222. Copyrighted 2001, American Medical Association.)

Stage 4. Stage 4 holes are full-thickness retinal defects similar to stage 3 holes but are associated with a complete vitreous separation (posterior vitreous detachment). Chronic macular holes can be stage 3 or stage 4 and are often associated with an epimacular membrane, a contracture of the internal limiting membrane, and small yellow spots (clumped xanthophyll) at the level of the retinal pigment epithelium at the base of the hole.

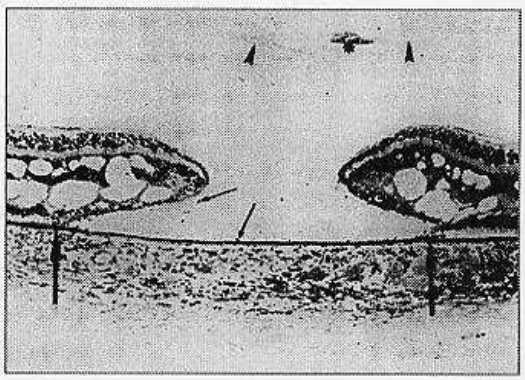

Figure 5. Macular hole histopathology—note defect, cystic foveal edema, and subretinal fluid at either side of the base of the hole in this section (arrowheads designate detached vitreous; asterisk designates operculum). (From Frangieh GT, Green WR, Engel HM. A histopathologic study of macular cysts and holes. *Retina.* 1981;1:318. Reprinted with permission from Elsevier Science.)

Histopathology

A macular hole is a full-thickness circular retinal defect at the fovea and is often associated with an operculum. Typically, this full-thickness defect ranges in size from less than 100 µm to greater than 800 µm in diameter. Additionally, a cuff of subretinal fluid surrounds the base of the macular hole, and cystoid foveal edema is usually present, as shown in Figure 5.

It remains unclear whether macular hole opercula include photoreceptor elements. The loss of photoreceptors was thought to influence visual potential following hole closure, but histopathological studies of macular hole opercula excised during vitrectomy have yielded conflicting results. Some researchers have concluded that opercula rarely, if ever, contain retinal fragments (and thus are better termed "pseudo-opercula"). However, a recent immunocytochemical study of opercula excised during vitrectomy showed a variety of operculum types, including those containing only glia and those containing numerous cones.

Clinical Presentation and Diagnosis

Patients with macular holes may experience relative central scotomata or metamorphopsia. This is not only due to the hole, but also to a localized neurosensory retinal detachment and foveal edema surrounding the

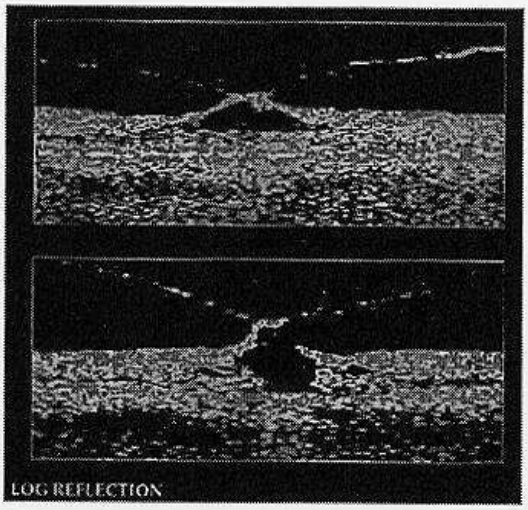

Figure 7. Optical coherence tomography images show the evolution of a foveal pseudocyst (top) to a stage 2 macular hole (bottom), demonstrating progression of the lesion from foveal detachment to full-thickness foveal defect. Note the attachment of the posterior vitreous cortex (thin linear yellow-green reflection) to the foveal center. (From Haouchine B, Massin P, Gaudric A. Foveal pseudocyst as the first step in macular hole formation: a prospective study by optical coherence tomography. *Ophthalmology.* 2001;108:19. Reprinted with permission from Elsevier Science.)

hole. Discovery of the symptoms are often accidental or sudden due to the insidious nature of the condition.

Amsler grid testing can be used to confirm a relative central scotoma or metamorphopsia. Visual acuity is often between 20/80 and 20/400. The mean, long-term, untreated visual acuity in the EDCCS was approximately 20/100. Ophthalmoscopy, preferably with contact lens biomicroscopy at the slit lamp, reveals a circular defect in the foveal region, subretinal fluid, and foveal edema (see Figure 6, cover).

Ancillary tests are often not necessary but may be useful to confirm the diagnosis and to rule out any lesions included in the differential diagnosis whose nature continues to be in doubt after ophthalmoscopy. Fluorescein angiography shows a transmission defect due to absence of xanthophyll pigment and retinal tissue within the hole. Surrounding subretinal fluid or edema may cause partial blockage of choroidal fluorescence, creating increased contrast with the hole. Ancillary tests such as optical coherence tomography and the scanning laser ophthalmoscope are not yet widely available and are often not necessary, but they may be helpful in certain situations to aid in diagnosis and to confirm or evaluate whether closure has occurred postoperatively. Optical coherence tomography—an imaging modality that uses optical reflectivity to produce high-longitudinal-resolution (10 μm) cross-sectional tomographs of ocular tissue—demonstrates the full-thickness foveal defect (see Figure 7). Serial optical coherence tomography has confirmed the Gass hypothesis that pathogenesis is related to traction from the vitreous cortex. The scanning laser ophthalmoscope uses a laser source to scan over an area of retina to be imaged on a video monitor. The scanning laser ophthalmoscope may be used to obtain high-contrast ophthalmoscopic images of the macular hole, as well as for fluorescein angiography and tomographic images of the macular hole. Autofluorescence of the macular hole has also been demonstrated using the argon laser mode of the confocal scanning laser ophthalmoscope.

Preoperative and postoperative macular perimetry testing may also be accomplished with the scanning laser ophthalmoscope by projecting target images directly on the macula and then measuring sensitivity in different macular locations. Preoperative microperimetry using the scanning laser ophthalmoscope shows that the visual loss associated with macular holes is related to the relative reduction of retinal function in the area of the surrounding neurosensory detachment as well as the absence of retinal function in the area of neurosensory defect. The size of the absolute scotoma in the area of neurosensory defect and that of the surrounding relative scotomata in the area of neurosensory detachment, as determined by microperimetry, correlates with the patient's visual acuity and duration of symptoms of the macular hole.

Two additional widely available ancillary tests that are useful in diagnosing macular holes are the Watzke-Allen slit-beam test and the laser aiming beam test. The Watzke-Allen test is performed with the patient wearing a macular contact lens. When the slit-lamp biomicroscope projects a narrow, vertical slit-light beam over the fovea, the patient with a macular hole will note a break or thinning in the beam that corresponds to the location of the hole. The laser aiming beam test is performed via a slit-lamp biomicroscope laser delivery system, with the patient also wearing a macular contact lens. Patients with a full-thickness macular hole will not be able to detect a 50-μm-diameter laser aiming beam projected within the hole, but they can detect it when it is directed to the surrounding retinal tissue.

Differential Diagnosis

A "pseudohole," a hole in an idiopathic epiretinal membrane (not in the retina), can usually be distinguished from a true hole without much difficulty because the pseudohole is often oval, rather than circular, due to the traction exerted by the membrane. In addition, with pseudoholes there is usually no, or a slight, transmission defect on fluorescein angiography, loss of visual acuity is mild to moderate, and results of the Watzke-Allen and laser aiming beam tests are negative. Optical coherence tomography shows no evidence of full-thickness hole formation in this situation. Other differential diagnoses that can be discerned with ophthalmoscopy and ancillary testing include foveal retinal pigment epithelial atrophy (dry age-related macular degeneration), cystoid macular edema (usually secondary to retinal vascular disease or ocular inflammation), idiopathic central serous chorioretinopathy, foveal drusen or retinal pigment epithelial detachment (usually with retention of good visual acuity), and choroidal neovascularization. Fluorescein angiography is a useful test to rule out these conditions.

Lamellar macular lesions are partial-thickness defects with intact outer retinal tissue. A flat, sharply circumscribed reddish area due to an aborted stage 1 lesion or chronic cystoid macular edema distinguishes them. In contrast to full-thickness macular holes, lamellar macular lesions reveal retinal tissue in the base of the lesion on contact lens biomicroscopy, have negative Watzke-Allen and laser aiming beam test results, and demonstrate intact outer retinal tissue on optical coherence tomography scans. Unlike full-thickness macular holes, lamellar macular lesions have no surrounding cuff of subretinal fluid, operculum, or yellow deposits in the base of the hole. Lamellar macular lesions do not progress to full-thickness macular holes.

Treatment

First described in 1869, macular holes were thought to be untreatable until 1991, when a pilot study series by Kelly and Wendel demonstrated that successful macular hole closure was possible with pars plana vitrectomy, delamination of the vitreous cortex, and fluid–gas exchange.

Current surgical treatment of full-thickness macular holes consists of a series of maneuvers. First, a three-port pars plana vitrectomy is performed. Second, the vitreous cortex is delaminated. Next, ancillary maneuvers, such as peeling of the internal limiting membrane, can be considered. Finally, tamponade of the hole with gas or silicone oil is performed. The rationale for each surgical step follows.

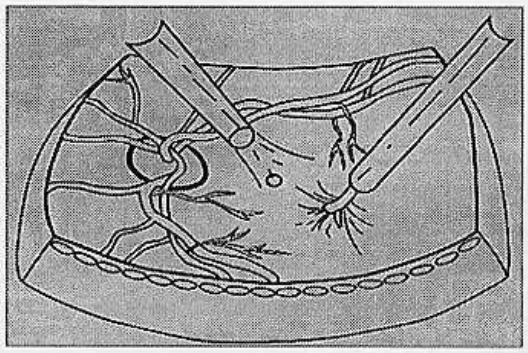

Figure 8. "Fish-strike sign," with silicone-tipped active extrusion cannula over the retinal surface to identify adherent cortical vitreous. (Reprinted with permission from Kelly NE, Wendel RT. Vitreous surgery for idiopathic macular holes. *Arch Ophthalmol.* 1991;109:655. Copyrighted 2001, American Medical Association.)

Pars Plana Vitrectomy/Delamination of Vitreous Cortex

Pars plana vitrectomy and delamination of the vitreous cortex remove anteroposterior, tangential, and circumferential forces keeping the hole open. Because the vitreous cortex is a clear structure, the following special technique is used to identify its presence and/or confirm its removal: after completion of the core pars plana vitrectomy, a cannula with a flexible silicone tip is introduced into the vitreous cavity through a pars plana sclerotomy site and is placed approximately 1 mm above the retinal surface, just below the inferotemporal arcade. Aspiration through the cannula is then applied at 150–200 mm Hg, and the cannula is gently elevated. If the posterior cortical vitreous remains attached to the retina, the cannula will bend posteriorly. Upon engaging the cortical layer, the tip of the cannula suddenly deviates perpendicularly toward the surface of the retina. This is called the "fish-strike" or "divining-rod" sign and is illustrated in Figure 8. Aspiration of the posterior vitreous cortex can also be carried out with the vitreous cutter. Next, the vitreous cortex is elevated and may be delaminated bimanually with an illuminated hook. This vitreous cortex membrane can then be cut and aspirated to the periph-

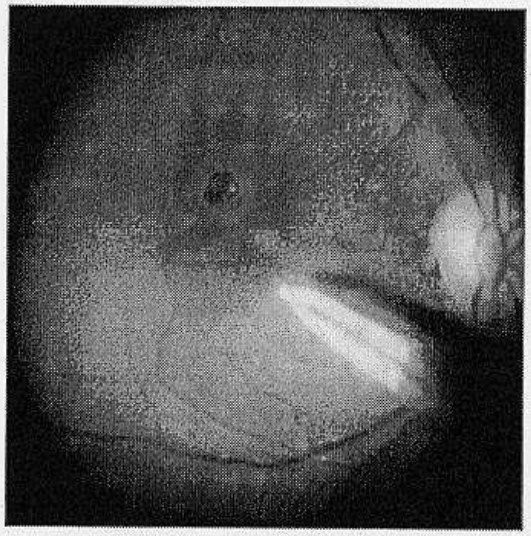

Figure 9. Operating microscope view demonstrating peeling of an indocyanine green–stained internal limiting membrane. (Reprinted with permission from Kadonosono K, Itoh N, Uchio E, et al. Staining of internal limiting membrane in macular hole surgery. *Arch Ophthalmol.* 2000;118: 1117. Copyrighted 2001, American Medical Association.)

ery using the vitrectomy suction and cutting instrument. After this maneuver, if sweeps with the silicone-tipped cannula close to the retina occur without deviation of the tip, the entire posterior cortex has been successfully removed.

Delamination of the Epiretinal Membrane

Following delamination of the vitreous cortex, various maneuvers have been performed to attempt to improve surgical success, the most common of which is peeling (delamination) of visible epiretinal membranes and/or the internal limiting membrane. Most surgeons advocate peeling visible epiretinal membranes associated with macular holes. In the Vitrectomy for Macular Hole Study Group, the prevalence of visible epiretinal membrane was 80% in pseudophakic eyes and 63% in phakic eyes and increased with severity of the hole. Considering the mechanical mechanisms of idiopathic macular hole formation, removal of visible epiretinal membrane around a macular hole seems to be a reasonable surgical approach.

Delamination of the Internal Limiting Membrane

The internal limiting membrane may harbor fibroblast-like cells, especially in stage 4 or chronic holes, causing contracture and maintaining hole patency. Histologic examination reveals layers of myofibrocytes and fibrous astrocytes. These cells that comprise clinically invisible epiretinal membranes may be secondary to macular hole formation in a failed reparative process. Enlargement of a macular hole may occur by the contraction of myofibroblasts on the inner surface of the internal limiting membrane. Peeling of the internal limiting membrane and adherent contractile epiretinal membrane removes this mechanical factor, which appears to contribute to hole patency and enlargement.

Indocyanine green (ICG) dye stains the internal limiting membrane. A 0.5% solution of ICG is often used to facilitate peeling of the internal limiting membrane by providing a contrast between the stained internal limiting membrane and the unstained retina. After pars plana vitrectomy and posterior vitreous cortex delamination, 0.2–0.4 ml of the 0.5% ICG solution is instilled directly over the macular region and allowed to remain there for approximately 3 minutes. After removal of the ICG with active suction, the internal limiting membrane (not the epiretinal membrane or retina) is left stained with ICG. This allows for visualization of this otherwise transparent, diaphanous structure. Once the membrane is visualized, the peel may be initiated with a bent microvitreoretinal blade, a diamond-dusted "scraper," or a blunt retinal pick. Intraocular microforceps are used to complete the peel throughout the posterior pole, from the temporal edge of the optic nerve to the temporal vascular arcades (see Figure 9). A complete fluid–gas exchange is then performed. Controversy remains regarding the need for internal limiting membrane peeling (with or without ICG staining). Related complications such as mechanical trauma to retinal elements, light toxicity, and ICG retinal pigment epithelial toxicity have been reported.

Adjuvants

Various surgical adjuvants have been used to attempt to improve surgical success. Those surgical adjuvants applied to the base of the macular hole that have not conclusively shown benefit include transforming growth factor B2, collagen plugs, thrombin-activated fibrinogen, thrombin, autologous platelet concentrate, and autologous serum. In theory, autologous plasmin

enzyme would allow for enzymatic manipulation of the posterior vitreous cortex and perihole tissue, causing an atraumatic posterior vitreous detachment and stimulating cell proliferation to close macular holes. In one small series, injection of 0.4 IU of autologous plasmin enzyme into the midvitreous cavity resulted in a spontaneous posterior vitreous separation in eight of nine patients; vitrectomy surgery and tamponade with 14% perfluorocarbon (C3F8) resulted in hole closure in all nine patients. Endolaser surgery at the base of the hole (at the retinal pigment epithelium, not the retina) may stimulate gliosis or release factors that favor hole closure and has been shown to be beneficial in a series of cases, but it is not typically used.

Tamponade of the Macular Hole

Tamponade of the hole with gas or silicone oil allows gliosis to occur, thereby sealing the hole while the hole is closed. Just prior to applying the gas tamponade with a fluid–air exchange, it is very important to perform indirect ophthalmoscopy with scleral indentation of the retinal periphery. This is performed to identify any iatrogenic retinal tears, which may become indistinct once a fluid–gas exchange is performed and may result in a postoperative rhegmatogenous retinal detachment if not properly identified and treated at this point. During the fluid–gas exchange, drainage of the subretinal fluid cuff should be avoided because this may lead to retinal pigment epitheliopathy. Tamponade of the macular hole with gas is best accomplished with the patient in facedown positioning to avoid gas–lenticular contact. A long-acting gas such as 12%–16% C3F8, with 1–2 weeks of facedown positioning, is often used. Following this period, 6 hours per day of facedown positioning is often suggested until the majority of gas is absorbed. No supine positioning for an extended period of time and no air travel are permitted while gas is in the eye. Approximately 12%–16% of the C3F8 gas gets absorbed totally in 4–6 weeks.

Eliminating or Reducing Duration of Facedown Positioning

The need for and duration of facedown positioning have become controversial issues. Filtered air (a short-acting gas requiring only 4 days of positioning) has been used successfully in conjunction with peeling of the internal limiting membrane. A small series using gas showed that success was still possible without facedown positioning; all phakic patients in this series underwent combined cataract extraction at the time of vitrectomy surgery. Patients who cannot position themselves reliably, for example, those with mental disorders or physical limitations such as significant cervical arthritis, may opt for silicone oil tamponade, which obviates the need for positioning. However, silicone oil tamponade requires another procedure to remove the oil 6–12 weeks after the initial surgery.

Other Options

Macular hole repair with minimal vitrectomy has recently been shown to be efficacious in a small series of patients who had persistent vitreous traction on a macular hole, demonstrated by optical coherence tomography. A microspatula knife was used to incise the vitreomacular connection. This was followed by a limited vitrectomy over the macula and a partial gas fill with 14% C3F8.

A macular scleral buckle is rarely used to counteract persistent traction on the hole, especially with the increasing use of internal limiting membrane peeling. A scleral buckle, however, may be used in patients with high myopia and a large posterior staphyloma and a macular hole associated with extensive subretinal fluid (retinal detachment).

Repair of Reopened Macular Holes

Various approaches exist for patients with a persistent or reopened macular hole (elevated/open or flat/open) following vitrectomy. Repeated vitrectomy has been advocated. Outpatient fluid–gas exchange is also an option, especially if there are no visible epiretinal membranes or if return to the operating room is undesirable for medical reasons. Some have combined the outpatient fluid–gas exchange with laser photocoagulation of the foveal retinal pigment epithelium.

Results of Macular Hole Surgery

Stage 1 Lesions (Foveal Cysts)

Because most patients with stage 1 lesions have relatively good vision, and the cysts may resolve on their own with the normal development of a complete posterior vitreous cortex separation, no surgical treatment is indicated. The Vitrectomy for Prevention of Macular Hole Study (terminated due to low recruitment) demonstrated no clear significant benefit of vitrectomy surgery for stage 1a and stage 1b lesions. This study showed that patients with stage 1 lesions with visual acuity better than 20/40 have a 30% risk for progres-

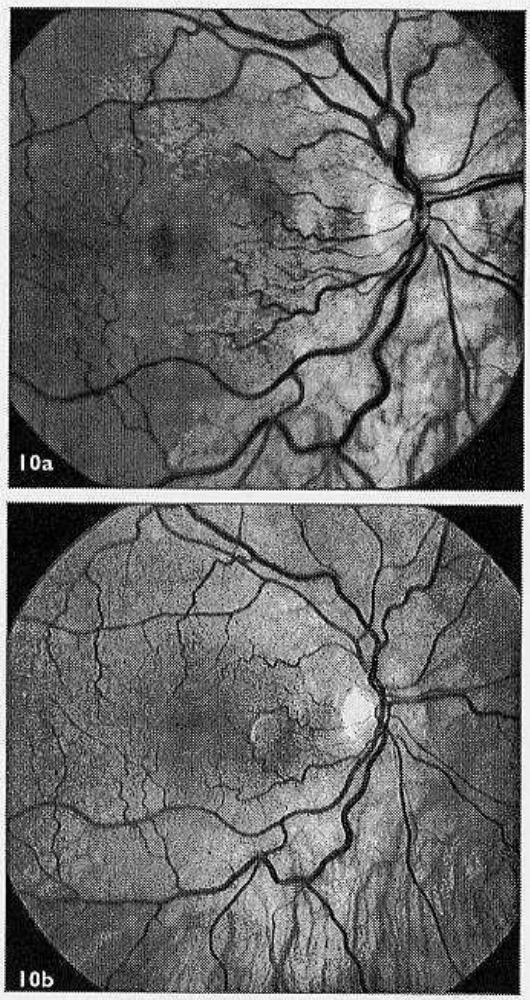

Figure 10. 10a: Preoperative appearance of a macular hole; note perihole epiretinal proliferation and retinal striae in the temporal macula. 10b: Postoperative appearance of re-established anatomy.

sion to a full-thickness macular hole, whereas those with visual acuity from 20/50 to 20/80 have a 66% risk. In the future, enzymatic separation of the posterior vitreoretinal interface may be considered for stage 1 lesions.

Full-Thickness Macular Holes (Stages 2–4)

The three possible anatomical outcomes of full-thickness macular hole surgery are defined by the position of the hole in relation to the retinal pigment epithelium (ie, elevated or flat) and whether the edges of the hole are visible (ie, open or closed). The elevated/open configuration represents a failed surgical attempt, and no improvement in vision occurs. In the flat/open configuration, acuity is rarely better than 20/50. The flat/closed configuration may be compatible with vision of 20/30 or better. Hyperfluorescence in the base of a macular hole noted on preoperative fluorescein angiography disappears with successful closure of the macular hole.

Surgical treatment of full-thickness macular holes most commonly results in improved visual acuity, improved stereopsis, and decreased distortion. This results in psychological comfort and relief as well as an improved quality of life for the patient. Postoperatively, visual improvement occurs due to closure of the hole, resolution of the neurosensory retinal detachment (cuff of subretinal fluid) surrounding the hole, and resolution of foveal edema (see Figure 10).

Scanning laser ophthalmoscope microperimetry demonstrates no detectable absolute scotoma and partial or complete resolution of the surrounding relative scotomata following successful macular hole closure with surgery. Surgery performed on more recent and smaller full-thickness macular holes has better success at improving vision. Scanning laser polarimetry—which measures retardation of reflected laser light, allowing estimation of retinal nerve fiber layer thickness—demonstrates progressive thinning of the retinal nerve fiber layer thickness as the stage of the macular hole advances. This suggests that surgery should be done at an early stage of full-thickness hole formation. Visual function continues to improve for 3 years after surgery according to one study.

The Vitrectomy for Treatment of Macular Hole Study Group demonstrated that pars plana vitrectomy with gas tamponade resulted in a clear benefit in closure rate, visual acuity, and word reading in patients with stage 2, 3, or 4 idiopathic macular holes (see Table 1). The surgical technique used in this study did not include peeling of the internal limiting membrane. (Surgeries were done June 1992-September 1993.)

A more recent study showed that internal limiting membrane peeling significantly improves visual and anatomic success in treatment of recent, chronic, and reopened idiopathic macular holes, as well as idiopathic macular holes that failed to close after initial vitrectomy surgery. The study also showed that peeling of the internal limiting membrane *eliminated* reopening of holes greater than 300 µm. In addition, a recent,

Table 1. Vitrectomy for Macular Hole Study Group: 6-Month Outcome Assessment

Stratified by randomized treatment			Stratified by hole closure within the surgery group		
No. ETDRS Lines	Surgery	Observed	No. ETDRS Lines	Closed	Not Closed
≥2 (improved)	11 (19)	3 (5)	≥1 (improved)	19 (48)	3 (19)
1 (improved)	12 (20)	6 (10)	0 (no change)	12 (30)	4 (25)
0 (no change)	16 (27)	34 (59)	0 (no change)	16 (27)	34 (59)
-1 (worse)	7 (12)	6 (10)	-1 (worse)	7 (12)	6 (10)
≤-2 (worse)	13 (22)	9 (16)	≤-1 (worse)	9 (23)	9 (56)
Total no. of eyes	59	58	Total no. of eyes	40	16
$P = .01$*			$P = .04$*		

ETDRS indicates Early Treatment Diabetic Retinopathy Study.
* Comparisons between groups using the χ^2 test.
(Reprinted from Freeman WR, Azen SP, Kim JW, et al. Vitrectomy for the treatment of full-thickness stage 3 or 4 macular holes. Results of a multicentered randomized clinical trial. The Vitrectomy for Treatment of Macular Hole Study Group. *Arch Ophthalmol.* 1997;115:11–21. Copyrighted 2001, American Medical Association.)

consecutive, noncomparative interventional case series found that better final visual acuity was correlated with a better preoperative visual acuity, shorter preoperative duration of the macular hole, and more complete internal limiting membrane peeling. Another study, however, demonstrated no statistically significant difference in macular hole closure rates or postoperative visual improvement in patients with idiopathic macular holes with internal limiting membrane peeling versus no peeling. In any case, with current surgical techniques, anatomic closure of the macular hole occurs in nearly 90% of idiopathic macular hole cases, and the majority of these will show improvement in vision, especially with a shorter duration (less than 6 months) of the macular hole. A recent series showed a 96% closure rate with pars plana vitrectomy for traumatic macular holes, with visual acuity improvement of two or more lines in 84% of the patients.

The results of surgery without facedown positioning have also been good. In one series, pars plana vitrectomy with delamination of the posterior vitreous cortex and epiretinal membrane (if present) and 15% C3F8 gas without facedown positioning resulted in successful macular hole closure in 26 of 33 eyes with one surgery. In another series, silicone oil was used for tamponade without facedown positioning, and this achieved an 80% success rate. In both studies, a significant improvement in vision occurred when the macular hole was sealed.

A series that addressed the efficacy of surgical intervention for chronic (>1 year; mean 4.2 years) macular holes demonstrated successful closure of the hole in 87% of patients; followup was 6 months or greater. The majority of these eyes had an improvement in vision. Membranectomy was an important factor for surgical success in these chronic cases.

Reopened or Persistent Macular Holes

A second vitrectomy for a persistent macular hole following initial vitrectomy resulted in a hole closure rate of 83% and visual acuity improvement in the majority of patients in one series (mean followup was 7.4 months). Another option for patients with a persistent or reopened macular hole following vitrectomy is an office-based, outpatient fluid–gas exchange and laser surgery of the foveal retinal pigment epithelium. This procedure achieved anatomic success in 12 of 13 eyes using 20% SF6 in one series and in 13 of 15 eyes using 20% C3F8 in another series. Vision improved two lines or more on Snellen testing in all patients with macular hole closure in the latter series. Another series of patients with failed vitrectomy for a macular hole showed hole closure following postoperative fluid–gas exchange in 17 of 23 eyes. All eyes with hole closure showed improved visual acuity of two or more Snellen lines in this series.

Macular Holes in Highly Myopic Eyes

Highly myopic eyes with macular holes can be successfully treated with pars plana vitrectomy and gas tamponade, but the anatomical closure rate may be lower in these eyes than in eyes with idiopathic macular holes. In one series, the myopic macular hole was closed with one surgery in 60% of eyes and with one or more surgeries in 85% of eyes. However, another more recent myopic macular hole series that used internal limiting membrane peeling demonstrated an 87.5% hole closure rate after one surgery and a 100% closure rate following two surgeries.

High myopes with a retinal detachment associated with a macular hole are also treated with pars plana vitrectomy and gas tamponade. Visual outcomes for treatment of a macular hole associated with a retinal detachment compare poorly with those of macular hole not associated with extensive subretinal fluid: anatomical closure rates are lower and reoperation rates are higher. Removing the macular internal limiting membrane may contribute to a higher initial success rate. In eyes with large posterior staphylomas, silicone oil tamponade and/or a macular scleral buckle may be used.

Effect of Age

Age does not play a role in the success or failure of surgery. One study demonstrated that macular hole surgery is beneficial in patients older than 80, with results similar to those obtained in patients younger than 80. One study did note a finding of reduced initial macular hole closure in eyes with significant macular drusen. However, a second operation improved closure rates, and visual outcomes were excellent once closure was accomplished.

Complications of Surgery

Complications of macular hole surgery are becoming less common with surgeons' increasing experience in this area. The retinal detachment rate has been reported to be between 2% and 11%, but once the retinal detachment is repaired, this complication usually does not play a role in the ultimate visual success. Intraoperative peripheral iatrogenic retinal breaks may occur (an incidence of 5.5% was noted in one prospective series), with the distribution tending to be in the inferior and temporal retina. This emphasizes the need for careful indirect ophthalmoscopy and scleral indentation of the retinal periphery, with special surveillance in the inferior and temporal retina, prior to gas–fluid exchange. A giant retinal tear has been reported in association with macular hole surgery, with poor visual results. Postoperative visual field defects—usually temporal, wedge-shaped defects correlated with the location of the infusion cannula—may be minimized or eliminated with intraoperative gas infusion pressures equal to or less than 30 mm Hg.

Increased intraocular pressure may occur in the first postoperative week but is usually transient and can be controlled with medication. Retinal pigment epithelial changes from light toxicity associated with the endoilluminator are uncommon but may be associated with visual field defects and choroidal neovascularization. These changes may be minimized by reducing the time that the macular region is exposed to endoillumination. (One potential drawback of peeling the internal limiting membrane is increased macular endoilluminator exposure time.)

Endophthalmitis occurs rarely, probably in less than 1 in 1000 patients. Late reopening of the hole has been reported at a rate of 5% in one series and 9.5% in another; these cases may be successfully closed with an additional procedure. Also, patients whose macular holes are not successfully closed initially usually respond with an additional procedure, as indicated earlier.

Ulnar neuropathy may be caused by pressure exerted on a bent elbow during facedown positioning. This is manifested by paresthesias, dysesthesias, pain, weakness, and muscle atrophy in the distribution of the ulnar nerve. Postvitrectomy facedown-positioning devices are commercially available; ergonomic support may enhance compliance and enhance patient comfort during the time of facedown positioning.

To maximize visual potential, almost all patients must undergo cataract surgery within 2 years of macular hole surgery. Cataract surgery may be performed either before or after macular hole surgery. Some have advocated combining pars plana vitrectomy for macular hole treatment with cataract extraction and lens implantation as a safe and effective alternative to separate pars plana and cataract surgeries.

Conclusion

Macular holes are a significant cause of loss in central visual acuity and are becoming more common as the population ages. The initial surgical technique had a hole closure rate of 58%. Refinements in the technique have increased this rate to greater than 90%, and complication rates have decreased. Visual acuity and visual function improve with treatment in the majority of patients. Educating referring doctors about the importance of early referral of patients with macular holes may enhance outcomes. With appropriate referral and successful treatment, the quality of life of these patients may be significantly improved.

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The author states that he has no financial relationships with the manufacturer of any commercial product discussed in this module.

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