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MAJOR REVIEW

Macular Hole

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Abstract. A macular hole is a full-thickness defect of retinal tissue involving the anatomic fovea, thereby affecting central visual acuity. Macular holes have been associated with myriad ocular conditions and originally were described in the setting of trauma. The pathogenesis of idiopathic, age-related macular holes remains unclear despite a litany of theories. Recently, Gass has described an updated biomicroscopic classification of macular holes and postulated that tangential vitreous traction may play a role. Cellular components surrounding the rim of macular holes may also contribute tangential traction forces and elevate the rim. Pseudomacular holes may be mistaken for macular hole lesions, despite careful clinical examination. Careful biomicroscopic examination with a contact lens and use of the Watzke and laser aiming beam tests help to ensure accurate diagnosis. Newer imaging technology, such as optical coherence tomography, helps distinguish true macular holes from pseudoholes and may provide additional insight into the pathogenesis of this condition. Surgical management with or without pharmacosurgical adjuncts can improve vision in select cases. The most common surgical complication is progressive lens opacification in phakic patients. (**Surv Ophthalmol 42**:393–416, 1998.

Key words. lamellar macular hole • macular hole • macular pseudohole • vitrectomy • vitreous

A macular hole is a full-thickness defect of retinal tissue involving the anatomic fovea and, primarily, the foveola of the eye. It has been a quarter of a century since Aaberg published his comprehensive review of macular holes, indicating that much progress remained to be made toward the understanding of their pathogenesis.[2] Although significant progress has been made toward an understanding of these lesions, significant controversy exists regarding the pathophysiology, natural history, and management of macular holes and precursor lesions.

Historically, macular holes were uncommon, were attributed to trauma, and were observed in young individuals. It is now understood that idiopathic macular hole affects as many as 100,000 people in the USA, generally afflicting healthy women in their seventh and eight decades (mean age, 65 years) of life who have normal refractive errors.[211]

I. Historical Associations and Theories of Pathogenesis

Early case descriptions of macular holes focused on young traumatized eyes, but it is now known that atraumatic "idiopathic" macular holes of the elderly comprise the vast majority of these lesions. At the start of the century, traumatic macular holes were believed to account for half of all cases of macular holes.[110] In a 1982 series, however, 83% were idiopathic and only 15% were due to accidental or surgical trauma.[140]

Early descriptions of macular hole were made in the second half of the 19th century, and it was not

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until early in this century that macular holes were recognized as a clinical entity by most ophthalmologists.[1] There are three basic historical theories regarding the etiology of macular holes: the traumatic theory, the cystic degeneration and vascular theory, and the vitreous theory.[1,2]

A. TRAUMATIC THEORY

In 1869 Knapp published the first case description of a macular hole in a patient with ocular trauma and an initial diagnosis of a macular hemorrhage.[118] He and most other early observers attributed macular holes to ocular trauma.[11,12,43,44,47,48,55,69,90,110,118,133,155,156,175,220] Two years later Noyes provided the first accurate and detailed ophthalmoscopic description of macular hole, which was secondary to blunt trauma in a 13-year-old girl.[155] He noted the difference in depth of focus from the retinal surface to the base of the lesion and probably was the first to recognize that the hallmark of the lesion was a full-thickness defect in retinal tissue within the center of the macula. In 1900 Ogilvie compiled the first case series in the English literature of holes at the macula, a review of 15 previously published cases, and proposed terminology including *macular hole*, as well as *floor* and *edge* of the macular hole.[156] Many of the first reported cases of macular holes were in young patients, and trauma was estimated to account for as many as 50%.[110] The majority of traumatic macular holes occur in men, whereas it is now known that the majority of age-related macular holes occur in women.

B. CYSTOID DEGENERATION THEORY

The first histopathologic descriptions of full-thickness and lamellar macular holes were provided by Fuchs (1901)[69] and Coats (1907).[44] Coats noted cystic intraretinal changes adjacent to the macular hole and surmised that these changes could be caused by trauma as well as other mechanisms. In some cases of trauma in which there was not immediate macular hole formation, trauma was believed to cause reactive vasoconstriction followed by vasodilation, thus leading to cystic degeneration of the central macula.[55,175] Cyst coalescence could then create a full-thickness macular hole.[66,133] Blunt ocular trauma could effect immediate macular hole formation from mechanical energy created by vitreous fluid waves and contrecoups macular necrosis or macular laceration.[90,155,156] Indirect ocular trauma had also been reported to cause macular hole formation. A lateral blow to the head, projectile objects within the orbit, or trauma to the orbital rim are examples of indirect trauma that have been associated with macular hole formation.[110,156]

Recognizing that cystoid degeneration was not only due to posttraumatic macular sequelae, Kuhnt concluded that macular holes were caused by cystoid degeneration in the macula, not necessarily related to trauma.[123] Increasingly, ophthalmologists recognized macular holes in an atraumatic setting. In 1970 Aaberg found that only 9% of eyes with a macular hole at a university setting were associated with trauma, compared with an earlier report of 50%.[2,110]

Cystoid degeneration of the central macula with resultant macular hole formation has been uncommonly described in association with a variety of conditions, including severe hypertension,[45,121] central retinal artery occlusion,[19] retinal venous occlusive disease,[209] Coats' disease,[21] syphilis,[136] solar maculopathy,[167] arc welding maculopathy,[214] electrocution,[40] and vitreous traction[133,166,219] (Table 1).

C. VASCULAR THEORY

Although trauma was once believed to be the primary or sole cause of macular holes, it was probably the histopathologic and clinical observations of cystoid degeneration in the surrounding tissue of macular holes that led to considerations of atraumatic causes and, in particular, the vascular theory of pathogenesis. Coats and Kuhnt together believed that aging-related changes of the retinal vasculature led to cystoid degeneration and subsequent macular hole formation.[44,123] This vascular theory, sometimes characterized as ocular angiospasm,[80] was the basis for a variety of interesting therapies (Table 2).

TABLE 1

Macular Hole Associations

Full-thickness macular hole
Trauma[118]
Topical pilocarpine[71]
Proliferative diabetic retinopathy[14]
Severe hypertensive retinopathy[45]
Optic disk coloboma[23]
High myopia[180]
Choroidal neovascularization[194]
Best's disease[81,141,177]
Adult vitelliform macular degeneration[154]
Retinal arteriovenous communication[153]
Alport's syndrome[145]
Scleral buckling for retinal reattachment[34,187]
Pneumatic retinopexy for retinal reattachment[172]
Vitrectomy for epiretinal membrane[187]
Accidental Nd:YAG laser[196]
Lightning[35]
Electrocution[40]
Welding[214]
Septic embolization[18a]
Choroidal melanoma[202b]
Lamellar macular hole
Topical pilocarpine[20]
Cystoid edema after cataract extraction[72]
Idiopathic parafoveal telangectasia[161]

D. VITREOUS THEORY

In 1912 Zeeman described the histopathology of overlying premacular vitreous condensation adjacent to foveal cystoid degeneration.[219] Twelve years later Lister implicated the vitreous in the pathogenesis of some macular holes amidst predominant traumatic and vascular/cystoid degeneration theories of the time.[133] As noted by Aaberg, Lister documented the theories of Elschnig, Leber, and Nordenson, describing anteroposterior fibrous vitreous traction bands, which were believed to cause macular distortion, traction retinal detachments, macular cystoid degeneration and, subsequently, macular holes.[2] Lister, however, could not completely reconcile this theory of contracting vitreous bands with his clinical observations of relatively clear vitreous, devoid of obvious vitreous traction bands, in his cases of macular holes.[133] Similarly, Aaberg did not observe a high incidence of persistent focal vitreoretinal adhesion (vitreous strands to the macular hole or operculum or adhesion of the posterior vitreous surface only at the macula) in eyes with macular holes; vitreous separation was noted in 84% of his cases.[1] Thus both modes of vitreous actions, contracting vitreous bands and preretinal condensation, were described in the early part of the century.[2] The exact mechanisms of vitreous pathophysiology, however, remained unclear.

Beginning in the 1960s, clinical and histopathologic studies began to highlight the relationship of the vitreous and the macula in eyes with macular holes. Several investigators concluded that traction, presumably anteroposterior forces, from the vitreous on the macula were important in the evolution of a macular hole. Jaffe[100] described 14 cases and Yoshioka[217] described 5 cases of macular hole in which they observed vitreomacular traction. Worst described the premacular vitreous bursa as a vitreous pocket attached to and anterior to the macula, which could exert anteroposterior traction from the bursa margins despite fluid in the prefoveal interface.[212,213] Avila and Jalkh, using a high-resolution lens, noted vitreoretinal traction arising from the vitreous base and concluded that persistent vitreous-to-macula adhesions were important in the pathogenesis of macular holes; 53% of their cases did not have posterior vitreous detachments.[17] Kakehashi et al reported that observations of vitreomacular attachment at the macula in patients with macular breaks supported the notion of anteroposterior traction, but they could not rule out the possibility of tangential macular traction.[105,106] Foos's histopathologic observations of firm vitreofoveal attachment plaques and an absence of these plaques in other areas of the macula supported a vitreous theory.[65] A case of macular hole formation after the instillation of pilocarpine eye drops implicated pharmacologically induced vitreomacular traction in the development of a macular hole.[71] The problem with these observations was that although a firm vitreofoveal adhesion was now known to be present within the macula, rarely did others observe obvious anteroposterior vitreous traction bands from the vitreous base to the fovea.

Other proponents of a vitreous theory emphasized that the process of vitreous separation from the macula was the critical event in the pathogenesis of a macular hole. Reese et al proposed that separation of the vitreous from the fovea could cause dissolution or avulsion of the fovea, leading to lamellar or full-thickness macular holes.[166] McDonnell et al noted that complete vitreous separation was observed in all macular hole cases and in all premacular hole lesions that evolved to macular holes during their study. Thus, McDonnell et al thought vitreous separation to be critical in the pathogenesis of a macular hole.[140] This theory has not been confirmed by more recent investigations. Because of the preponderance of women with macular hole, McDonnell and others speculated that systemic estrogen fluctuations might promote destabilizaiton and liquefaction of the vitreous, leading to vitreous separation and macular hole formation.[121,140] Unfortunately, no control group observations were made in these studies, and others have been unable to confirm this relationship.[137]

A number of other reports, however, described lower rates (12–27%) of vitreous detachment in eyes with macular holes.[7,73] thereby challenging the necessity of vitreous separation in the development of a macular hole. In Akiba et al's 1990 study using dynamic clinical examination with an aspheric lens (+58.6 diopter [D] El Bayadi-Kajiura), all 15 eyes classified as macular cystic lesions and all 43 eyes classified as early macular holes (92% with crescent or horseshoe-shaped holes and 8% with small cen-

TABLE 2

Historical Systemic Therapies for Macular Hole

	Year	Author[Reference]
Abstinence from tobacco Sedation Hormones Minerals Vitamins	1943	Gifford[80]
Anxiolytics Vasodilators	1950	Croll and Croll[48]
Acetylcholine Nicotinic acid Calcium chloride Potassium iodide	1953	Amsler[15]
Retrobulbar atropine Retrobulbar prisicoline	1967	Hruby[98]

tral holes) progressed to fully developed macular holes without the occurrence of posterior vitreous detachment.[7] These findings strongly suggested that most idiopathic macular holes develop in the absence of posterior vitreous detachment.[7] In our view, these authors correctly point out that one must observe the vitreous condition during the development of macular hole (not only after a macular hole has developed) to determine the relationship of the vitreous to macular hole.

Data on the relationship of the vitreous to macular hole formation are muddled by multiple problems, including the definition of vitreous separation (partial versus complete, vitreofoveal versus vitreomacular), the lack of uniform criteria used for vitreous separation (clinical: Weiss ring, posterior vitreous lacuna, posterior hyaloid; echographic: B-scan ultrasonography; intraoperative: with endoilluminator and retinal pick or silicone-tipped cannula), and the timing of the observation of the vitreous. Was the observation single or prospective? For example, was vitreous attachment or separation noted before, after, or during the evolution of a macular hole? Because posterior vitreous detachment is a common event in the age group of those at greatest risk for formation of idiopathic macular hole, it is difficult to ascribe a causal relationship between these two events. In our view, it seems that the process of a posterior vitreous separation (defined as detachment of the posterior hyaloid from the macula) is not essential to macular hole formation. In fact, it is reported that macular holes can develop despite having a preexisting complete posterior vitreous separation.[84]

E. INVOLUTIONAL MACULAR THINNING

Morgan and Schatz proposed a mechanism that they described as *involutional macular thinning*, incorporating vitreous, vascular, and cystic degeneration theories.[151] The macular lesion was described as "thin, mildly atrophic fovea that has lost its normal architecture and appearance." The foveal lesion was a subtle abnormal depression with variably associated retinal cystic changes or a surrounding yellow ring. Of 95 eyes with involutional macular thinning, 27% developed full-thickness macular holes during a follow-up period ranging between 3 months and 10 years (mean: 4.5 years). In the first step of this schema, choroidal vascular changes lead to altered submacular choroidal vascular perfusion, leading to focal foveal, retinal and pigment epithelial changes. Alterations in the retinal pigment epithelium, as detected by fluorescein angiography, were identified as an independent risk factor for macular hole formation. These vascular changes then lead to cystic degeneration of the retina, which produces permanent structural changes in the fovea or in the retinal pigment epithelium, leading to involutional macular thinning. The final step in the pathogenesis of a macular hole in this theory is vitreous traction on thinned foveal tissue.[151,152] These authors did not specify the nature of the vitreous traction in their theory, but presumably it was generated from attached posterior vitreous, the other independent risk factor for macular hole development in involutional macular thinning. Interestingly, two eyes with a complete posterior vitreous separation were observed to develop a macular hole despite the lack of an apparent vitreous attachment.

II. Recent Concepts of Pathogenesis and the Revised Gass Classification

In 1988 Gass[76] and then Johnson and Gass[102] described a classification scheme for idiopathic macular holes and their precursor lesions. In these works they incorporated their ideas on the pathogenesis of these lesions, highlighting the concept of *tangential vitreous traction* (Table 3). Gass has recently provided an updated biomicroscopic classification and anatomic interpretation of macular hole formation (Figs. 1A and 1B).[74]

Spontaneous tangential traction of the external part of the prefoveolar cortical vitreous detaches foveolar retina, thereby creating an intraretinal yellow spot approximately 100–200 μm in diameter (stage 1A[74,76] [Fig. 2A]). The yellow color may result from intraretinal xanthophyll pigment. The foveal retina then elevates to the level of the surrounding perifoveal retina, elongating the foveal retina around the umbo. This transforms the yellow spot to a small donut-shaped yellow ring (stage 1B[74] [Fig. 2B]). This anterior traction is different from that described by Avila et al,[17] who described anteroposterior vitreous traction originating from the vitreous base and transmitted by shrinking transvitreal vitreous fibers.

Stage 1 lesions often demonstrate fine radiating retinal striae best observed with retroillumination. Vision is typically in the 20/25–20/70 range. No obvious vitreous separation from the optic disk or macula is detected by biomicroscopy. Eventually the centrifugal displacement of the retinal receptors, xanthophyll, and radiating nerve fibers leads to a dehiscence of the retinal receptor layer at the umbo.[74] Biomicroscopic detection may be precluded by the semitranslucent prefoveolar vitreous condensation that in some cases includes the internal limiting membrane and horizontally oriented Müller cell processes that bridge the macular hole.[74] An occult macular hole is a new concept in Gass's revised classification scheme. The center of the yellow ring may often appear reddish in color and the yellow ring itself develops a serrated or irregular edge. The hole

TABLE 3

Historical Timeline of Macular Hole Theories

Year	Author	Description
1869	Knapp	First case description of macular hole (traumatic)[118]
1871	Noyes	First detailed clinical description of macular hole (traumatic)[155]
1900	Kuhnt	Atraumatic theories of cystic retinal degeneration leading to macular hole[123]
1901	Fuchs	Early histopathologic descriptions of macular hole including cystic retinal changes[44,69]
1907	Coats	
1912	Zeeman	Histopathologic recognition of premacular vitreous condensation[219]
1924	Lister	Vitreous forces and "vitreous traction bands" (anteroposterior) may cause macular holes[133]
1967	Reese et al	Vitreous separation critical to macular hole formation[166]
1982	McDonnell et al	Possible female hormonal influece on vitreous separation and macular hole formation[140]
1983	Avila et al	Vitreous separation not necessary in formation of a macular hole[7,17,73,84]
1986	Morgan and Schatz	Involutional macular thinning is a premacular hole condition[151]
1988	Gass	Tangential vitreous traction and Gass biomicroscopic classification of Johnson premacular hole and macular hole lesions[76,102]
1995	Gass	Centrifugal displacement of retinal receptors with umbo dehiscence Reappraisal of biomicroscopic classification of premacular hole and macular hole lesions[74]

may become evident in two ways. More often it appears as an eccentric hole caused by separation of the prefoveolar vitreous cortex from the edge of the round, previously occult macular hole. Spontaneous vitreofoveal separation may then occur, creating a semitranslucent prefoveal opacity (pseudo-operculum) that is often larger than the underlying occult foveolar hole.[74] The yellow ring appears at the edge of the centrifugally displaced retinal receptors and disappears, presumably because of relief of prefoveolar vitreous traction on the edge of the expanding occult macular hole[74] (Fig. 2C). The first biomicroscopically identifiable full-thickness retinal defect is a stage 2 hole (redefined as less than 400 μm in diameter) and may be obscured by the overlying pseudo-operculum[74] (Figs. 2D and 2E). Most macular hole opercula probably do not harbor retinal receptors; they are composed of vitreous condensation and reactive glial proliferation.[74,135] These generally enlarge to stage 3 holes (400 μm and greater) (Fig. 2F). Approximately half of stage 3 holes will demonstrate nodular yellow deposits on the surface of the retinal pigment epithelium in the base of the hole, and nearly all will demonstrate a shallow surrounding neurosensory macular detachment.[76] Stage 3 holes (partial vitreomacular separation) may then evolve to stage 4 macular holes (complete separation of the vitreous from the entire macular surface and optic disk)[74] (Fig. 2G). Vision usually varies between 20/70 and 20/400 in stage 3 or 4 lesions. An overlying operculum may be observed and, with time, there may be fine radiating retinal striae (26%) drusen or yellow-white deposits (42%), atrophy of the retinal pigment epithelium, and a circular pigmented demarcation line within the area of the hole and surrounding retinal detachment[76,193] (Fig. 2H). Epiretinal membranes, cystic degeneration of the retina, and underlying cuffs of subretinal fluid that create shallow macular detachments are also observed.

These reports by Gass focused attention on the different types of mechanical forces on the macula generated by attached vitreous, provided descriptive and standardized terminology of macular holes and associated lesions, and theorized possible explanations for arrested macular hole development with vitreofoveal separation.[74,76,102]

Another ultrastructural histopathologic report supports the concept of prefoveolar vitreous contraction in the evolution of macular holes.[216] This report provided histopathologic descriptions derived from 12 surgical macular hole cases. The internal limiting membrane was intentionally peeled, and suggested that macular holes appear to form from contraction of the prefoveal vitreous and that the hole enlarges because of contraction of myofibroblasts on the inner surface of the internal limiting membrane.[216] These contractile elements may cause traction elevation of Henle's nerve fiber layer surrounding a macular hole.[113]

III. Differential Diagnosis and Diagnostic Testing

Many macular lesions simulate macular holes or macular hole precursor lesions (stages 1A and 1B). The ophthalmologist's most valuable tool is a careful contact lens biomicroscopic evaluation of the lesion. Narrowing the slit-lamp beam and off-centering the incident light to study the contour of the macula and vitreous interface either directly or with retroillumination are helpful as well. Visual acuity can be misleading because macular holes may occasionally be found with 20/40 vision but generally occur with visual acuity of 20/80 or worse.[188]

A. USEFUL DIAGNOSTIC TESTS: WATZKE AND LASER AIMING BEAM

The most useful diagnostic tests for discriminating full-thickness macular holes from other lesions are the Watzke and the laser aiming beam tests. The Watzke test is performed at the slit-lamp biomicroscope by using a macular lens and placing a narrow vertical slit beam through the fovea; a positive test is noted when the patient detects a break in the bar of light (Fig. 3). The laser aiming beam test is performed similarly by using a macular lens and placing the 50-μm laser-photocoagulator aiming beam within a lesion; a positive test is observed when the patient cannot detect the aiming beam within the lesion but is able to detect it in surrounding intact tissue. A positive Watzke sign is reported by most patients,[205] and the use of the laser aiming beam is probably more sensitive and specific for full-thickness macular holes.[138]

B. OTHER DIAGNOSTIC TESTS

Other ancillary testing is generally not necessary or helpful in distinguishing macular holes from simulating lesions. For example, Amsler grid abnormalities are sensitive to macular lesions but not specific to macular hole lesions.[138,193] Macular holes do not cause absolute scotomas detectable by Amsler grid testing.[193] However, bowing in of the Amsler grid lines and micropsia are commonly appreciated, perhaps because of the edema of the surrounding retinal tissue separating the outer photoreceptors. Fluorescein angiography that demonstrates early central hyperfluorescence may be present in true (79%)[199] and pseudomacular holes (63%)[114] and, therefore, is generally not helpful in distinguishing these lesions. B-scan ultrasonagraphy is predictive of the vitreomacular relationship[54,119] and, therefore, may be helpful in staging a macular hole lesion and planning a surgical approach, but it is not sensitive enough to distinguish macular holes from masquerade lesions.

C. NEWER IMAGING TECHNOLOGY

New imaging technologies may be helpful but are not widely available. Scanning-laser ophthalmoscopy has been used to study macular holes,[5,202a] but may not add significant diagnostic or preoperative information to a careful biomicroscopic examination. Confocal laser tomography,[18,206] laser biomicroscopy,[111,157] and optical coherence tomography[92,165] are helpful in distinguishing the status of the vitreous and macula. These techniques take advantage of the imaging advantages offered by coherent light and interferometry to improve the resolution of the vitreomacular interface. Optical-coherence tomography is helpful in distinguishing full-thickness macular holes from lamellar macular holes and macular cystic lesions[92] (Fig. 4).

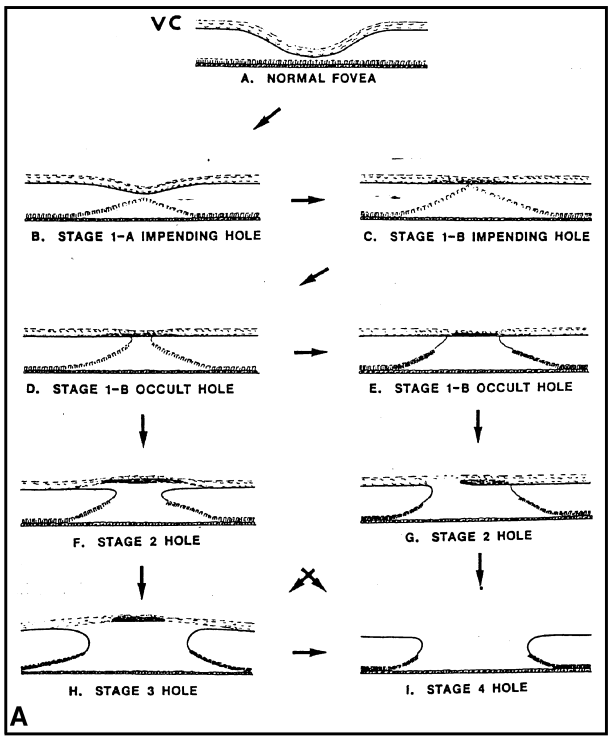


Fig. 1A. 1995 Gass biomicroscopic classification of macular hole (diagram). States of development of a senile macular hole. (A) Normal fovea. Layer of vitreous (vc) lying on internal limiting membrane of retina. (B) Stage 1A impending hole. Early contraction of outer part of vitreous cortex with foveolar detachment. (C) Stage 1B impending hole. Further vitreous contraction and condensation of the prefoveolar vitreous cortex with foveal detachment. (D) and (E) Stage 1B occult hole. Dehiscence of the retinal receptor layer at the umbo with centrifugal retraction of the retinal receptors. (F) Stage 2 hole with early separation of condensed prefoveolar vitreous cortex with formation of pseudo-operculum that is larger than the hole. (G) Stage 2 hole with tear in vitreous cortex at junction of the prefoveolar vitreous cortex and edge of macular hole. (H) Stage 3 hole with pseudo-operculum. (I) Stage 4 hole after posterior vitreous separation. (Reprinted from Gass[74] with permission of the author and the Ophthalmic Publishing Company.)

D. DIFFERENTIAL DIAGNOSIS OF MACULAR HOLE

The most common lesions simulating a full-thickness macular hole are an epiretinal membrane with a pseudomacular hole, impending macular holes, and lamellar macular holes[10,77,88,114,186] (Table 4). Pseudomacular holes associated with epiretinal membranes have a median visual acuity of 20/30 and retinal vascular tortuosity and compression.[63] They are not associated with a rim of subretinal fluid

TABLE

BIOMICROSCOPIC CLASSIFICATION OF AGE-RELATED MACULAR HOLE

STAGE	BIOMICROSCOPIC FINDINGS	ANATOMIC INTERPRETATION	
		OLD	NEW
1-A (impending hole)	Central yellow spot, loss of foveolar depression, no vitreofoveolar separation	Early serous detachment of foveolar retina	Same
1-B (impending or occult hole)	Yellow ring with bridging interface, loss of foveolar depression, no vitreofoveolar separation	Serous foveolar detachment with lateral displacement of xanthophyll	Same for small ring. For larger ring, central occult foveolar hole with centrifugal displacement of foveolar retina and xanthophyll, with bridging contracted prefoveolar vitreous cortex. Cannot detect transition from impending to occult hole.
2	Eccentric oval, crescent, or horse-shoe retinal defect inside edge of yellow ring	Hole (tear) in peripheral foveolar retina	Hole (tear) in contracted prefoveolar vitreous bridging round retinal hole, no loss of foveolar retina
	Central round retinal defect with rim of elevated retina		
	With prefoveolar opacity	Hole with operculum,* rim of retinal detachment	Hole with pseudo-operculum,† rim of retinal detachment
	Without prefoveolar opacity	Hole, no posterior vitreous detachment from optic disk and macula	Same
3	Central round ≥ 400 μm diameter retinal defect, no Weiss's ring, rim of elevated retina		
	With prefoveolar opacity	Hole with operculum, no posterior vitreous detachment from optic disk and macula	Hole with pseudo-operculum, no posterior vitreous detachment
	Without prefoveolar opacity	Hole, no posterior vitreous detachment from optic disk and macula	Same
4	Central round retinal defect, rim of elevated retina, Weiss's ring		
	With prefoveolar opacity‡	Hole with operculum and posterior vitreous detachment from optic disk and macula	Hole with pseudo-operculum and posterior vitreous detachment from optic disk and macula
	Without prefoveolar opacity	Hole and posterior vitreous detachment from optic disk and macula	Same

*Operculum contains foveolar retina
†Pseudo-operculum contains no retinal receptors.
‡Usually found near temporal border of Weiss's ring.

B

Fig. 1B. 1995 Gass biomicroscopic classification of macular hole. (Reprinted from Gass[75] with permission of the author and the Ophthalmic Publishing Company.)

(Fig. 5A). Lamellar macular holes (Fig. 5B) are sharply circumscribed, partial-thickness defects of the macula representing either aborted full-thickness lesions or a complication of chronic cystoid macular edema.[72,161] They are characterized by a flat, reddish-hue-type lesion with intact outer retinal tissue. Careful contact lens biomicroscopic evaluation will reveal retinal tissue in the base of the lesion and

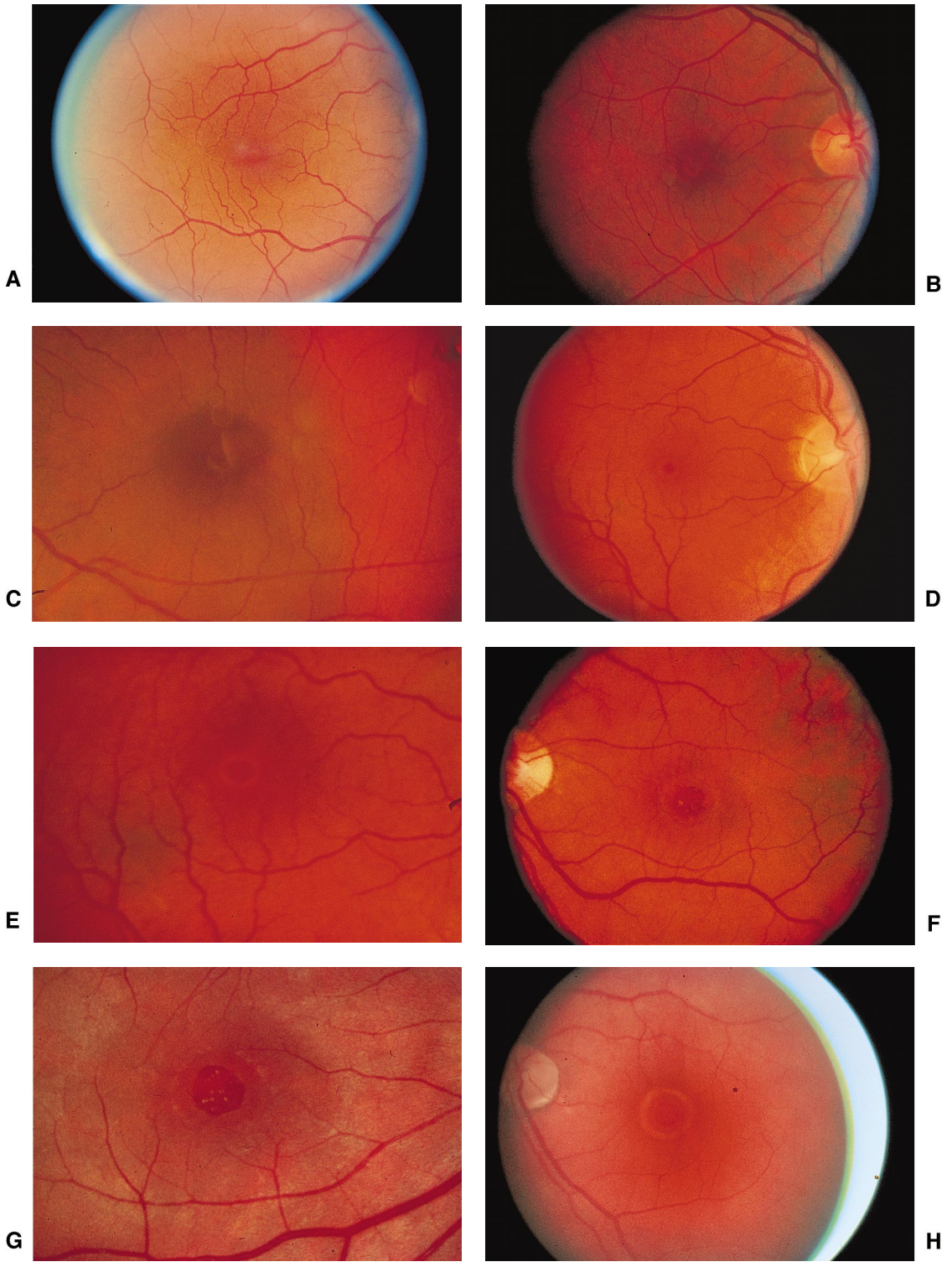


Fig. 2. *A:* Stage 1A macular lesion. A foveolar intraretinal yellow lesion with loss of normal foveal depression. Visual acuity is 20/30. *B:* Stage 1B macular lesion. A foveolar yellow ring is present with subtle retinal striae and adjacent thinning of retinal tissue comprising a reddish halo. Visual acuity is 20/30. *C:* Stage 1B macular lesion, probable occult macular hole. Condensation of the prefoveolar vitreous is present overlying the temporal aspect of the yellow ring, comprising an early pseudo-operculum. Visual acuity is 20/40. *D:* Stage 2 macular hole. Within the foveal yellow ring there is a central foveolar retinal dehiscence less than 200 μm in greatest diameter and no detectable subretinal fluid. Visual acuity is 20/60. *E:* Stage 2 macular hole. A small central foveolar dehiscence is present. *F:* Stage 3 macular hole. This is a generally well-circumscribed, oval, 500 μm, full-thickness retinal defect. Note the yellow clumps of presumed glial cells in the base of the macular hole and the large surrounding cuff of subretinal fluid. The posterior hyaloid is attached at the optic nerve and the major temporal retinal arcades. Visual acuity is 20/100. *G:* Stage 4 macular hole. The full-thickness retinal defect is surrounded by an epiretinal membrane and elevated by a large rim of subretinal fluid. Yellow deposits are noted in the base of the macular hole. The posterior vitreous hyaloid is completely separated. Visual acuity is 20/300. *H:* Stage 4 macular hole with a nonpigmented demarcation line beneath the neurosensory detachment.

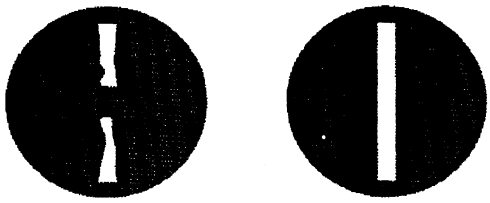


Fig. 3. Watzke sign. A narrow slit beam of light is placed through the fovea to elicit the Watzke sign. A positive Watzke sign is identified when the patient observes a complete break in the beam of light and is compatible with a macular hole (*left*). A negative sign is described when there is no break in the bar of light (*right*). It may be helpful to ask the patient to draw what he/she observes. Bending or distortion of the observed slit beam is not specific to full-thickness macular hole.

no evidence of subretinal fluid. Lamellar macular holes do not progress to full-thickness lesions.[77] Distinguishing features of true macular holes are drusenlike yellowish deposits in the base of the hole, a cuff of subretinal fluid, a distinct margin around the hole, and an overlying operculum.[188] Patients with pseudomacular holes report a negative Watzke sign and can see a laser aiming beam when it is directed within the lesion.

E. DIFFERENTIAL DIAGNOSIS OF PREMACULAR HOLE LESIONS

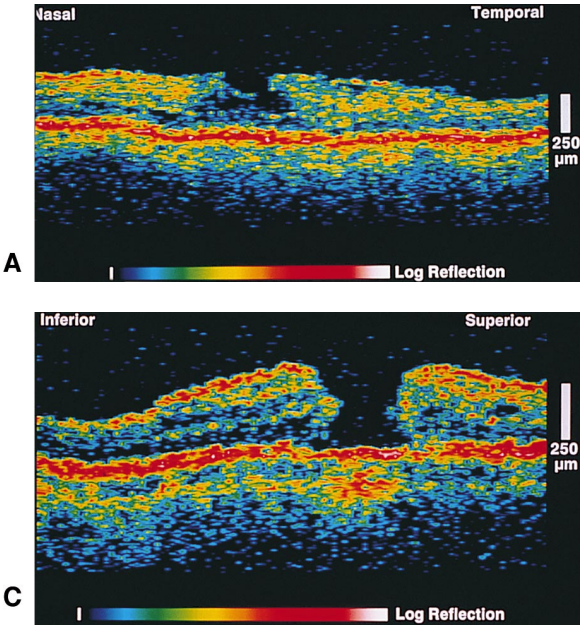
Premacular hole lesions (stage 1A) are also simulated by a wide variety of other macular lesions (Table 4). Macular "cysts" is a misnomer for true stage 1 macular hole lesions because they are not true cysts lined by epithelium. Simulating yellow macular lesions are observed in pseudo-opercula;[78] vitreomacular traction; cystoid macular edema; macular neurosensory elevations such as in central serous retinopathy; degenerations of the retinal pigment epithelium demonstrating drusen (Fig. 5C); vitelliform and pattern dystrophy lesions; acute solar maculopathy; posttraumatic maculopathy;[86] and occasional inflammatory or infectious chorioretinopathies. Macular yellow rings (stage 1B) are rarely simulated by any disorder other than a stage 2 hole.

The clinician's most important diagnostic tool again is careful slit-lamp biomicroscopic examination with a macular contact lens. Key features of true stage 1 macular hole lesions are yellow intraretinal spot or ring; loss of the foveal depression, but not significant elevation above the surrounding tissue; and an absence of vitreofoveal separation. Vitreomacular traction often demonstrates elevation of foveal tissue above the plane of the retina. Stages 1A and 1B lesions are not accompanied by extrafoveal serous macular elevation, as observed in central serous retinopathy. Central drusen and pattern lesions are at the level of the retinal pigment epithelium, while the yellow lesions of stages 1A and 1B are intraretinal. The only yellow lesions that evolve from a yellow foveal cystic lesion to a yellow ring are stage 1 premacular holes.

IV. Histopathology

A. FULL-THICKNESS MACULAR HOLE

Two large histopathologic series have reported on macular holes.[66,89] Histopathologic examination of



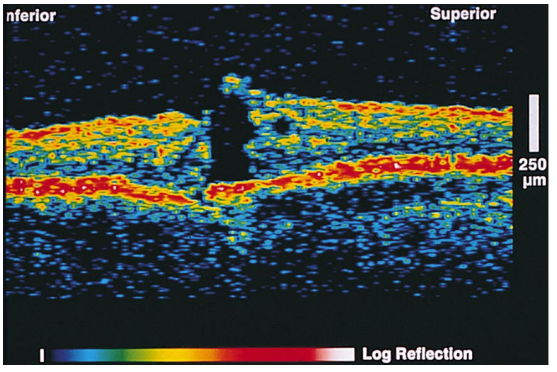


Fig. 4. A: Optical coherence tomography of lamellar macular hole. The dark discontinuity of the retinal reflections corresponds to the lamellar foveal defect. *B:* Optical coherence tomography of stage 2 macular hole. Some early intraretinal cystic changes are noted. *C:* Optical coherence tomography of stage 3 macular hole. There is only minimal evidence of associated subretinal fluid in this image plane. (Reprinted from Hee et al[92] with permission of the author and the Ophthalmic Publishing Company.)

TABLE 4

Macular Hole and Premacular Hole Mimickers

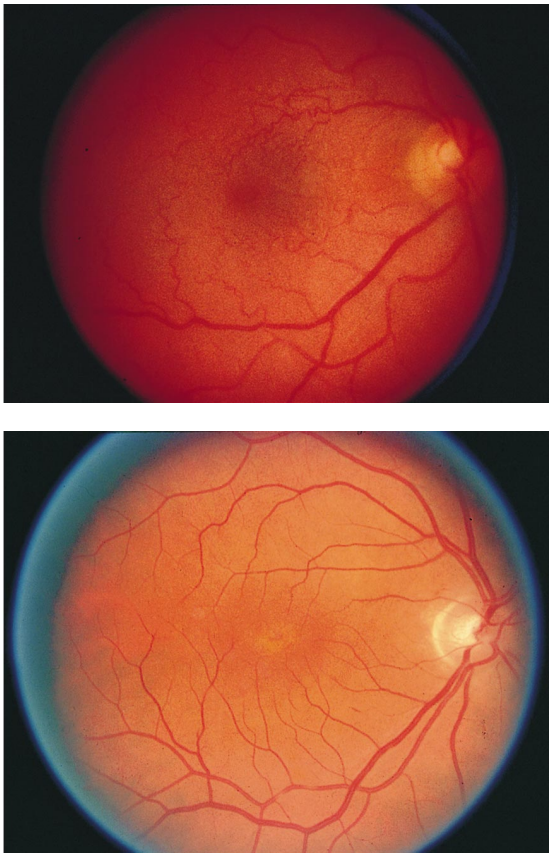
Macular hole
Epiretinal membrane with pseudomacular hole
Lamellar macular hole
Chronic cystoid macular edema
Impending macular hole (stages 1A and 1B)
Premacular hole
Pseudo-opercula
Vitreomacular traction
Cystoid macular edema
Central serous retinopathy
Central druse
Pattern of vitelliform dystrophy
Solar maculopathy
Inflammatory maculopathy

full-thickness macular holes demonstrates round or oval retinal defects surrounded by rounded retinal edges and a cuff of detached neurosensory retina with subretinal fluid (Figs. 6A and 6B). In the most recent series, 79% of 21 eyes with full-thickness–age-related macular holes demonstrated cystoid macular edema (Fig. 6C) and 68% had epiretinal membranes. Photoreceptor atrophy was variable (200–750 μm, mean: 480 μm from the edge of the retinal margin)[89] in this group of globes, some of which had longstanding macular holes (Fig. 6D). In some of the eyes, a thin, tapered layer of cortical vitreous was noted that may effect traction on the edges of the macular hole. Artifactitious changes in the vitreous during gross examination and microscopic processing prohibited detailed description of the vitreous condition. One group has demonstrated myofibril contractile elements surrounding the edges of macular holes.[216]

Two cases of probable spontaneously resolved macular holes have also been reported[89] (Figs. 7A and 7B). In these specimens, there was no surrounding cuff of subretinal fluid and the photoreceptors were reapposed to Bruch's membrane (Figs. 7C and 7D). One eye demonstrated hyperplastic retinal pigment epithelium at the margin of the retinal defect, which appeared to seal the macular hole.

B. LAMELLAR MACULAR HOLE

Histopathology of lamellar macular holes has also been described.[72,89] Lamellar macular holes are characterized by a partial loss of neurosensory retina, which resembles a sharply circumscribed round or petal-shaped, red depression in the inner retinal surface.[77] In half of these eyes, there was evidence of a thin layer of an epiretinal vitreous membrane that might have been causing tangential traction.[89]



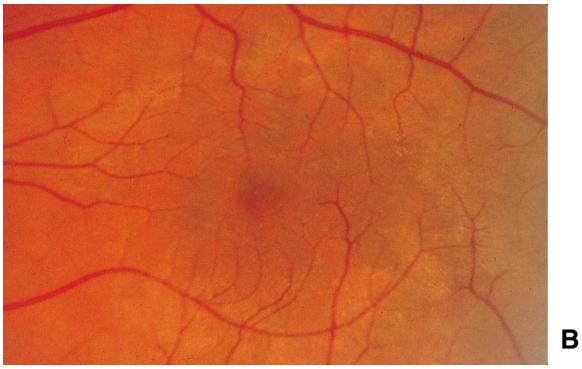


Fig. 5. A: Pseudomacular hole/epiretinal membrane. The most common misdiagnosis of a full-thickness macular hole is an epiretinal membrane that creates a circular central depression without a true retinal defect. Note the tortuosity of the macular vessels and subtle retinal striae. The Watzke sign was negative and the visual acuity was 20/25. *B:* Pseudomacular hole/lamellar macular defect. A lamellar macular defect is a flat, reddish lesion with partial loss of inner foveal tissue, no macular subretinal fluid, and negative Watzke and laser aiming beam tests. *C:* Pseudopremacular hole/foveal drusen. Isolated foveal drusen may simulate premacular hole lesions; however, these lesions are not intraretinal like true premacular holes. They are located at the level of the retinal pigment epithelium and are not associated with a loss of foveal depression.

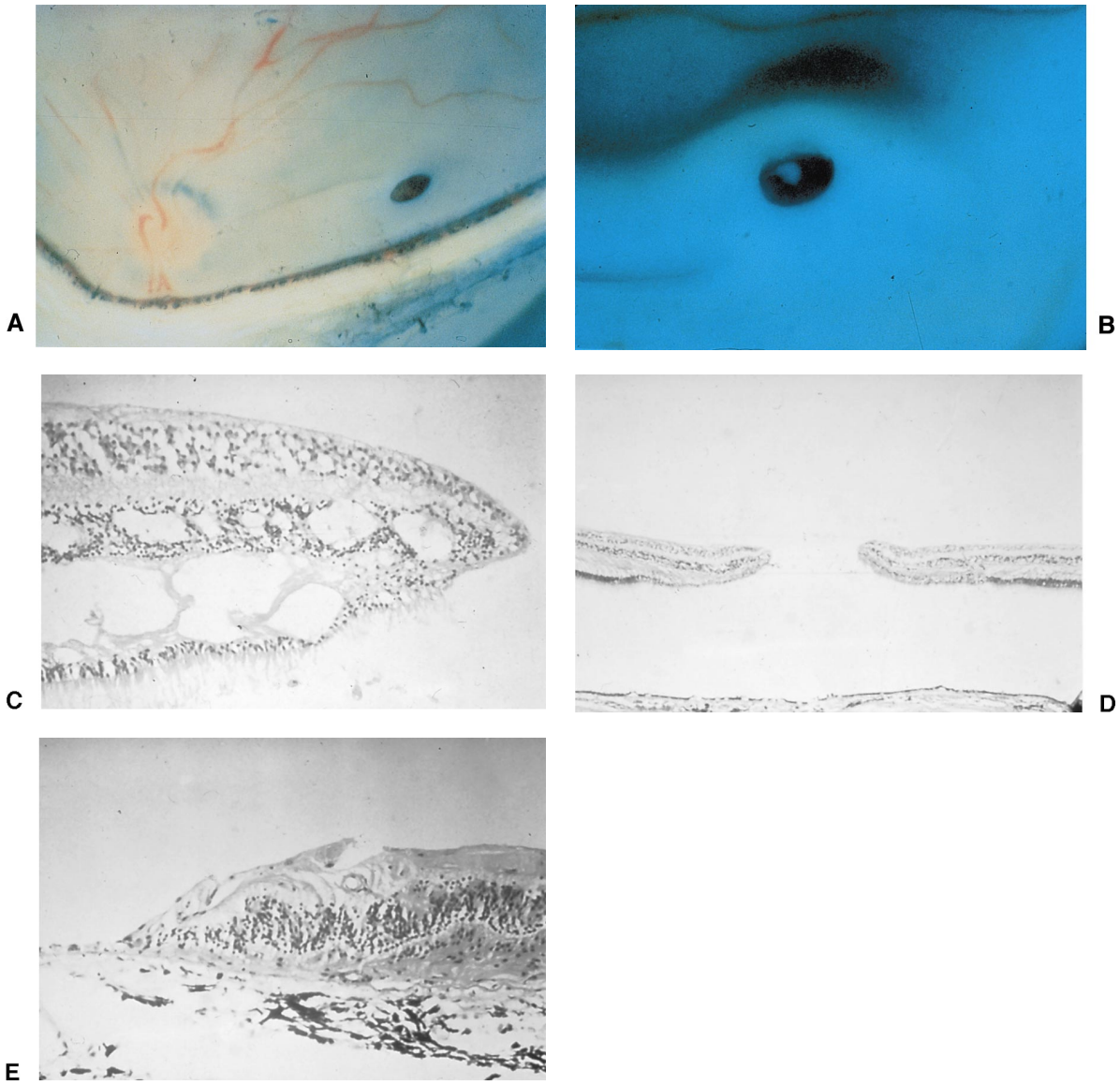


Fig. 6. *A*: Gross appearance of an eye with age-related macular hole. *B:* Gross appearance of an age-related macular hole with an overlying operculum and a surrounding macular detachment. *C:* Microscopic appearance of intraretinal cystoid edema, rounded and everted edges of macular hole, and photoreceptor atrophy, particularly near the edge of the hole (110 × magnification, hematoxylin and eosin). *D:* Microscopic appearance of macular hole with an associated macular retinal detachment (artifactitious) and photoreceptor atrophy (35 × magnification, hematoxylin and eosin) (Fig. 6A–D reprinted from Guyer et al[89] with permission of the author and the Ophthalmic Publishing Company). *E:* Microscopic appearance of a spontaneously sealed macular hole with a thin discontinuous fibroglial layer on the surface of the retina (70 × magnification). Other spontaneously sealed macular holes can demonstrate hyperplastic retinal pigment epithelium on the retinal surface. (Courtesy of W. R. Green.)

C. PREMACULAR HOLE LESIONS

To date, there are no clinicopathologic correlations on stages 1A or 1B macular lesions. Clinically, they appear cystic but are likely not true cysts lined by epithelium.

D. PREMACULAR VITREOUS AND OPERCULA

The histopathology of tissue removed during vitreous surgery for impending macular holes has been described.[36,190] In one study, the primary tissue specimen was a thin sheet of acellular premacular vitreous collagen verified by electron microscopy.[190] This thin layer of cortical vitreous is difficult to detect biomicroscopically and may be present even when there is an apparent posterior vitreous detachment. These findings corroborate a previous scanning electron microscopy study demonstrating persistent prefoveal cortical vitreous despite spontaneous vitreous detachment in normal eyes.[112] The second report

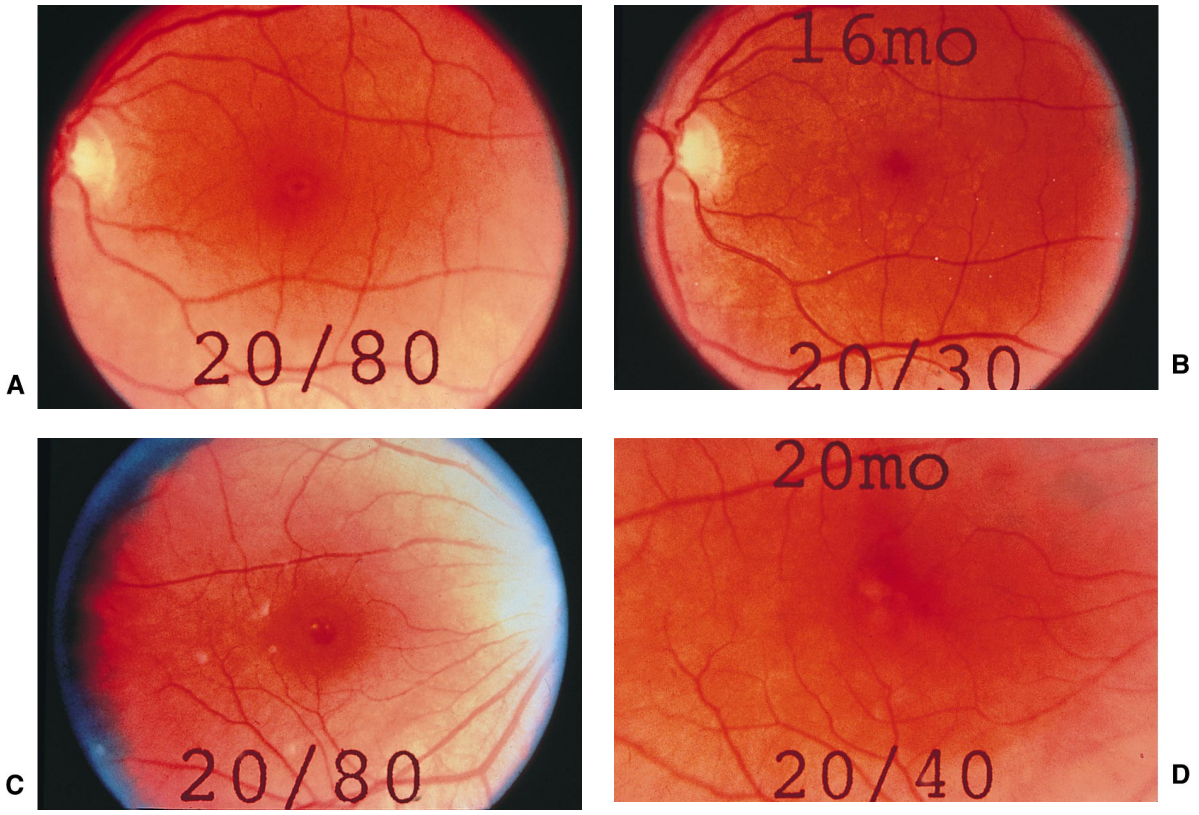


Fig. 7. *A:* Spontaneous resolution of a stage 1B macular hole. The patient presented with 20/80 vision and a stage 1B macular hole. *B:* Sixteen months later the patient's visual acuity improved from 20/80 to 20/30 with the macular lesion resolving into a flat, reddish-hue lesion. *C:* Spontaneous resolution of a full-thickness macular hole. This patient presented with 20/80 vision and a full-thickness macular hole. There was a cuff of submacular fluid and yellow deposits were noted at the level of the retinal pigment epithelium. *D:* Twenty months later the patient's vision improved from 20/80 to 20/40 and the macular hole had partially resolved into a flat, reddish-hue lesion without subretinal fluid. (Reprinted from Guyer[87] with permission of the author and the Ophthalmic Publishing Company.)

used immunocytochemical labeling of the premacular vitreous sheet and demonstrated a cellular, potentially contractile glial and retinal pigment epithelial cells in the surgical specimens[36] consistent with prior studies on the vitreoretinal interface.[65] Contractile elements have been identified using ultrastructural analysis of tissue removed with the internal limiting membrane surrounding full-thickness macular holes.[216]

Interesting reports on surgically retrieved opercula overlying full-thickness macular holes reveal that at least some opercula do not represent displaced neurosensory photoreceptors.[135,59a] The opercula were composed of a proliferation of dislodged fibrous astrocytes and Müller cells. This observation is consistent with Gass's revised theory on macular hole pathogenesis, which is characterized by a dehiscence at the umbo with lateral displacement of photoreceptors; the operculum represents the overlying prefoveal tissue and not necessarily neurosensory retina. Whether this tissue represents a reparative biologic response or a clue to the pathogenesis of an umbo dehiscence remains unclear.[76] Future clinicopathologic reports may help to clarify this issue.

There are two reports on the histopathology of surgically treated macular holes.[70,134] These clinicopathologic studies demonstrated that macular holes can be sealed by fibrous astrocytes and Müller cells without significant inflammation or disruption of the underlying retinal pigment epithelium or cystoid macular edema. There is a closer reapproximation of retinal edges compared with spontaneously resolved macular holes,[89,134] suggesting that surgically treated holes may seal in different ways than spontaneously resolved macular holes. The same fibrous astrocytes and Müller cells that have been shown to help seal surgically treated macular holes may also contribute to epiretinal membrane formation and recurrent macular holes if the reparative process goes awry.[60]

V. The Natural History of Premacular Holes, Fellow Eyes, and Full-Thickness Macular Holes

A. PREMACULAR HOLE LESIONS, STAGES 1A AND 1B

The natural history of stage 1 lesions has been controversial. Some of the reports predate the 1988 Gass classification and thus describe the history of macular yellow cystic lesions. The best information currently available on the natural history of stage 1 lesions is derived from the Vitrectomy for Prevention of Macular Hole Study Group, which reported that 14 (40%) of 35 patients randomized to observation progressed to a full-thickness macular hole over a 2-year–follow-up period.[51] Generally, a stage 1A lesion progresses to a stage 1B lesion within a few weeks to a few months.[51] Stage 1 lesions progressing to full-thickness lesions do so in an average time of 4.1 months (range: 1–13 months) after diagnosis.[51] Prior reports estimated the progression rate of stage 1 or other premacular hole lesions to be 10–75%.[6,8,16,33,74,77,87,96,102,140,152] Several of these prior studies were limited by their retrospective nature.

In general, resolution of a stage 1 lesion is accompanied by vitreofoveal separation and a change in the appearance and morphology of the macular lesion.[85,104] Sixty percent of stage 1 lesions abort macular hole formation. The resolved fovea may appear normal or may demonstrate the red-faceted slightly depressed lesion characteristic of a lamellar macular hole. There may be an overlying yellow pseudo-operculum suspended anterior to the fovea, which may be confused with a stage 1 lesion itself.[77,78,204] Lamellar macular holes do not progress to macular holes.[77,102] Moreover, posterior vitreous detachment is generally believed to confer protection from macular hole evolution,[6,8,64,77,96,204,210] although one small series of five patients was believed to develop macular hole despite a complete posterior vitreous detachment (Weiss ring and intraoperative confirmation in three of five cases).[84]

The visual acuity of stage 1 lesions ranges between 20/25 and 20/80. Initial visual acuity is believed to predict progression to full-thickness macular hole.[120,140] Recent data from the Vitrectomy for Prevention of Macular Hole Study Group revealed that eyes with stage 1 macular holes and best-corrected visual acuity between 20/50 and 20/80 had a 66% (10 of 15 eyes) rate of progression to full-thickness macular hole, whereas eyes with best-corrected visual acuity between 20/25 and 20/40 had a 30% (6 of 20 eyes) risk of progression to full-thickness macular hole.[120] Clearly, the risk of progression to macular hole is significantly higher in eyes with stage 1 macular holes with best-corrected visual acuity of 20/50 or worse. It may be that some of these eyes with worse visual acuity may have occult macular holes with umbo dehisence, which is obscured by overlying prefoveal tissue.

B. RISK FACTORS FOR FULL-THICKNESS MACULAR HOLE

While the demographic features of age-related macular hole patients are widely recognized, risk factors for development of full-thickness lesions are more controversial. The Eye Disease Case-Control Study Group reported on the demographics and risk factors for idiopathic macular hole, comparing 198 subjects with macular hole and 1,023 matched controls. Seventy-two percent of subjects with macular hole were female;[58] explanations for this female preponderance are speculative. Only 3% of subjects with idiopathic macular hole were less than 55 years of age. This study did not find an association of macular hole with hysterectomy, hypertension, or cardiovascular disease in contrast to prior reports.[140,152] Interestingly, the most significant risk factor for macular hole formation was increased plasma fibrinogen (greater than 2.95 g/L), which more than doubled the risk for macular hole formation;[58] again, explanations are speculative. Estrogen users were at a reduced risk for hole formation.[58] The Eye Disease Case-Control Study Group did not examine two ocular characteristics that have been previously been associated with macular hole formation:[151] macular retinal pigment epithelial changes (involutional macular thinning) and macular vitreous attachment.

C. STAGE 2 LESIONS

According to the revised Gass classification, stage 1B occult holes become manifest (stage 2 holes) either after early separation of the contracted prefoveolar vitreous cortex from the retina surrounding a small hole or as an eccentric can opener–like tear in the contracted prefoveolar vitreous cortex at the edge of larger stage 2 holes.[74]

The majority of stage 2 holes demonstrate progression to stages 3 and 4 macular holes with subsequent loss of vision. The most optimistic study reported a 33% resolution rate, with 67% progressing to larger stage 3 and 4 lesions.[87] With 12 months of prospective follow-up, Kim et al observed 71% progression to stages 3 or 4.[109] Hikichi et al reported a 96% (N = 48 eyes) progression of stage 2 lesions to stages 3 or 4, although only 4% remained in stage 2. No eyes demonstrated resolution during a median follow-up period of 4 years (range: 2–8 years).[95] Eighty-five percent of stage 2 eyes enlarged their hole size to greater than 400 μm and 64% experienced vitreomacular separation. Visual acuity de-

creased two or more Snellen lines during the follow-up period in 34 (71%) of 48 eyes; the prevalence of this was significantly higher in eyes with vitreomacular attachment at the final examination (28 of 34, 82%) than in eyes with vitreomacular separation at the final examination (6 of 14, 43%). These authors concluded that even though vitreomacular separation may improve the prognosis of a macular hole, stage 2 lesions usually develop an enlarged hole and lead to decreased visual acuity.[95,96] Most stage 2 holes progress and enlarge to stages 3 or 4 within 6 months.

Rarely, there may be spontaneous resolution of a full-thickness macular hole with resultant good visual acuity.[49] Stages 2, 3, or 4 macular holes may experience spontaneous resolution. Because of the infrequency of the event, it is unknown if smaller macular holes are more likely to spontaneously resolve than larger ones.

D. STAGE 3 AND 4 MACULAR HOLES

Most full-thickness macular holes greater than 400 μm retain peripheral vision but suffer loss of central vision to the level of 20/100 and worse, typically 20/100–20/400.[101] Some stage 3 or 4 lesions will enlarge their hole and a minority will undergo progressive loss of central visual acuity. Hikichi et al reported that attached vitreous and smaller macular holes (less than 400 μm) were features associated with enlargement.[93,94] They also reported that 32 (55%) of 58 eyes with a stage 3 lesion and 5 (16%) of 31 eyes with a stage 4 lesion underwent macular hole enlargement during the median follow-up period of 3 years. Visual acuity decreased two or more lines of Snellen equivalent during the follow-up period in 17 (29%) eyes with a stage 3 lesion and 4 (13%) eyes with a stage 4 lesion.[96]

Visual deterioration may be related to increasing and chronic subretinal fluid, cystoid retinal changes, or photoreceptor atrophy. Less commonly, loss of central and then peripheral vision is related to a progressive retinal detachment. This is most commonly associated with myopia 6 D or greater.[1,147,215] Progression of retinal detachment beyond the foveal area is rare in patients without high myopia or evidence of anteroposterior vitreous traction. In Aaberg's series, 6 of 81 eyes demonstrated retinal detachment, with 5 eyes greater than 6 D myopic;[1] macular holes were equally distributed between emmetropic, hyperopic, and myopic eyes. Another report revealed that retinal detachment occurred in 16 of 17 eyes, with macular hole and myopia of 6 D or greater.[215]

Occasionally, spontaneous retinal reattachment and visual improvement (5–12% of stages 3 or 4) may occur.[87,140,151,218] The mechanism of spontaneous reattachment is unclear, although two cases have been reported in association with epiretinal membrane formation[22,130] and vision improving to the 20/20–20/30 level. Patients with macular holes demonstrate on microperimetry an absolute scotomata corresponding to the hole and a relative scotomata corresponding to the surrounding neurosensory detachment.[3,182] The mechanism for visual recovery after spontaneous reattachment of the retina may be similar to that after successful surgical repair (Fig. 8).[183]

E. FELLOW EYES OF PATIENTS WITH MACULAR HOLES

Patients with a unilateral macular hole are understandably concerned about the prognosis for their fellow eye. The majority of fellow eyes will not develop a macular hole. The risk of fellow eye involvement has been reported to be from 3 to 22%.[6,33] In a large retrospective study, Lewis reported that patients with incomplete macular holes (stage 1, aborted stage 1, lamellar) or full-thickness holes had a 19% incidence of bilaterality at 48 months follow-up.[131] Normal fellow eyes have a very low incidence (0–2%) of macular hole formation, particularly if there is a pre-existent posterior vitreous detachment.[6,64,87,152,202] However, Lewis et al reported that of 32 patients with full-thickness macular holes in the first eye, 13% developed full-thickness holes in the fellow eye within 48 months.[131] Fellow eyes with macular stage 1 lesions and vitreous attachment are probably at a similar risk for hole formation as previously described (about 40%).

Focal electroretinography may further refine the prognosis of a fellow eye.[26] In a prospective study, Birch et al performed focal electroretinography in both eyes of 35 patients with a unilateral full-thickness macular hole. Abnormal fellow eye foveal electroretinography amplitude was significantly related to subsequent macular hole formation compared with fellow eyes that did not develop macular hole, suggesting that this test can provide an objective measure of macular function to help identify eyes at risk for macular hole formation.[26] At this time, we do not routinely perform focal electroretinography on normal fellow eyes but believe this intriguing data deserves further investigation.

VI. Management of Macular Hole Lesions

Because the majority of patients with macular hole suffer from unilateral loss of central vision with a preserved fellow eye, indications for intervention have been questioned.[62,207] Nevertheless, many vitreoretinal surgeons offer surgical intervention to afflicted patients because of the potential for a better visual outcome, refinements in surgical technique, and up

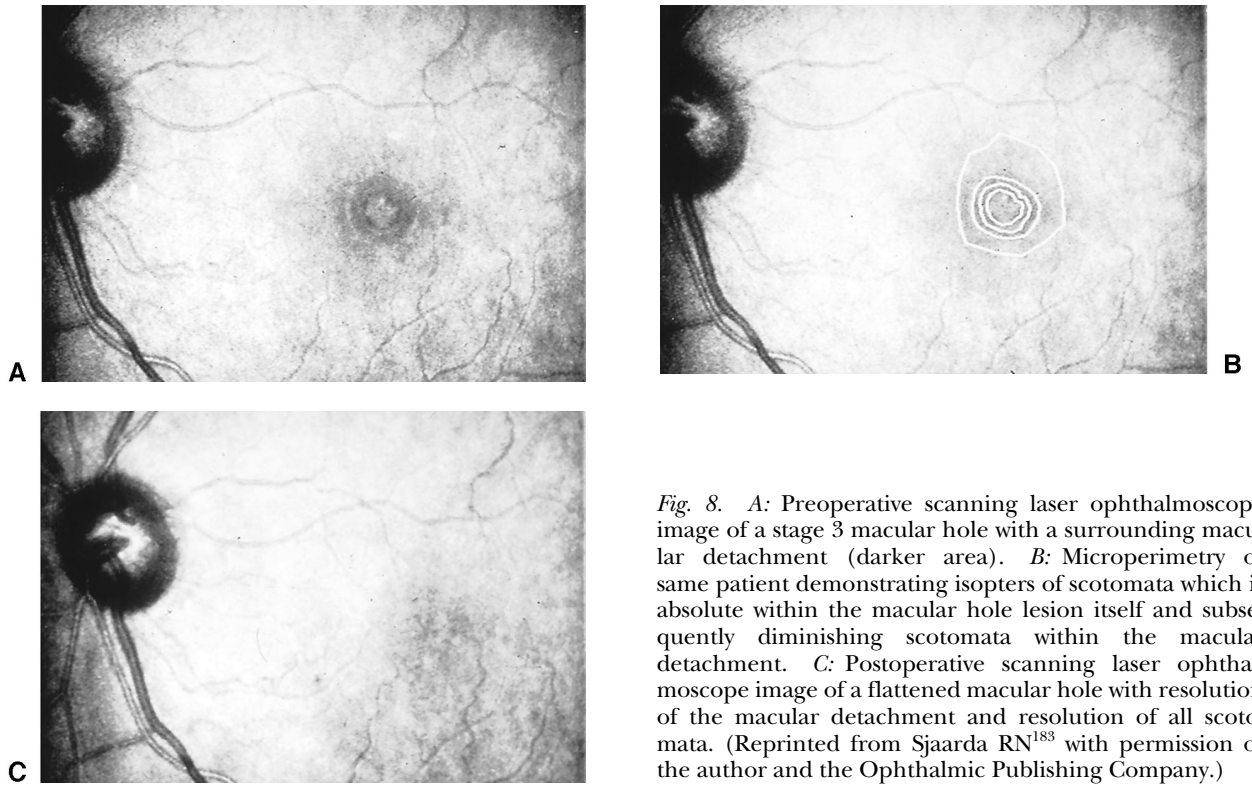


Fig. 8. A: Preoperative scanning laser ophthalmoscope image of a stage 3 macular hole with a surrounding macular detachment (darker area). *B:* Microperimetry of same patient demonstrating isopters of scotomata which is absolute within the macular hole lesion itself and subsequently diminishing scotomata within the macular detachment. *C:* Postoperative scanning laser ophthalmoscope image of a flattened macular hole with resolution of the macular detachment and resolution of all scotomata. (Reprinted from Sjaarda RN[183] with permission of the author and the Ophthalmic Publishing Company.)

to a 20% chance that the fellow eye will become affected. The first step in the management of a macular hole lesion is to reconfirm the diagnosis because pseudomacular holes are commonly misdiagnosed as full-thickness macular holes. The management of premacular hole lesions has been guided by the prospective, randomized, controlled clinical reports of the Vitrectomy for Prevention of Macular Hole Study Group.

Historically, therapy for macular holes has evolved from anxiolytics and vasodilator therapies[80] to current day strategies using intraocular gas tamponade and vitrectomy surgery. Until recently, most surgeons focused their attention on retinal detachments that were associated with macular hole and high myopia. Meyer-Schwickerath, in 1961, proposed cerclage, subretinal fluid drainage, and light laser photocoagulation employing scleral buckling techniques to flatten a macular hole.[146] Subsequent reports in the next two decades advocated variations on this theme, including y-shaped plombs,[61,125] silver clips,[115–117,168] scleral resection,[24] "armed" silicone implant[127] or buckles,[129,178] diathermy,[13,53] laser photocoagulation,[146] cryotherapy, silicone oil,[25,91] and intravitreal gas[27,28,124,126,139,144,149,150]—often without vitrectomy—to flatten the macula and associated retinal detachment. With the advent of vitrectomy techniques, macular hole-associated retinal detachments were repaired with vitrectomy and intraocular gas.[195,203] Not surprisingly, many of the subjects of these reports were greater than 6 D myopic. In 1982 Gonvers and Machemer were the first to recommend vitrectomy, intravitreal gas, and prone positioning for retinal detachments secondary to macular hole.[83] Four years later, Chigrell and Billington recommended vitrectomy and internal gas tamponade for the treatment of macular holes.[42]

A. FULL-THICKNESS MACULAR HOLE

In 1991 Kelly and Wendel reported on vitrectomy, removal of cortical vitreous and epiretinal membranes, and strict facedown gas tamponade to stabilize or improve vision in full-thickness–age-related macular holes.[107] Their hypothesis was that by removing tangential vitreous and membrane forces, they could flatten the macular hole and possibly reduce the adjacent cystic retinal changes and neurosensory macular detachment. The overall results of their initial report were a 58% anatomic success rate and visual improvement of two or more lines in 42% of eyes (73% of anatomically successful eyes) (Figure 9).

A critical surgical step is the induction of a posterior vitreous detachment with an actively aspirated (100–250 mm Hg) soft-tipped silicone suction cannula, which is swept over the retinal surface near the major retinal vascular arcades and temporal to the macula or adjacent to the optic nerve; engagement of the often invisible cortical vitreous with active suction results in the "fish strike" sign or bending of the

soft silicone cannula. However, repetitive engagement of the cannula near the optic disk could mechanically traumatize nerve fibers. Translucent hyaloid is then elevated by a combination of side-to-side and anteroposterior movements by the cannula alone or with the aid of a bent microvitreoretinal blade,[142] retinal pick, or lighted knife. Using the retinal pick or similar instrument, prepapillary elevation of the hyaloid is achieved by engaging a portion of the Weiss ring and moving from the center of the optic disk outward, just over the substance of the optic rim. Using this maneuver over several clock hours of the optic disk and rotating the instrument through the clock hours of the attachments at the optic disk will complete the Weiss ring and facilitate macular posterior hyaloid elevation. The hyaloid excision is then performed to the posterior equatorial zone. Because surface cortical vitreous can be difficult to identify, one report advocates the use of autologous blood to stain this tissue,[173] although we have not found this to be necessary. In addition, fine and often friable epiretinal membranes are removed using a microbarbed microvitreoretinal blade or diamond-dusted silicone cannula[131a] to create a surgical plane and fine end-gripping tissue forceps stripping, which often causes small retinal hemorrhages near the macular hole. The surgical goal is to remove enough of the surrounding membrane, when present, to relieve traction that could prevent flattening of the edges of the macular hole. The peripheral retina is inspected carefully for iatrogenic retinal tears, which are often not associated with sclerotomy sites and are likely related to the process of vitreous separation.[184] A total air-fluid gas exchange is performed to dessicate the vitreous cavity, and accumulated posterior retinal fluid is followed by a nonexpansile concentration of long-acting gas. It is helpful to temporarily plug the sclerotomies and wait 10 minutes or longer to remove as much vitreous fluid as possible.[170] Residual vitreous cortex will appear as a gelatinous substance on and above the surface of the retina at the time of air-fluid exchange[176] and should prompt a posterior vitreous redissection under fluid. Strict facedown positioning to position the gas bubble against the macular hole for at least 1 week and as long as 3 or 4 weeks is as important as the technical components of the procedure.

In their second report, Wendel et al improved their overall results to 73% anatomic success and 55% of patients improving two or more lines of visual acuity.[208] This group and other investigators have noted that macular hole surgery is more successful in patients with macular holes of less than 6 months duration compared with those up to 2 years or longer.[174] In a small series, one group noted that surgery on long-standing stage 3 macular holes (1 year duration) or longer can result in 58% anatomic success rate with improvement in central visual acuity, although recovery of central vision may be delayed for 6 months or longer.[159] An uncontrolled series of surgery for stage 2 macular holes demonstrated that 61% improved visual acuity, 27% remained stable, and 12% progressed to a stage 3 macular hole with worse vision;[171] 61% of these eyes had a final visual acuity of 20/50 or better.

A prospective, randomized and controlled series by the Vitrectomy for Treatment of Macular Hole Study Group for stage 2 macular holes showed that vision was improved in eyes that were operated on compared with observed eyes, using the potential acuity meter and word reading test, but not by Early Treatment Diabetic Retinopathy Study vision testing;[109] postvitrectomy cataracts were not removed in this study and may have accounted for the discrepancy in visual function as tested using Early Treatment Diabetic Retinopathy Study methods. This same group provided short-term (6 months after randomization) results for stages 3 and 4 macular holes.[68] They demonstrated some visual benefit as measured by the potential acuity meter and word reading tests and marginal benefit ($P = 0.05$) by Early Treatment Diabetic Retinopathy Study vision testing. More frequent adverse advents were noted in surgically treated versus control eyes, with the most common being macular retinal pigment epithelium changes.[17a] Compared with control eyes, eyes randomized to surgery demonstrated a progression of nuclear cataract (83%), which potentially confounds postoperative visual assessment.

Glaser et al first reported on the novel use of growth factors in the surgical management of macular holes. These investigators described using intravitreal bovine transforming growth factor-β_2 (TGF-β_2) with pars plana vitrectomy and fluid-gas exchange for full-thickness macular hole and reported anatomic success rates of about 90%.[82,128,169,189] In contradistinction to the surgical technique by Kelly and Wendel, these investigators did not strip surrounding epiretinal membranes in some cases.[128] Their surgical success rate was better with longer acting gas tamponade with 16% perfluoropropane than with air[198] but was associated with significant nuclear sclerotic cataract formation (75% requiring cataract extraction) with follow-up greater than or equal to 24 months.[197] Unfortunately, production of recombinant TGF-β_2 (nonbovine derived) did not yield similarly successful surgical results as bovine TGF-β_2 and was associated with significant elevations of intraocular pressure.[200]

Surgical maneuvers, such as peeling of the epiretinal membrane or internal limiting membrane (T. Rice, unpublished) or small radial incisions[31] surrounding the macular hole have been recommended to improve flattening of the macular rim if a macular traction membrane is difficult to delami-

nate. However, most of the membranes can be removed without resorting to retinotomy. In our experience, removal of the residual cortical vitreous and epimacular membranes seems to provide the greatest chance for anatomic success. Laser photocoagulation alone to the edge of a macular hole has been reported to help flatten the surrounding neurosensory detachment, but only 3 (17%) of 18 subjects achieved a visual acuity of 20/100 or better.[179]

Autologous blood products,[32,79,122] such as platelets, serum,[132] and plasma and commercial thrombin,[29] and other biologic modifiers have also been used to help seal macular holes, although their role in macular hole surgery remains investigational at present. These modifiers are placed on the macular hole after pars plana vitrectomy, posterior hyaloid removal, and air-fluid gas exchange. Subsequent facedown positioning is still required. Preliminary reports suggest that platelets may be a safe surgical adjunct to macular hole surgery,[122] and one small controlled series demonstrated a greater than 90% anatomic success rate with platelets compared with a 65% anatomic success rate without.[79] One report described 5 (8%) of 60 patients who developed a hypopyon without unusual pain and responded to topical steroids on the first postoperative day after administration of autologous fibrinogen and bovine thrombin (20 to 80 unit).[158] Future clinical investigations will determine the role, if any, of these surgical adjuvants particularly because adjuvants may not be necessary to achieve successful surgical results.[192a]

Controversy exists regarding the indications for treatment of a full-thickness macular hole because the majority of these subjects will not develop a macular hole in their fellow eye, and one group has noted that with careful refraction many eyes with full-thickness macular hole may enjoy better visual acuity than previously believed.[67] Hillis and Fine opine that more and longer-term data be generated with respect to potential benefits and risks of vitrectomy for macular hole surgery in light of the results reported by the Vitrectomy for Treatment of Macular Hole Study Group.[97] However, refinements in surgical techniques have clearly made recovery of central acuity possible in this group of patients. If surgical intervention is elected, the ideal surgical candidate has a recent onset, small, full-thickness macular hole with progressive loss of vision and will have no problems maintaining a facedown postoperative position. On the other hand, many patients with unilateral, symptomatic macular hole of less than 1-year duration may enjoy a significant long-term visual benefit if surgery is successful.[129a,174] Furthermore, some patients with longstanding macular holes may even experience improvement with surgery (J. T. Thompson, unpublished data). Bilateral visual function may improve after macular hole surgery, particularly if the fellow eye is abnormal.[164] Perhaps preoperative diagnostic testing, such as laser interferometry, will help select candidates with postoperative visual potential.[192] We agree that surgery for patients with very small macular holes and good vision or with questionable full-thickness defects and stable vision should be deferred until there is evidence of progression.[181]

B. COMPLICATIONS

The immediate complication for the surgical patient is the strict, 1-week, facedown positioning requested by most surgeons. Positioning difficulties due to neck, back, sinus or other disease prompt a reconsideration of macular hole surgery, although one group has demonstrated comparable anatomic success without rigorous positioning.[201] Potential surgical candidates also need to be informed about possible surgical complications, including the high rate of subsequent nuclear cataract progression (up to 81% after 2 years),[197] and at least 25% of patients will require postoperative cataract surgery.[107,171] Simultaneous cataract and macular hole surgery have been reported.[147a,201] Patients who undergo consecutive macular hole and cataract extraction surgery can enjoy improved vision, although they are not immune to complications such as late reopening of the macular hole or cystoid macular edema.[148,185]

Other surgical complications of intraocular surgery for macular hole have been reported, including retinal tears (3%),[160] rhegmatogenous retinal detachment (14%),[160] enlargement of the hole (2%),[160] late reopening (2–7%),[57,160,160a] and photic toxicity or retinal pigment epithelial alterations (1%),[17a,39,56,160,163] exudative retinal detachment,[4] glaucoma,[41] and proliferative vitreoretinopathy.[46] Clearly, some of the surgical complications are not unique to macular hole surgery, although others are related to manipulation of the macular hole and associated posterior vitreous. The 14% incidence of rhegmatogenous retinal detachment reported by Park et al is high compared with my surgical experience. The incidence of retinal detachments may be lower than reported by Park et al because that study reemphasized the need to perform a careful peripheral retinal examination with depression at the time of surgery.

Many surgeons now favor performing a fluid-gas exchange without direct contact with retinal pigment epithelium and take care to change the endoilluminator position to avoid photic toxicity. Several case series have identified visual field defects after uncomplicated vitrectomy surgery and intraocular gas tamponade for macular hole; the most common defect is dense and wedge-shaped and affects the temporal field.[30,30a,59,108,160b,162] The field defects may be symptomatic; the central vision can improve, despite peripheral field defects. The true incidence is not known because of a lack of prospective data, and the

mechanisms of this condition are not well understood. It may be related to mechanical trauma during posterior hyaloid separation or fluid-gas exchange or intraocular gas toxicity. Future studies will help elucidate this finding and determine whether this phenomenon is primarily related to macular hole surgery or is more generalized, as one report suggests.[108]

For primary surgical failures (hole not flattened), another vitrectomy may result in successful flattening of the macular hole and visual improvement.[59b,99] Late reopening of an initially successful macular hole has been observed nearly 2 years after the initial vitrectomy, and these lesions may respond to repeat vitrectomy and intraocular gas tamponade.[57] Others have suggested macular laser photocoagulation with[52] or without intraocular gas tamponade for primary[179] or recurrent macular hole failures (late reopening after primary flattening).[52]

C. PREMACULAR HOLE LESIONS

Because tangential vitreous traction is believed to play a role in the formation of macular holes, removal of cortical vitreous should reduce the rate of progression of stages 1A and 1B premacular hole lesions to full-thickness macular holes. Smiddy et al,[191] and then Jost et al,[103] reported small, uncontrolled pilot series on the technical feasibility of vitrectomy surgery for impending macular holes. In another small, uncontrolled series Chan described intravitreal injection of an expansile gas bubble without vitrectomy surgery to induce a posterior vitreous detachment with resolution of stages 1A (7 of 7) and 1B (3 of 4) premacular hole lesions.[38]

The Vitrectomy for Prevention of Macular Hole Study subsequently reported multicenter, prospective, randomized data on vitrectomy surgery and careful peeling of the cortical vitreous for presumed stages 1A and 1B lesions. A full-thickness macular hole developed in 10 (37%) of 27 patients in the vitrectomy group compared with 14 (40%) of 35 patients randomized to observation (P = 0.81). This study could not demonstrate a significant benefit of vitrectomy surgery for stages 1A and 1B lesions and the study was terminated because of low recruitment. As noted previously, this group also reported that visual acuity may be predictive of full-thickness macular hole formation.[120] At present, we do not recommend vitrectomy surgery for these premacular hole lesions, but rather suggest careful follow-up because a significant proportion will develop full-thickness macular holes within a year.

Others question the role of tangential vitreous traction in the pathogenesis of macular hole, as surgical peeling of cortical vitreous did not reduce the rate of full-thickness macular hole formation in the Vitrectomy for Prevention of Macular Hole Study.[143] It may be that some premacular hole stage 1 lesions were actually occult macular holes as noted intraoperatively by Jost et al or that the intervention may have been too late in the disease process.[50,103] The surgical procedure itself may have caused macular hole formation, although this was not a commonly recognized complication intraoperatively. On the other hand, it may be that tangential traction may only be part of the pathogenesis of this condition and other retinal, retinal pigment epithelial, or choroidal factors may also be important.[50,132a,151,202c] One small study advocated vitrectomy without premacular cortical vitreous stripping for impending macular holes.[37]

VII. Summary

The advent of vitreoretinal microsurgical techniques has sparked a renewed interest in age-related

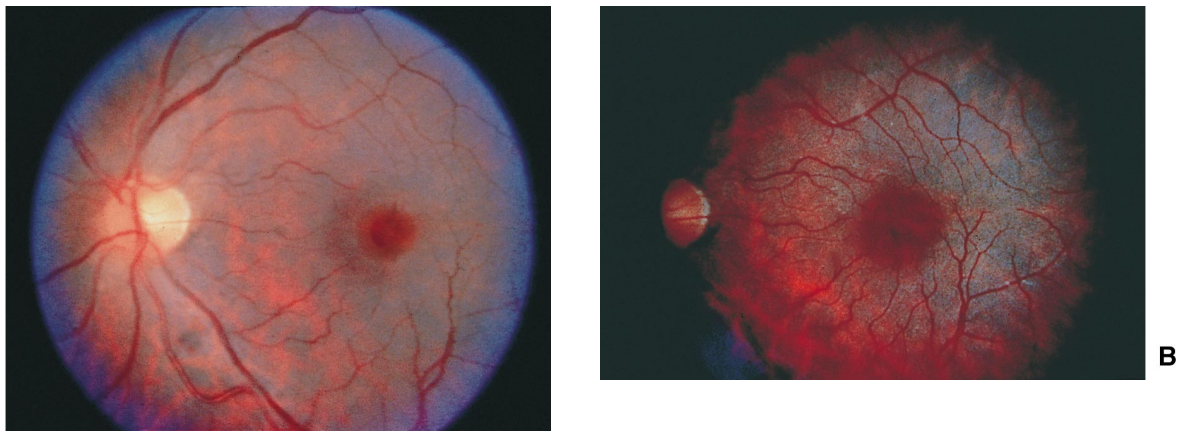


Fig. 9. A: Preoperative appearance of macular hole. Preoperatively, there is submacular fluid and elevation of the edges of the macular hole. *B:* Postoperative appearance after pars plana vitrectomy and intraocular gas tamponade. Postoperatively, the lesion is flat and the borders of the lesion are imperceptible. (Reprinted from Kelly and Wendel[107] with permission of the authors and the Ophthalmic Publishing Company.)

macular hole and, particularly, its management. Progress in management of macular hole lesions has progressed despite a probably incomplete understanding of the pathogenesis of macular hole. Although there have been a variety of theories on the pathogenesis of this condition, Gass's tangential vitreous theory has garnered recent support. This theory, in conjunction with a better understanding of the cellular components at the edges of and on the surface of macular hole lesions, including cells with contractile properties, serves as the basis for our current concepts of macular hole evolution. Tangential vitreous traction, foveal wound healing, cellular metaplasia to contractile elements, and degenerative retinal and subretinal cells all likely serve as the major influences in the pathogenesis of age-related macular hole.

Macular hole lesions are often misdiagnosed. The ophthalmologist's most valuable tool in discriminating macular hole lesions from mimickers is a careful contact lens biomicroscopic evaluation of the lesion. A positive Watzke sign or laser aiming beam test can be helpful, but these are subjective tests. Careful biomicroscopic evaluation along with the knowledge of the distinguishing clinical features of true macular holes from pseudoholes will minimize misdiagnosis.

The natural history of macular hole lesions varies. Stage 1 lesions with good visual acuity (better than 20/40) have a 30% risk for progression to a full-thickness macular hole, whereas those with worse visual acuity (20/50–20/80) have a 66% risk. The majority of stage 2 macular holes (67–98%) progress to stage 3 or 4 macular holes. Uncommonly (5–12%), full-thickness macular holes demonstrate spontaneous flattening, and improvement in vision can occur. Fellow eyes of patients with macular hole are at low risk if there are no macular changes (1–10% risk of developing macular hole), whereas fellow eye stage 1 lesions are probably at similar risk to first eye stage 1 lesions, as described previously.

The management of macular hole has evolved from an untreatable condition to a microsurgical procedure with considerable potential success. Interestingly, the Vitrectomy for Treatment of Macular Hole Study Group was unable to demonstrate a consistent short-term visual benefit for eyes with full-thickness macular hole undergoing vitrectomy surgery. Longer follow-up as well as visual function evaluation after cataract extraction may provide additional and more practical information. The surgical approach continues to evolve, however, and most surgeons favor pars plana vitrectomy with an intraocular gas tamponade, which has anatomic success rates at high as 90% and visual success rates as high as 75% of anatomically flattened cases. The intriguing issue of surgical biologic modifiers remains unsettled at this time. The spectrum of surgical complications is not unique to macular hole vitrectomy surgery, with the most common long-term complication being cataract progression. The successful macular hole surgeon is as meticulous about case selection as he or she is about surgical technique.

References

1. Aaberg TM: Macular holes. Am J Ophthalmol 69:555–562, 1970
2. Aaberg TM: Macular holes: A review. Surv Ophthalmol 15:139–162, 1970
3. Acosta F, Lashkari K, Reynaud X: Characterization of functional changes in macular holes and cysts. Ophthalmology 98:1820–1823, 1991
4. Akduman L, Del Priore LV, Kaplan HJ: Exudative retinal detachment as a complication of macular hole surgery. Ophthalmology 103 (Suppl):124, 1996
5. Akiba J, Ishiko S, Hikichi T, et al: Imaging of epiretinal membranes in macular holes by scanning laser opthalmoscopy. Am J Ophthalmol 121:177–180, 1996
6. Akiba J, Kakehashi A, Arzabe CW, Trempe CL: Fellow eyes in idiopathic macular hole cases. Ophthalmic Surg 23:594–597, 1992
7. Akiba J, Quiroz MA, Trempe CL: Role of posterior vitreous detachment in idiopathic macular holes. Ophthalmology 97:1610–1613, 1990
8. Akiba J, Yoshida A, Trempe CL: Risk of developing a macular hole (see comments). Arch Ophthalmol 108:1088–1090, 1990
9. Alexandridis E, Kohl EH: Treatment of retinal detachment with macular hole. Graefes Arch Clin Exp Ophthalmol 224:11–12, 1986
10. Allen AW, Gass JD: Contraction of a perifoveal epiretinal membrane simulating a macular hole. Am J Ophthalmol 82:684–691, 1976
11. Alt A: Remarks of holes in the macula lutea and fovea centralis with the report of a new case. Am J Ophthalmol 30:97–106, 1913
12. Alvarex-Luna RS: Edema de Berlin y agupero de la macula. Arch Soc Oftal Hisp-Amer 7:221–225, 1947
13. Amemiya T, Iida T: Results and complications of surgery of retinal detachment with a macular hole. Ophthalmologica 181:88–92, 1980
14. Amemiya T, Yoshida H: Macular hole in diabetic maculopathy. Ophthalmologica 177:188–191, 1978
15. Amsler M: Earliest symptoms of diseases of the macula. Br J Ophthalmol 37:521–537, 1953
16. Atmaca LS: Follow-up of macular holes. Ann Ophthalmol 16:1064–1065, 1984
17. Avila MP, Jalkh AE, Murakami K: Biomicroscopic study of the vitreous in macular breaks. Ophthalmology 90:1277–1283, 1983

17a. Banker AS, Freeman WR, Kim JW, et al.: Vision-threatening complications of surgery for full-thickness macular holes. Vitrectomy for Macular Hole Study Group. Ophthalmol 104:1442–1452, 1997

18. Bartsch DU, Intaglietta M, Bille JF, et al: Confocal laser tomographic analysis of the retina in eyes with macular hole formation and other focal macular diseases. Am J Ophthalmol 108:277–287, 1989

18a. Beatty S, Harrison RJ, Roche P: Bilateral macula holes resulting from spetic embolization. Am J Ophthalmol 123: 557–559, 1997

19. Bedell AJ: Photographic study of holes in macular region and associated changes. Am J Ophthalmol 10:890–894, 1927
20. Benedict WL, Shami M: Impending macular hole associated with topical pilocarpine (letter). Am J Ophthalmol 114:765–766, 1992
21. Bengisu N: Coats disease and a macular hole. Ann Oculist 201:158–162, 1968

22. Bidwell AE, Jampol LM: Macular holes and excellent visual acuity. Arch Ophthalmol 106:1350, 1988
23. Biedner B, Klemperer I, Dagan M, Yassur Y: Optic disc coloboma associated with macular hole and retinal detachment. Ann Ophthalmol 25:350–352, 1993
24. Binder S, Riss B: Advances in intraocular techniques in the treatment of retinal detachments arising from holes of the posterior pole. Br J Ophthalmol 67:147–149, 1983
25. Binder S, Zugner M, Velikay M: Does vitrectomy followed by intraocular gas tamponade offer sufficiently effective treatment of retinal detachment due to holes in the posterior pole? Int Ophthalmol 11:25–30, 1987
26. Birch DG, Jost BF, Fish GE: The focal electroretinogram in fellow eyes of patients with idiopathic macular holes. Arch Ophthalmol 106:1558–1563, 1988
27. Blankenship GW, Ibanez LS: Treatment of myopic macular hole and detachment. Intravitreal gas exchange. Ophthalmology 94:333–336, 1987
28. Blodi CF, Folk JC: Treatment of macular hole retinal detachments with intravitreal gas (letter). Am J Ophthalmol 98:811, 1984
29. Blumenkranz MS, Coll GE, Chang S, Morse LS: Use of autologous plasma-thrombin mixture as adjuvant therapy for macular hole. Ophthalmol 101 (Suppl):69, 1994
30. Boldt HC, Munden PM, Folk JC, Mehaffey MG: Visual field defects after macular hole surgery. Am J Ophthalmol 122:371–381, 1996

30a. Bopp S, Lucke K, Hille U: Peripheral visual field loss after vitreous surgery for macular hole. Graefes Arch Clin Exp Ophthalmol 235:362–371, 1997

31. Bovino JA, Marcus DF: Radial retinotomy in the macula. Retina 4:123–125, 1984
32. Bresgen M, Heimann K: Idiopathic macular foramen: new aspects of staging and possible therapeutic concepts (German). Klin Monatsbl Augenheilkd 206:2–12, 1995
33. Bronstein MA, Trempe CL, Freeman HM: Fellow eyes with macular holes. Am J Ophthalmol 92:757–761, 1981
34. Brown GC: Macular hole following rhegmatogenous retinal detachment repair. Arch Ophthalmol 106:765–766, 1988
35. Campo RV, Lewis RS: Lightning-induced macular hole. Am J Ophthalmol 97:792–794, 1984
36. Campochiaro PA, Van NE, Vinores SA: Immunocytochemical labeling of cells in cortical vitreous from patients with premacular hole lesions (see comments). Arch Ophthalmol 110:371–377, 1992
37. Chambers RB, Davidorf FH, Gresak P, Stief W: Modified vitrectomy for impending macular holes. Ophthalmic Surg 22:730–734, 1991
38. Chan CK, Wessels IF, Friedrichsen EJ: Treatment of idiopathic macular holes by induced posterior vitreous detachment. Ophthalmology 102:757–767, 1995
39. Charles S: Retinal pigment epithelial abnormalities after macular hole surgery (letter). Retina 13:176, 1993
40. Chavanne H: Pseudo-trou maculaire par electrocution. Bull Soc Ophtalmol Fr 271–275, 1958
41. Chen C: Glaucoma following macular hole surgery. Ophthalmology 103 (Suppl):124, 1996
42. Chigrell AH, Billington B: The treatment of macular holes by pars plana vitrectomy and internal SF6 exchange. Graefes Arch Clin Exp Ophthalmol 224:67–68, 1986
43. Clapp CS: Hole at the macula. Ophthal Rec 22:79–84, 1913
44. Coats G: The pathology of macular holes. Roy London Hosp Rep 17:69–96, 1907
45. Cohen SM, Gass JDM: Macular hole following severe hypertensive retinopathy. Arch Ophthalmol 112:878–879, 1994
46. Coll GE, Chang S, Lewis H: Macular hole surgery and proliferative vitreoretinopathy. Ophthalmology 103 (Suppl):125, 1996
47. Collins ET: Unusual changes in the macular region (? the results of injury). Trans Ophthal Soc UK 20:196–197, 1900
48. Croll LJ, Croll M: Hole in the macula. Am J Ophthalmol 33:248–252, 1950
49. da Cruz L, Constable IJ, Barry CJ: Spontaneous resolution of a full-thickness macular hole with good visual acuity. Arch Ophthalmol 115:130–131, 1997
50. de Bustros S: Author's reply. Ophthalmology 101:1765, 1994
51. de Bustros S: Vitrectomy for prevention of macular holes. Results of a randomized multicenter clinical trial. Vitrectomy for Prevention of Macular Hole Study Group. Ophthalmology 101:1055–1059, 1994
52. Del Priore LV, Kaplan HJ, Bonham FD: Laser photocoagulation and fluid-gas exchange for recurrent macular hole. Retina 14:381–382, 1994
53. Dellaporta A: Endodiathermy for retinal detachment with macular hole (letter). Am J Ophthalmol 95:405–407, 1983
54. Dugel PU, Smiddy WE, Byrne SF, et al: Macular hole syndromes. Echographic findings with clinical correlation. Ophthalmology 101:815–821, 1994
55. Duke-Elder WS: System of Ophthalmology. St. Louis, CV Mosby, 1967
56. Duker JS: Retinal pigment epitheliopathy after macular hole surgery (letter). Ophthalmology 100:1604–1605, 1993
57. Duker JS, Wendel RT, Patel AC, Puliafito CA: Late reopening of macular holes following initial successful vitreous surgery. Ophthalmology 101:1373–1378, 1994
58. Eye Disease Case-Control Study Group: Risk factors for idiopathic macular holes. Am J Ophthalmol 118:754–761, 1994
59. Ezra E, Arden GB, Riordan-Eva P, et al: Visual field loss following vitrectomy for stage 2 and 3 macular holes. Br J Ophthalmol 80:519–525, 1996

59a. Ezra E, Munro PM, Charteris DG, et al: Macular hole opercula. Ultrastructural features and clinicopathological correlation. Arch Ophthalmol 115:1381–1387, 1997

59b. Ezra E, Aglward WG, Gregor ZJ: Membranectomy and autologous serum for the retreatment of full-thickness macular holes. Arch Ophthalmol 115:1276–1280, 1997

60. Fekrat S, Wendel RT, de la Cruz Z, Green WR: Clinicopathologic correlation of an epiretinal membrane associated with a recurrent macular hole. Retina 15:53–57, 1995
61. Feman SS, Hepler RS, Straatsma BR: Rhegmatogenous retinal detachment due to macular hole. Management with cryotherapy and a Y-shaped sling. Arch Ophthalmol 91:371–372, 1974
62. Fine SL: Vitreous surgery for macular hole in perspective. Is there an indication? (editorial). Arch Ophthalmol 109: 635–636, 1991
63. Fish RH, Arnand R, Izbrand DJ: Macular pseudoholes: Clinical features and accuracy of diagnosis. Ophthalmology 99:1665–1670, 1992
64. Fisher YL, Slakter JS, Yannuzzi LA, Guyer DR: A prospective natural history study and kinetic ultrasound evaluation of idiopathic macular holes. Ophthalmology 101:5–11, 1994
65. Foos RY: Vitreoretinal junction; topographical variations. Invest Ophthalmol Vis Sci 11:801–808, 1972
66. Frangieh GT, Green WR, Engel HM: A histopathologic study of macular cysts and holes. Retina 1:311–336, 1981
67. Freeman WR: Vitrectomy surgery for full-thickness macular holes. Am J Ophthalmol 2:233–235, 1992
68. 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 (see comments). Arch Ophthalmol 115:11–21, 1997
69. Fuchs E: Zur veranderung der macula lutea nach contusion. Ztschr Augenheilk 6:181–186, 1901
70. Funata M, Wendel RT, de la Cruz Z, Green WR: Clinicopathologic study of bilateral macular holes treated with pars plana vitrectomy and gas tamponade. Retina 12:289–298, 1992
71. Garlikov RS, Chenoweth RG: Macular hole following topical pilocarpine. Ann Ophthalmol 7:1313–1316, 1975
72. Gass JD: Lamellar macular hole: a complication of cystoid macular edema after cataract extraction. Arch Ophthalmol 94:793–800, 1976
73. Gass JD: Clinicopathologic correlation of surgically removed macular hole opercula (letter). Am J Ophthalmol 121:453–455, 1996
74. Gass JD: Reappraisal of biomicroscopic classification of

stages of development of a macular hole. Am J Ophthalmol 119:752–759, 1995
75. Gass JD: Risk of developing macular hole (letter). Arch Ophthalmol 109:610–612, 1991
76. Gass JD: Idiopathic senile macular hole: Its early stages and pathogenesis. Arch Ophthalmol 106:629–639, 1988
77. Gass JD, Joondeph BC: Observations concerning patients with suspected impending macular holes. Am J Ophthalmol 109:638–646, 1990
78. Gass JD, VanNewkirk M: Xanthic scotoma and yellow foveolar shadow caused by a pseudo-operculum after vitreofoveal separation. Retina 12:242–244, 1992
79. Gaudric A, Massin P, Paques M, et al: Autologous platelet concentrate for the treatment of full-thickness macular holes. Graefes Arch Clin Exp Ophthalmol 233:549–554, 1995
80. Gifford SR: An evaluation of ocular angiospasm. Trans Am Ophthalmol Soc 48:19–30, 1943
81. Glacet BA, Coscas G: Full-thickness macular hole and retinal detachment complicating Best's disease. Eur J Ophthalmol 3:53–54, 1993
82. Glaser BM, Michels RG, Kuppermann BD, et al: Transforming growth factor-beta 2 for the treatment of full-thickness macular holes: A prospective randomized study. Ophthalmology 99:1162–1172, 1992
83. Gonvers M, Machemer R: A new approach to treating retinal detachment with macular hole. Am J Ophthalmol 94:468–472, 1982
84. Gordon LW, Glaser BM, Ie D, et al: Full-thickness macular hole formation with a pre-existing complete posterior vitreous detachment. Ophthalmology 102:1702–1705, 1995
85. Greven CM, Slusher MM, Czyz CN: The natural history of macular pseudoholes. Ophthalmology 103 (Suppl):124, 1996
86. Gross JG, Freeman WR: Posttraumatic yellow maculopathy. Retina 10:37–41, 1990
87. Guyer DR, de Bustros S, Diener WM, Fine SL: Observations on patients with idiopathic macular holes and cysts. Arch Ophthalmol 110:1264–1268, 1992
88. Guyer DR, Green WR: Idiopathic Macular Holes and Precursor Lesions. Proceedings of the Symposium on Retina and Vitreous, New Orleans Academy of Ophthalmology. New York, Kugler Publications, 1993, pp 135–162
89. Guyer DR, Green WR, de Bustrus S, Fine SL: Histopathologic features of idiopathic macular holes and cysts. Ophthalmology 97:1045–1051, 1990
90. Haab O: Die traumatische durchlocherung der macula lutea. Ztschr Augenheilk 3:113–126, 1900
91. Haut J, Van EG, Flammand M: Treatment of macular hole retinal detachment with silicone oil, with or without argon laser photocoagulation. Ophthalmologica 187:25–28, 1983
92. Hee MR, Puliafito CA, Wong C, et al: Optical coherence tomography of macular holes. Ophthalmology 102:748–756, 1995
93. Hikichi T, Akiba J, Trempe CL: Effect of the vitreous on the prognosis of full-thickness idiopathic macular hole. Am J Ophthalmol 116:273–278, 1993
94. Hikichi T, Trempe CL: Risk of decreased visual acuity in full-thickness idiopathic macular holes. Am J Ophthalmol 116:708–712, 1993
95. Hikichi T, Yoshida A, Akiba J, et al: Prognosis of stage 2 macular holes. Am J Ophthalmol 119:571–575, 1995
96. Hikichi T, Yoshida A, Akiba J, Trempe CL: Natural outcomes of Stage 1, 2, 3, and 4 idiopathic macular holes (see comments). Br J Ophthalmol 79:517–520, 1995
97. Hillis A, Fine SL: Verdict on macular hole surgery: More data needed (editorial). Arch Ophthalmol 115:112, 1997
98. Hruby K: Slit lamp examination of vitreous and retina. Baltimore, Williams and Wilkins, 1967
99. Ie D, Glaser BM, Thompson JT, et al: Retreatment of full-thickness macular holes persisting after prior mitrectomy: a pilot study. Ophthalmology 100:1787–1793, 1993
100. Jaffe NS: Vitreous traction at the posterior pole of the fundus due to alterations in the vitreous posterior. Trans Am Acad Ophthalmol Otolaryng 71:642–652, 1967
101. James M, Feman SS: Macular holes. Graefes Arch Clin Exp Ophthalmol 215:59–63, 1980
102. Johnson RN, Gass JD: Idiopathic macular holes: Observations, stages of formation, and implications for surgical intervention. Ophthalmology 95:917–924, 1988
103. Jost BF, Hutton WL, Fuller DG, et al: Vitrectomy in eyes at risk for macular hole formation. Ophthalmology 97:843–847, 1990
104. Kakehashi A, Schepens CL, Akiba J, et al: Spontaneous resolution of foveal detachments and macular breaks. Am J Ophthalmol 120:767–775, 1995
105. Kakehashi A, Schepens CL,Trempe CL: Vitreomacular observations. II. Data on the pathogenesis of idiopathic macular breaks. Graefes Arch Clin Exp Ophthalmol 234:425–433, 1996
106. Kakehashi A, Schepens CL, Trempe CL: Vitreomacular observations. I. Vitreomacular adhesion and hole in the premacular hyaloid. Ophthalmology 101:1515–1521, 1994
107. Kelly NE, Wendel RT: Vitreous surgery for idiopathic macular holes: Results of a pilot study (see comments). Arch Ophthalmol 109:654–659, 1991
108. Kerrison JB, Haller JA, Elman M, Miller NR: Visual field loss following vitreous surgery. Arch Ophthalmol 114:564–569, 1996
109. Kim JW, Freeman WR, Azen SP, et al: Prospective randomized trial of vitrectomy or observation for stage 2 macular holes. Am J Ophthalmol 121:605–614, 1996
110. Kipp CJ: Macular holes: a clinical contribution. Trans Am Ophthalmol Soc 11:518–528, 1908
111. Kiryu J, Shahidi M, Ogura Y, et al: Illustration of the stages of idiopathic macular holes by laser biomicroscopy. Arch Ophthalmol 113:1156–1160, 1995
112. Kishi S, Demaria C, Shimizu K: Vitreous cortex remnants at the fovea after spontaneous vitreous detachment. Int Ophthalmol 9:253–260, 1986
113. Kishi S, Kamei Y, Shimizu K: Tractional elevation of Henle's fiber layer in idiopathic macular holes. Am J Ophthalmol 120:486–496, 1995
114. Klein BR, Hiner CJ, Glaser BM, et al: Fundus photographic and fluorescein angiographic characteristics of pseudoholes of the macula in eyes with epiretinal membranes. Ophthalmology 102:768–774, 1995
115. Kloti R: Surgical technique with a silver clamp in detachment caused by a macular hole. Bibl Ophthalmol 70:246–252, 1966
116. Kloti R: Silver clip for central retinal detachments with macular hole. Mod Probl Ophthalmol 12:330–336, 1974
117. Kloti R: An operating method for retinal detachment due to macular holes. Ophthalmologica 148:42–56, 1964
118. Knapp H: Ueber isolerte zerreissungen der aderhaut in folge von traumen auf dem augapfel. Arch Augenklinik 1:6–29, 1869
119. Kokame GT: Clinical correlation of ultrasonographic findings in macular holes. Am J Ophthalmol 119:441–451, 1995
120. Kokame GT, de Bustros S: Visual acuity as a prognostic indicator in Stage I macular holes. The Vitrectomy for Prevention of Macular Hole Study Group. Am J Ophthalmol 120:112–114, 1995
121. Kornzweig AL, Feldstein M: Studies of the eye in old age. II. Hole in the macula: A clinico-pathologic study. Am J Ophthalmol 33:243–247, 1950
122. Korobelnik JF, Hannouche D, Belayachi N, et al: Autologous platelet concentrate as an adjunct in macular hole healing: a pilot study. Ophthalmology 103:590–594, 1996
123. Kuhnt H: Uber eine eigenthumliche veranderung der netzhaut ad maculam (retinitis atrophicans sive rareficans centralis). Ztschr Augenheilk 3:105–112, 1900
124. Kuriyama S, Matsumura M, Harada T, et al: Surgical techniques and reattachment rates in retinal detachment due to macular hole (see comments). Arch Ophthalmol 108:1559–1561, 1990
125. Laatikainen L, Harju H: Macular hole and retinal detachment. Acta Ophthalmol (Copenh) 61:337–342, 1983
126. Lai YK: Treatment of macular hole retinal detachment (see comments). Br J Ophthalmol 74:201–202, 1990
127. Landolfo V, Albini L, Romano A: Macular hole-induced retinal detachment: treatment with an "armed-silicone" implant. Ophthalmic Surg 17:810–812, 1986

128. Lansing MB, Glaser BM, Liss H, et al: The effect of pars plana vitrectomy and transforming growth factor-beta 2 without epiretinal membrane peeling of full-thickness macular holes. Ophthalmology 100:868–871, 1993
129. Leaver PK, Cleary PE: Macular hole and retinal detachment. Trans Ophthalmol Soc UK 95:145–147, 1975
129a. Leonard RE, Smiddy WE, Flynn HW, Fever W: Long-term visual outcomes in patients with successful macular hole surgery. Ophthalmol 104:1648–1652, 1997
130. Lewis H, Cowan GM, Straatsma BR: Apparent disappearance of a macular hole associated with development of an epiretinal membrane. Am J Ophthalmol 102:172–175, 1986
131. Lewis ML, Cohen SM, Smiddy WE, Gass JD: Bilaterality of idiopathic macular holes. Graefes Arch Clin Exp Ophthalmol 234:241–245, 1996
131a. Lewis JM, Park I, Ohji M, et al: Diamond-dusted silicone cannula for epiretinal membrane separation during vitreous surgery. Am J Ophthalmol 124:552–554, 1997
132. Liggett PE, Skolik SA, Horio B, et al: Human autologous serum for the treatment of full-thickness macular holes. Ophthalmology 102:1071–1076, 1993
132a. Lipham WJ, Smiddy WE: Idiopathic macular hole following vitrectomy: implications for pathogenesis. Ophthalmic Surg Lasers 28:633–639, 1997
133. Lister W: Holes in the retina and their clinical significance. Br J Ophthalmol 8:1–20, 1924
134. Madreperla SA, Geiger GL, Funata M, et al: Clinicopathologic correlation of a macular hole treated by cortical vitreous peeling and gas tamponade. Ophthalmology 101:682–686, 1994
135. Madreperla SA, McCuen BW, Hickingbotham D, Green WR: Clinicopathologic correlation of surgically removed macular hole opercula. Am J Ophthalmol 120:197–207, 1995
136. Manschot WA, von Winning CH: Hole in the macula due to syphilis. 36:261–262, 1953
137. Margherio RR, Schepens CL: Macular breaks. I. Diagnosis, etiology, and observations. Am J Ophthalmol 74:219–232, 1972
138. Martinez J, Smiddy WE, Kim J, Gass JD: Differentiating macular holes from macular pseudoholes. Am J Ophthalmol 117:762–767, 1994
139. Matsumura M, Kuriyama S, Harada T, et al: Surgical techniques and visual prognosis in retinal detachment due to macular hole. Ophthalmologica 204:122–133, 1992
140. McDonnell PJ, Fine SL, Hillis AI: Clinical features of idiopathic macular cysts and holes. Am J Ophthalmol 93:777–786, 1982
141. Mehta M, Katsumi O, Tetsuka S, et al: Best's macular dystrophy with a macular hole. Acta Ophthalmol (Copenh) 69:131–134, 1991
142. Mein CE, Flynn HJ: Recognition and removal of the posterior cortical vitreous during vitreoretinal surgery for impending macular hole. Am J Ophthalmol 111:611–613, 1991
143. Melberg NS, Williams DF: More on macular holes. Ophthalmology 101:1764–1765, 1994
144. Menchini U, Scialdone A, Visconti C, Brancato R: Pneumoretinopexy in the treatment of retinal detachment with macular hole. Int Ophthalmol 12:213–215, 1988
145. Mete UO, Karaaslan C, Ozbilgin MK, et al: Alport's syndrome with bilateral macular hole. Acta Ophthalmologica Scand 74:77–80, 1996
146. Meyer-Schwickerath G: Indications and limitations of light coagulation of the retina. Trans Am Ophthalmol Soc 63:725–738, 1959
147. Mikuni M, Kobayashi S, Yaoeda H: Treatment of retinal detachment with macular hole. Nippon Ganka Kiyo 18:659–668, 1967
147a. Miller JH, Googe JM, Hoskins JC: Combined macular hole and cataract surgery. Am J Ophthalmol 123:705–707, 1997
148. Miller-Meeks MJ, Simpson JL: Outcomes of cataract extraction in previously vitrectomized eyes for repair of macular hole. Ophthalmology 103 (Suppl):124, 1996
149. Miyake Y: A simplified method of treating retinal detachment with macular hole: Long-term follow-up. Arch Ophthalmol 104:1234–1236, 1986
150. Miyake Y: A simplified method of treating retinal detachment with macular hole. Arch Ophthalmol 97:243–245, 1984
151. Morgan CM, Schatz H: Involutional macular thinning: A premacular hole condition. Ophthalmology 93:153–161, 1986
152. Morgan CM, Schatz H: Idiopathic macular holes. Am J Ophthalmol 99:437–444, 1985
153. Munoz FJ, Rebolleda G, Cores FJ, Bertrand J: Congenital retinal arteriovenous communication associated with a full-thickness macular hole. Acta Ophthalmol (Copenh) 69:117–120, 1991
154. Noble KG, Chang S: Adult vitelliform macular degeneration progressing to full-thickness macular hole (letter). Arch Ophthalmol 109:325, 1991
155. Noyes HD: Detachment of the retina, with laceration at the macula lutea. Trans Am Ophthalmol Soc 1:128–129, 1871
156. Ogilvie FM: On one of the results of concussion injuries of the eye ("holes" at the macula). Trans Ophthalmol Soc UK 20:202–229, 1900
157. Ogura Y, Shahidi M, Mori MT, et al: Improved visualization of macular hole lesions with laser biomicroscopy. Arch Ophthalmol 109:957–961, 1991
158. Olsen TW, Sternber P, Martin DF, et al: Postoperative hypopyon after intravitreal bovine thrombin for macular hole surgery. Am J Ophthalmol 121:575–577, 1996
159. Orellana J, Lieberman RM: Stage III macular hole surgery. Br J Ophthalmol 77:555–558, 1993
160. Park SS, Marcus DM, Duker JS, et al: Posterior segment complications after vitrectomy for macular hole. Ophthalmology 102:775–781, 1995
160a. Pasques M, Massin P, Santiago PY, et al: Late reopening of successfully treated macular holes. Br J Ophthalmol 81: 658–662, 1997
160b. Pasques M, Passin P, Santiago PY, et al: Visual field loss after vitrectomy for full-thickness macular holes. Am J Ophthalmol 124:88–94, 1997
161. Patel B, Duvall J, Tullo AB: Lamellar macular hole associated with idiopathic juxtafoveolar telangiectasia. Br J Ophthalmol 72:550–551, 1988
162. Pendergast SD, McCuen BW: Visual field loss after macular hole surgery. Ophthalmology 103:1069–1077, 1996
163. Poliner LS, Tornambe PE: Retinal pigment epitheliopathy after macular hole surgery (see comments). Ophthalmology 99:1671–1677, 1992
164. Polk TD, Smiddy WE, Flynn HW Jr: Bilateral visual function after macular hole surgery. Ophthalmology 103:422–426, 1996
165. Puliafito C, Hee M, Lin C, et al: Imaging of macular diseases with optical coherence tomography. Ophthalmology 102:217–229, 1995
166. Reese AB, Jones IS, Cooper WC: Macular changes secondary to vitreous traction. Am J Ophthalmol 64:544–549, 1967
167. Rosen E: Solar retinitis. Br J Ophthalmol 32:23–35, 1948
168. Rosengren B: The silver plomb method in macular holes. Trans Ophthalmol Soc UK 86:49–53, 1966
169. Rubin JS, Glaser BM, Thompson JT, et al: Vitrectomy, fluid-gas exchange and transforming growth factor beta-2 for the treatment of traumatic macular holes. Ophthalmology 102:1840–1845, 1995
170. Rubin JS, Thompson JT, Sjaarda RN, et al: Efficacy of fluid-air exchange during pars plana vitrectomy. Retina 15:291–294, 1995
171. Ruby AJ, Williams DF, Grand MG, et al: Pars plana vitrectomy for treatment of stage 2 macular holes. Arch Ophthalmol 112:359–364, 1994
172. Runge PE, Wyhinny GJ: Macular hole secondary to pneumatic retinopexy: Case report. Arch Ophthalmol 106:586–587, 1988
173. Ryan EA, Lee S, Chern S: Use of intravitreal autologous blood to identify posterior cortical vitreous in macular hole surgery. Arch Ophthalmol 113:822–823, 1995
174. Ryan EH, Gilbert HD: Results of surgical treatment of recent-onset full-thickness idiopathic macular holes. Arch Ophthalmol 112:1545–1553, 1994
175. Samuels B: Cystic degeneration of the retina. Arch Ophthalmol 4:476–486, 1930
176. Saxena S, Melberg NS, Thomas MA: Management of idiopathic macular holes. Ophthalmic Surg Lasers 27:618–627, 1996

177. Schachat AP, de la Cruz Z, Green WR, Patz A: Macular hole and retinal detachment in Best's disease. Retina 5:22–25, 1985
178. Schepens CL, Okamura ID, Brockhurst RJ: The scleral buckling procedures. I. Surgical techniques and management. Arch Ophthalmol 58:797–811, 1957
179. Schocket SS, Lakhanpal V, Xiaoping M, et al: Laser treatment of macular holes. Ophthalmology 95:574–582, 1988
180. Siam A: Macular hole with central retinal detachment in high myopia with posterior staphyloma. Br J Ophthalmol 53:62–63, 1969
181. Sjaarda RN: Macular hole. Int Ophthalmol Clin 35:105–122, 1995
182. Sjaarda RN, Frank DA, Glaser BM, et al: Assessment of vision in idiopathic macular holes with macular microperimetry using the scanning laser ophthalmoscope. Ophthalmology 100:1513–1518, 1993
183. Sjaarda RN, Frank DA, Glaser BM, et al: Resolution of an absolute scotoma and improvement of relative scotomata after successful macular hole surgery. Am J Ophthalmol 116:129–139, 1993
184. Sjaarda RN, Glaser BM, Thompson JT, et al: Distribution of iatrogenic retinal breaks in macular hole surgery. Ophthalmology 102:1387–1392, 1995
185. Sjaarda RN, Thompson JT, Murphy RP: Visual outcome following consecutive macular hole surgery and cataract extraction. Ophthalmology 103 (Suppl):124, 1996
186. Slezak H: On findings resembling holes and cysts of the posterior pole. Graefes Arch Klin Exp Ophthalmol 173:168–174, 1967
187. Smiddy WE: Atypical presentations of macular holes (see comments). Arch Ophthalmol 111:626–631, 1993
188. Smiddy WE, Gass JD: Masquerades of macular holes. Ophthalmic Surg 26:16–24, 1995
189. Smiddy WE, Glaser BM, Thompson JT, et al: Transforming growth factor-beta 2 significantly enhances the ability to flatten the rim of subretinal fluid surrounding macular holes: Preliminary anatomic results of a multicenter prospective randomized study. Retina 13:296–301, 1993
190. Smiddy WE, Michels RG, de Bustros S, et al: Histopathology of tissue removed during vitrectomy for impending idiopathic macular holes. Am J Ophthalmol 108:360–364, 1989
191. Smiddy WE, Michels RG, Glaser BM, de Bustros S: Vitrectomy for impending idiopathic macular holes. Am J Ophthalmol 105:371–376, 1988
192. Smiddy WE, Thomley ML, Knighton RW, Feuer WJ: Use of the potential acuity meter and laser interferometer to predict visual acuity after macular hole surgery. Retina 14:305–309, 1994
192a. Smiddy WE, Pimentel S, Williams GA: Macular hole surgery without using adjunctive additives. Ophthalmic Surg Lasers 28:713–717, 1997
193. Smith RG, Hardman LSJ, Galloway NR: Visual performance in idiopathic macular holes. Eye 4:190–194, 1990
194. Smith T, Magargal LE, Donoso LA, et al: Choroidal neovascularization in an eye with a macular hole. Ann Ophthalmol 21:331–332, 1989
195. Stirpe M, Michels RG: Retinal detachment in highly myopic eyes due to macular holes and epiretinal traction. Retina 10:113–114, 1990
196. Thach AB, Lopez PF, Snady-McCoy LC, et al: Accidental Nd:YAG laser injuries to the macula. Am J Ophthalmol 119:767–773, 1995
197. Thompson JT, Glaser BM, Sjaarda RN, Murphy RP: Progression of nuclear sclerosis and long-term visual results of vitrectomy with transforming growth factor beta-2 for macular holes. Am J Ophthalmol 119:48–54, 1995
198. Thompson JT, Glaser BM, Sjaarda RN, et al: Effects of intraocular bubble duration in the treatment of macular holes by vitrectomy and transforming growth factor-beta 2. Ophthalmology 101:1195–1200, 1994
199. Thompson JT, Hiner CJ, Glaser BM, et al: Fluorescein angiographic characteristics of macular holes before and after vitrectomy with transforming growth factor beta-2. Am J Ophthalmol 117:291–301, 1994
200. Thompson JT, Sjaarda RN, Glaser BM, Murphy RP: Increased intraocular pressure after macular hole surgery. Am J Ophthalmol 121:615–622, 1996
201. Tornambe PE, Poliner LS, Grote KD: Macular hole surgery without face-down positioning. A pilot study. Retina 17:179–185, 1997
202. Trempe CL, Weiter JJ, Furukawa H: Fellow eyes in cases of macular hole: Biomicroscopic study of the vitreous. Arch Ophthalmol 104:93–95, 1986
202a. Tsujikawa M, Ohji M, Fujikado T, et al: Differentiating full-thickness macular holes from impending macular holes and macular pseudoholes. Br J Ophthalmol 81:117–122, 1997
202b. Uffer S, Zografos L: Macular hole in a case of choroidal melanoma. Eur J Ophthalmol 7:115–118, 1997
202c. Tsujikawa M, Saito Y, Lewis JM, Tano Y: Secondary vitrectomy for the treatment of macular holes occuring after vitrectomy. Ophthalmis Surg Lasers 28:336–337, 1997
203. Vallat M: Surgical treatment of retinal detachment from macular hole. Graefes Arch Clin Exp Ophthalmol 224:238–239, 1986
204. Van Newkirk MR, Gass JDM, Callanan D, et al: Follow-up and ultrasonagraphic examination of patients with macular pseudo-operculum. Am J Ophthalmol 117:13–18, 1994
205. Watzke RC, Allen L: Subjective slitbeam sign for macular disease. Am J Ophthalmol 68:449–453, 1969
206. Weinberger D, Stiebel H, Gaton DD, et al: Three dimensional measurements of idiopathic macular holes using a scanning laser tomograph. Ophthalmology 102:1445–1449, 1995
207. Weingeist TA: Surgical management of idiopathic macular holes. Ophthalmology 100:1607–1608, 1993
208. Wendel RT, Patel AC, Kelly NE, et al: Vitreous surgery for macular holes (see comments). Ophthalmology 100:1671–1676, 1993
209. Williamson FA: Two cases of thrombosis of the retinal vein, one showing a hole, the other a star at the macula. Br J Ophthalmol 6:67–73, 1922
210. Wiznia RA: Reversibility of the early stages of idiopathic macular holes. Am J Ophthalmol 107:241–245, 1989
211. Woods DO: Idiopathic macular hole. J Ophthalmic Nurs Tech 14:57–66, 1995
212. Worst JGF: The bursa intravitrealis premacularis, in New Developments in Ophthalmology, The Hague, Junk, 1976, pp 275–279
213. Worst JGF: Cisternal systems of the fully developed vitreous body in the young adult. Trans Ophthalmol Soc UK 97:550–554, 1977
214. Wurdemann HV: The formation of a hole in the macula: Light burn from exposure to electric welding. Am J Ophthalmol 19:457–460, 1936
215. Yaoeda H: Clinical observation on macular hole. Nippon Ganka Gakkai Zasshi 71:1723–1736, 1967
216. Yooh HS, Brooks HL Jr, Capone A Jr, et al: Ultrastructural features of tissue removed during idiopathic macular hole surgery. Am J Ophthalmol 122:67–75, 1996
217. Yoshioka H: Clinical studies on macular hole. III. On the pathogenesis of the senile macular hole. Nippon Ganka Gakkai Zasshi 72:575–584, 1968
218. Yuzawa M, Watanabe A, Takahashi Y, Matsui M: Observation of idiopathic full-thickness macular holes: follow-up observation. Arch Ophthalmol 112:1051–1056, 1994
219. Zeeman WPC: Uber Loch-und cystenbildung der fovea Centralis. Graefes Arch Clin Exp Ophthalmol 80:259–269, 1912
220. Zentmayer W: Hole at the macula. Ophthalmol Rec 18: 198–200, 1909

Outline

I. Historical associations and theories of pathogenesis
   A. Traumatic theory
   B. Cystoid degeneration theory

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