Reappraisal of Biomicroscopic Classification of Stages of Development of a Macular Hole

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• PURPOSE: To update the biomicroscopic classification and anatomic interpretations of the stages of development of age-related macular hole and provide explanations for the remarkable recovery of visual acuity that occurs in some patients after vitreous surgery.

• METHODS: Recent biomicroscopic observations of various stages of macular holes are used to postulate new anatomic explanations for these stages.

• RESULTS: Biomicroscopic observations include the following: (1) the change from a yellow spot (stage 1-A) to a yellow ring (stage 1-B) during the early stages of foveal detachment is unique to patients at risk of macular hole; (2) the prehole opacity with a small stage 2 hole may be larger than the hole diameter; and (3) the opacity resembling an operculum that accompanies macular holes is indistinguishable from a pseudo-operculum found in otherwise normal fellow eyes.

• CONCLUSIONS: The change from a yellow spot (stage 1-A) to a yellow ring (stage 1-B) is caused primarily by centrifugal displacement of retinal receptors after a dehiscence at the umbo. The hole may be hidden by semiopaque contracted prefoveolar vitreous cortex bridging the yellow ring (stage 1-B occult hole). Stage 1-B 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. Most prehole opacities probably contain no retinal receptors (pseudo-opercula). Surgical reattachment of the retina surrounding the hole and centripetal movement of the foveolar retina induced by gliosis may restore foveal anatomy and function to near normal.

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KELLY AND WENDELL[1] AND OTHERS[2-4] HAVE REPORTED excellent recovery of visual acuity after vitrectomy in some patients with age-related macular hole. As many as 48% of patients undergoing surgery may regain visual acuity of 20/40 or better.[4] The rationale for the surgery and the presumed explanation for its success was reattachment of the retina surrounding the macular hole. It seems unlikely, however, that reattachment of the 200- to 500-μm-wide rim of retinal detachment surrounding a 400- to 500-μm defect in the foveolar retina can be the only explanation for the remarkable visual improvement that occurs in some patients after surgery.

The present classification of stages of macular hole development is based largely on biomicroscopic observations and presumed anatomic changes, not clinicopathologic correlations.[5] Previous anatomic interpretations of these stages have suggested that most macular holes develop as the result of a 360-degree tear in the peripheral foveola, with loss of the central retina in formation of an operculum, which is demonstrable in approximately 75% of macular holes.[5]

The purposes of this report are to update the biomicroscopic classification and anatomic interpretation of the stages of development of age-related macular holes and to provide possible explanations for the unexpected good visual results after surgical treatment of patients with this disorder. This reinterpretation of biomicroscopic observations suggests the following: (1) that most macular holes begin as an occult central neurosensory retinal dehiscence at the umbo followed

by centrifugal retraction and concentration of the nearly full complement of retinal receptors, (2) that this mechanism of hole formation is usually accompanied by the appearance of a prehole opacity consisting of the contracted and condensed vitreous cortex but no retinal receptor cells (pseudo-operculum), and (3) that a peripheral foveolar tear in the neurosensory retina with operculum formation probably occurs infrequently.

The following key concepts redefine the anatomic interpretation of the biomicroscopic classification: (1) while spontaneous contraction and condensation of the vitreous cortex probably involve a broad area of the posterior vitreoretinal interface, they are focally intense in the region of the foveolar and perifoveolar area; (2) this focal condensation of the prefoveolar vitreous cortex, which is normally transparent, causes it, in most cases, to become semitransparent and biomicroscopically visible as an interface, when it bridges a macular hole, or as a prefoveolar opacity indistinguishable from an operculum, after vitreofoveal separation; (3) the retinal xanthophyll, which is highly concentrated within the retinal receptors comprising the 400- to 500-μm-diameter foveolar retina, is most likely responsible for the yellow spot seen in stage 1-A lesions; and (4) the yellow ring of stage 1-B lesions, particularly in its later stages of development, is probably primarily caused by centrifugal displacement of the foveolar receptor cells with xanthophyll and not by displacement of the xanthophyll alone.

MATERIAL AND METHODS

SINCE PUBLICATION OF THE BIOMICROSCOPIC CLASSIFICATION of age-related macular holes in 1987, I have examined more than 100 patients with various stages of macular hole formation.

RESULTS

ALTHOUGH A YELLOW SPOT IN THE CENTER OF THE fovea may occur biomicroscopically in any disorder that causes serous foveal retinal detachment, the change from a yellow spot (stage 1-A) to a yellow ring (stage 1-B) is peculiar to foveal detachment occurring in patients at risk for developing a macular hole. Biomicroscopic evidence of a full-thickness macular hole may appear initially as (1) a small round central hole in the center of the yellow ring in the absence of a prehole vitreous opacity, (2) as a round central hole associated with a prehole vitreous opacity that may be larger in diameter than the hole, and (3) most often as an eccentric hole beginning at the inner margin of the yellow ring and later extending 360 degrees, to form a prehole vitreous opacity smaller in diameter than the hole. Approximately 75% of fully developed macular holes are associated with a prehole opacity resembling an operculum. These opacities are indistinguishable biomicroscopically from pseudo-opercula that occur after spontaneous vitreofoveal separation in eyes with normal function and biomicroscopic appearance.

Figure 1 illustrates diagrammatically the presumed anatomy of the various stages of macular hole development. The Table summarizes the biomicroscopic classification of stages of development of a macular hole, as well as the old and new anatomic interpretation of these stages. Spontaneous tangential contraction of the external part of the prefoveolar cortical vitreous detaches the foveolar retina, and a yellow spot appears (stage 1-A hole; Fig 1B). As the foveal retina elevates to the level of the surrounding thick perifoveal retina, the retinal receptor layer is stretched or elongated, and thinning of the foveolar retina around the umbo causes a change from yellow spot to a small donut-shaped yellow ring lesion (stage 1-B, impending macular hole; Fig. 1C). This change from a yellow spot to a ring is followed by a break in the continuity of the receptor cell layer at the umbo, structurally the weakest point in the retina. The retinal receptors, their radiating nerve fibers, and the xanthophyll retract centrifugally beneath the contracted vitreous cortex, and the yellow ring enlarges and develops a more well defined central semitranslucent zone (stage 1-B lesion, occult macular hole; Figs. 1D and 2, top left). Initially, the internal limiting membrane of the foveolar retina and the thin layer of horizontally oriented Mueller cell processes separating it from the retinal receptor cells may not be involved in the central retinal break. Regardless, as long as the contracted prefoveolar vitreous cortex bridges the hole, it may be visible biomicroscopically as a semitranslucent interface. Thus the change from a stage

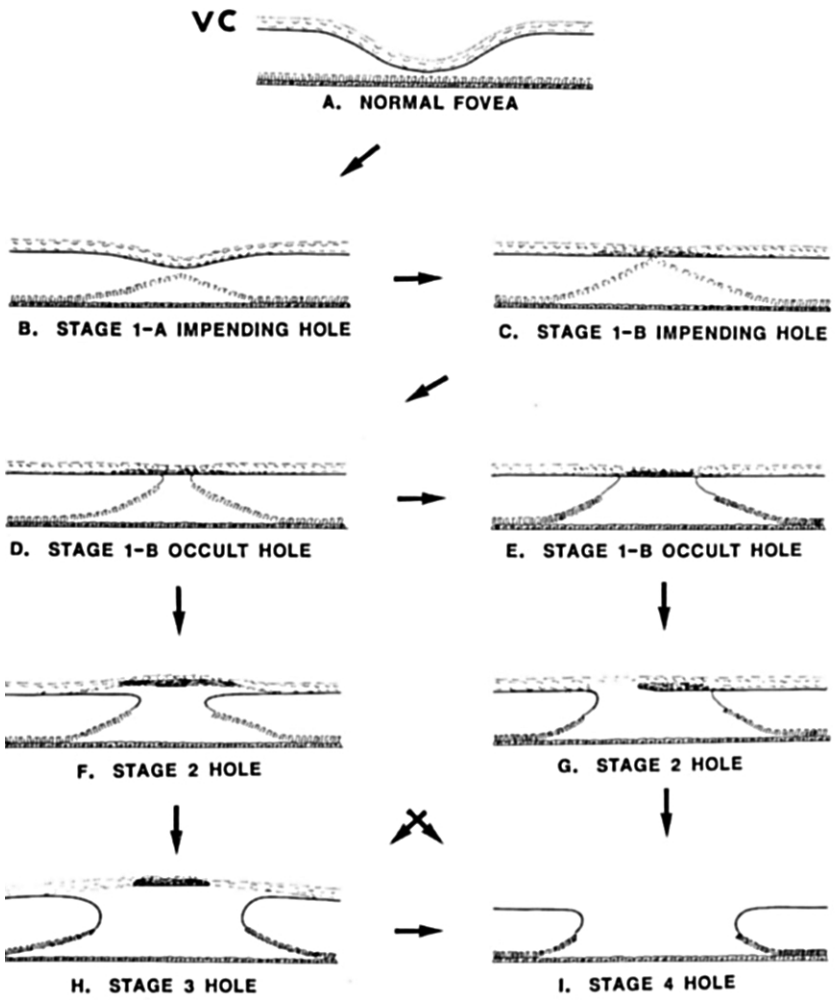

Fig. 1 (Gass). Stages of development of a senile macular hole. A, Normal fovea. Layer of vitreous cortex (vc) lying on internal limiting membrane of retina. B, Stage 1-A impending hole. Early contraction of outer part of vitreous cortex with foveolar detachment. C, Stage 1-B impending hole. Further vitreous contraction and condensation of the prefoveolar vitreous cortex with foveal detachment. D and E, Stage 1-B 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.

1-B impending hole to a stage 1-B occult hole cannot be detected biomicroscopically. Reactive proliferation of Mueller cells and retinal astrocytes occurring within the area of the receptor cell dehiscence may contribute to the opacification of the tissue bridging the defect and, in some cases, may cause ruffled edges of the retinal dehiscence surrounded by fine radiating retinal folds (Fig. 2, top left). Spontaneous vitreofoveal separation may occur soon after the central retinal dehiscence, and the contracted prefoveolar vitreous cortex becomes visible as a semitranslucent prehole opacity lying anterior to a small foveolar hole (stage 2 hole; Fig. 1F). Initially the diameter of this opacity is often larger than that of the foveolar hole. In a few patients with early stage 1-B lesions, separation of the prefoveolar vitreous cortex may be accompanied by avulsion of part of the foveolar retina and by true operculum formation. Biomicroscopy, however, cannot determine the presence or absence of retinal tissue in the prehole opacity. In some patients,

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.

the contracted prefoveolar vitreous cortex, either while it remains attached to and bridges the macular hole or after it separates from the perifoveolar retina, may be transparent and undetectable biomicroscopically. In such cases very small stage 2 holes without a prehole opacity may be evident. In most patients, however, the contracted vitreous cortex is semitransparent and remains attached to the inner

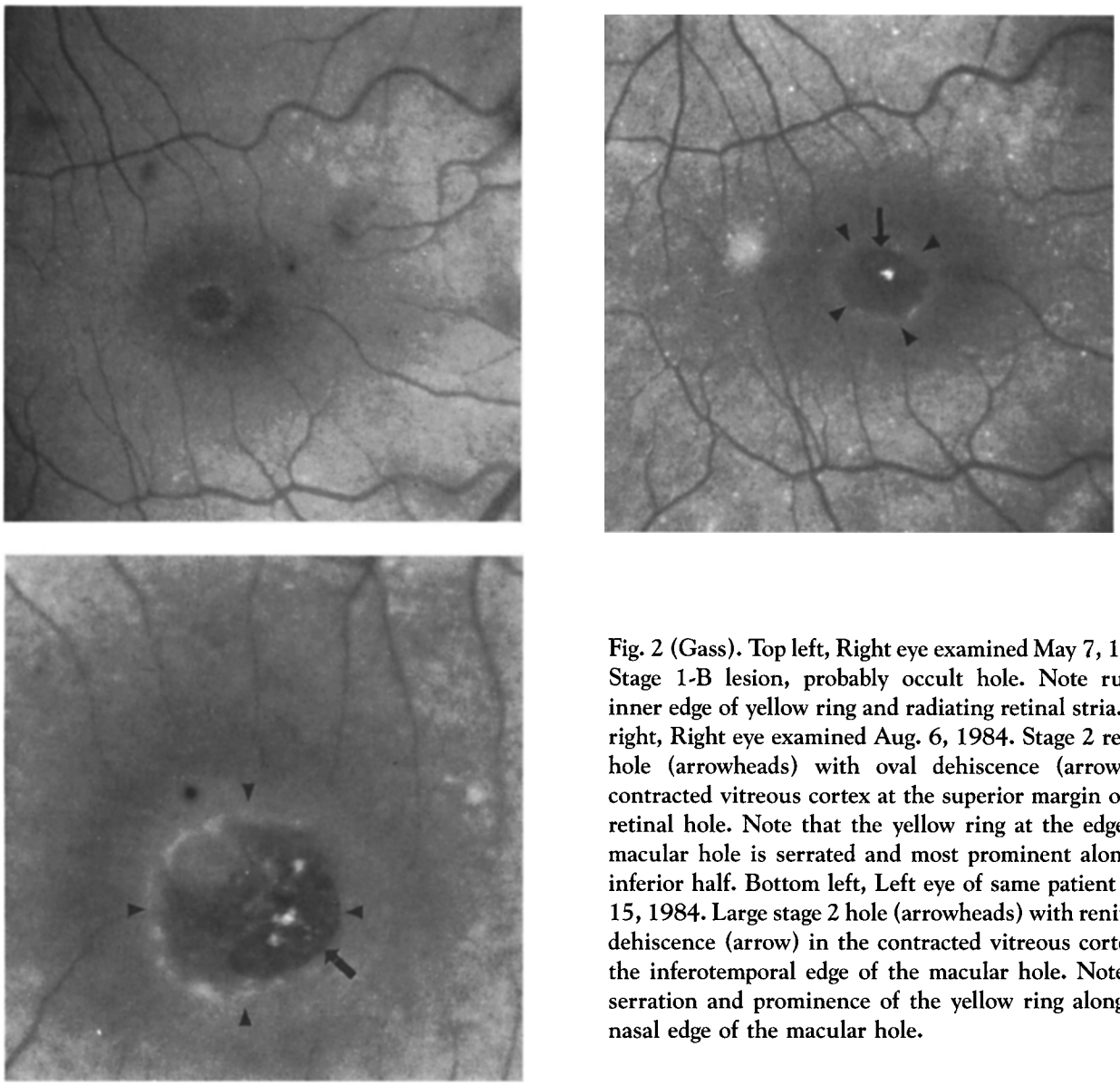

Fig. 2 (Gass). Top left, Right eye examined May 7, 1984. Stage 1-B lesion, probably occult hole. Note ruffled inner edge of yellow ring and radiating retinal stria. Top right, Right eye examined Aug. 6, 1984. Stage 2 retinal hole (arrowheads) with oval dehiscence (arrow) in contracted vitreous cortex at the superior margin of the retinal hole. Note that the yellow ring at the edge the macular hole is serrated and most prominent along its inferior half. Bottom left, Left eye of same patient Oct. 15, 1984. Large stage 2 hole (arrowheads) with reniform dehiscence (arrow) in the contracted vitreous cortex at the inferotemporal edge of the macular hole. Note the serration and prominence of the yellow ring along the nasal edge of the macular hole.

retinal surface surrounding the retinal hole as the foveolar retina continues to retract centrifugally (stage 1-B occult hole; Fig. 1E). Biomicroscopically there is progressive enlargement of the yellow ring, which may become serrated along the inner margin that corresponds to the edge of the occult round retinal hole (Fig. 2). Eventually the first biomicroscopic evidence of a dehiscence may occur in the semitransparent vitreous cortex at the inner edge of the yellow ring (stage 2 hole; Figs. 1G and 2, top right and bottom left). In the area of the dehiscence, the serration of the yellow ring disappears, presumably because of relief of traction on the edge of the retinal hole, and the yellow pigmentation fades, possibly as a result of diffusion of xanthophyll out of the retina in this area. Over a period of days or weeks, further enlargement of the macular hole and additional contraction of the prefoveolar vitreous cortex cause a 360-degree tear in the contracted prefoveolar vitreous cortex at the edge of the retinal hole, separating it from the less condensed vitreous cortex surrounding the hole. The prefoveal vitreous cortex is visible biomicroscopically as an opacity (pseudo-operculum) suspended anterior to the hole on the posterior surface of the thin layer of transparent vitreous gel that bridges the hole and lies along the inner retinal

surface in the macula. Centrifugal retraction of the foveolar retinal receptors continues until the diameter of the hole, in all but a few cases, reaches 400 to 600 μm (stage 3 hole; Fig. 1H). All stages of progressive enlargement of the hole are considered to be stage 2 holes. Since the ultimate diameter of the hole is variable, for purposes of classification, I suggest that all holes less than 400 μm in diameter be considered as stage 2 holes. After separation of the vitreous from the entire macular surface and optic disk, the hole is designated as stage 4, irrespective of its diameter (Fig. 1I).

DISCUSSION

IF THE ANATOMIC INTERPRETATIONS SUMMARIZED IN Figure 1 are correct, then the implications include the following: (1) most macular holes develop as the result of a central retinal dehiscence at the umbo, followed by centrifugal displacement of the relatively normal complement of retinal receptors; (2) this dehiscence occurs soon after the change from a yellow spot (stage 1-A impending hole) to a yellow ring lesion (stage 1-B impending hole), but in most cases it is not detectable with a thin slit beam as a defect in the center of the ring because of the presence of the semitranslucent condensed cortical vitreous that bridges the hole (stage 1-B occult hole); (3) most of the prehole opacities overlying stage 2 and stage 3 holes are condensed prefoveal vitreous cortex (pseudo-opercula), not opercula; and (4) after successful vitreous surgery, which includes tamponade of the hole with an intravitreal gas bubble and which is done within one year after commencement of hole formation, the anatomy of the central retina and its visual function may be restored to near normal levels in some patients as a result of retinal reattachment and centripetal repositioning of the retinal receptors.

If this description of the anatomic changes occurring in macular hole development is correct, histopathologic examination of the prehole opacities should show that most of them are composed of vitreous cortical collagen and are accompanied in some cases by internal limiting membrane of the retina, Mueller cell processes, and reactive glial proliferation, but not by retinal receptor cells. Although retinal opercula have been observed histopathologically in two eyes, one with posttraumatic macular hole and the other with an idiopathic macular hole, they have not been observed in most idiopathic macular holes studied histopathologically.[6,7]

The yellow spot seen in a stage 1-A impending hole is seen in serous detachment of the foveal retina caused by other disorders, for example, idiopathic central serous retinopathy and epiretinal membranes.[8] The change from the yellow spot to a yellow ring, however, occurs only with foveolar detachment caused by the anatomic changes and forces generated at the vitreoretinal interface occurring during macular hole formation. Approximately 50% of the patients who initially have stage 1 lesions experience spontaneous vitreofoveal detachment and return of visual acuity to near normal levels.[5,9] Most of these patients have stage 1-B lesions at the time of initial examination.[5] The macula in these patients typically returns to a normal appearance or, in approximately one third of patients, shows evidence of one or more inner lamellar holes. Most, but not all, patients whose macula returns to normal have a pseudo-operculum suspended immediately in front of the foveola. These findings provide further evidence that some, or perhaps most, of the prefoveolar opacities in stage 2 and 3 holes are pseudo-opercula. Failure to find pseudo-opercula in all patients after spontaneous vitreofoveal separation suggests that the contracted prefoveolar vitreous cortex in some patients is transparent and not detectable. Inner lamellar holes presumably develop as the result of a superficial dehiscence of the internal limiting membrane during stage 1-A or early stage 1-B macular hole formation.

Although no data are available concerning the relative size of yellow ring lesions that progress to a macular hole compared with those that do not, it is probable that there is a direct relationship between the ring diameter, visual acuity, and the chance for hole development. Some patients with relatively large stage 1-B yellow rings, however, may abort the process, with return of the macula to normal appearance and function. In such cases the retinal internal limiting membrane, Mueller cell processes, and proliferating retinal glial tissue, which bridge the defect caused by centrifugal displacement of the neurosensory retina, may act as a scaffold and stimulus to centripetal replacement of the foveolar retina to its

normal position after spontaneous vitreofoveal separation and retinal reattachment. The pseudo-operculum that develops in some patients after spontaneous retinal reattachment may cast a yellow shadow on the retina during slit-lamp biomicroscopy.[10] This observation is further evidence suggesting a central retinal receptor dehiscence that allows diffusion of the retinal xanthophyll into the condensed vitreous cortex before its separation from the retinal surface. After reattachment of the retina and closure of the receptor cell defect, which occur either spontaneously or after vitreous surgery, the mild hyperfluorescence usually evident in stage 1-B lesions and the more intense fluorescence present in most stage 2, 3, and 4 holes are no longer demonstrable in most patients. This disappearance of the hyperfluorescence suggests that there is a return of xanthophyll to the retinal receptors as well as glial tissue in the foveolar area.

Before the appearance of a slit-beam defect within the yellow ring, I have been unable to determine which stage 1-B lesions will progress and which will abort. The size of the ring and the level of visual acuity will probably be helpful but not completely reliable in predicting progression. In a previous study, I found that seven of ten patients with stage 1 impending holes that progressed to a stage 3 hole had visual acuity of 20/70 or worse at the initial examination, whereas seven of nine patients who aborted the process had visual acuity of 20/50 or better at the initial examination.[5] Until more data concerning the relationship between ring diameter and risk of hole formation and concerning the success of vitreous surgery are available, it is advisable to observe patients for biomicroscopic evidence of a full-thickness dehiscence within the yellow ring and a visual acuity of 20/70 or worse before surgery is considered. Even the presence of a biomicroscopic defect within the ring does not absolutely guarantee that a full-thickness hole is present. It is probable that in some patients the contracted prefoveolar vitreous cortex and the attenuated foveolar retina are sufficiently transparent that they cannot be detected biomicroscopically.

The recovery of 20/20 visual acuity, the disappearance of the focal hyperfluorescence corresponding with the hole angiographically, and the disappearance of absolute central scotomas observed in some patients after macular hole surgery indicate that centripetal movement of the paracentral retinal receptors and their xanthophyll may occur after retinal reattachment.[11] This hypothesis is supported also by the histopathologic studies of Funata and associates[12] and Madreperla and associates.[13] Gross anatomic and histopathologic examination of both eyes of a patient whose visual acuity improved from 20/400 to 20/40 in both eyes after macular hole surgery showed closure of the macular holes, reattachment of the retina, and return of xanthophyll to the center of the macula. In the left eye, closure of the hole was associated with glial proliferation and probable centripetal displacement of the retinal receptors. In the right eye, retinal reattachment and merging of the edges of the hole were not associated with gliosis. In another patient preoperative visual acuity was 20/80 and the postoperative visual acuity was 20/40.[13] One month postoperatively the patient died, and histopathologic examination showed closure of the hole and close approximation of the retinal receptors centrally by proliferating Mueller cells.[13]

In summary, I postulate that one of the important reasons for the reported surgical success in the treatment of macular holes is that, contrary to previous belief, most macular holes begin as a central retinal dehiscence and not as the result of a foveolar tear and operculum formation. Circumstantial evidence supports the following hypotheses: (1) the progressively enlarging yellow ring seen during the early stages of development of a macular hole is caused by centrifugal displacement of the foveolar retinal receptor cells, as well as the xanthophyll, after a central retinal dehiscence; (2) many of the lesions that we now classify as stage 1-B, because of a biomicroscopically discernible interface within the yellow ring, are occult holes that began centrally soon after the change from a yellow spot to a yellow ring lesion; (3) stage 1-B occult holes in some patients may close spontaneously after vitreoretinal separation; (4) the eccentric holes that develop near the inner margin of the yellow ring are tears in the condensed vitreous cortex and not the retina; and (5) most of the prehole vitreous opacities previously referred to as retinal opercula are instead contracted prefoveolar vitreous cortex or pseudo-opercula. Until these hypotheses are either verified or refuted by light and electron microscopic examination of prehole opacities, I suggest caution in making a diagnosis of a

macular hole before the patient develops biomicroscopic evidence of either a central or paracentral full-thickness hole in the foveolar area.

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