

Treatment of Macular Holes

By: Reena Mehta and Jill Rosenboom

Senior Project

Advisor: Dr. Walter Betts

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Macular holes are a disorder that continues to baffle both the ophthalmologic and optometric communities. To this day very little conclusive evidence is known about the origins of macular holes. The first case involving a macular hole was described in literature over one hundred years ago, and treatment has only become an option since the 1990's. The focus of this paper deals with the recent treatment modalities along with their outcomes and success rates. By way of a literature search, this paper will attempt to address the following topics regarding macular holes:

1. Classification by different stages
2. Identification of signs and symptoms
3. Differential diagnosis
4. Proper protocol and management
5. Surgeries and treatments available
6. Surgical outcomes and success rates

Before diving into the technicalities of the paper, it is important to give some background information that will assist in the identification of macular holes. It is a current and longstanding practice to grade macular holes by stages. The qualifications and stages of macular holes are credited to the work of Mr. J. D. Gass. The following is the Gass Classification System of Macular Holes:

Stage 1 Macular Holes:

Stage 1A (Impending hole):

Marked by a central yellow spot, loss of foveolar depression, and no vitreal foveolar separation (6).

Stage 1B (Impending or Occult hole):

Identified by the presence of a yellow ring with bridging interface and loss of foveolar depression and by the lack of vitreal foveolar separation (6). No abnormality is typically seen with fluorescein angiography (FA) (4).

Stage 2 Macular Holes:

A full thickness macular hole less than 400 micrometers in diameter (6). The defect is first noticed around the inner edge of the yellow ring or spot (4). FA may reveal a round window defect or it may be normal (4).

Stage 3 Macular Holes:

A full thickness macular hole, wider than 400 micrometers in diameter, without a PVD (6). May have a surrounding cuff of edema and fluid with or without an obvious overlying opacity (pseudo-epithelium) (4). FA may show window defect corresponding with the hole (4).

Stage 4 Macular Holes:

A full thickness macular hole, wider than 400 micrometers in diameter, with a PVD (6). Should be diagnosed only when an

obvious Weiss ring is visualized in front of the optic nerve head

(3).

While each stage has its own unique qualifications, the patient's signs and symptoms may not be as specific. Individuals with a Stage 1 macular hole usually have relatively good visual acuity (20/20 to 20/40) with minimal distortion (11). On the other hand, Stage 2 macular holes typically have a loss of visual acuity, a central scotoma, and distortion (11). Stage 3 and 4 macular holes have the same signs and symptoms as Stage 2 holes. In addition to being differentiated into stages, macular holes can also be categorized as either acute or chronic. The well known appearance of *breadcrumbs in a basket* normally occurs in chronic macular holes of stage 3 or 4 (11). These breadcrumbs are small yellow spots of clumped xanthophyll, which are visualized at the level of the RPE, at the base of the hole (11).

Most macular holes are considered idiopathic (6). Trauma, as well as pathological myopia, laser exposure, electrical current, and pilocarpine usage have also been possible causes of macular hole formation. (6). The current, most accepted theory involves tangential vitreomacular and anterioposterior traction on the fovea (6). This traction is believed to be the result of focal shrinkage of foveal vitreous (6). Another relevant theory involves the degeneration of macular cysts into macular holes. It is believed that involuntional macular thinning, which occurs with cortical vascular ischemic changes, may be the cause for cystic changes in the macula (6). It is hypothesized that the cysts may rupture and become a macular hole as a result of traction from a posterior vitreous detachment (6). While this is a possible theory, it's not as highly regarded.

There are many conditions that may resemble macular holes. The most commonly confused condition is an epiretinal membrane, otherwise known as a pseudohole. It becomes difficult to distinguish between the two conditions when the epiretinal membrane has discontinuity, contraction, or a circumferential edge in or near the fovea (4). Clinically, a pseudohole is associated with much better visual acuity and is not accompanied by a halo of fluid, yellow deposits, or an operculum (6). Differentiation can be made easier by using contact-lens biomicroscopy. This will show both the epiretinal membrane and the normal retina beneath the membrane. The best differential diagnosis between the two conditions is the missing characteristic cuff of retinal detachment or edema around the pseudo-hole. Epiretinal membranes are often found in association with macular holes, therefore careful observation is necessary.

Cystoid macular edema (CME) may also look similar to a full thickness macular hole, especially when a large central cyst is present (4). Differentiation requires the clinician to be alert and notice the presence of other ocular conditions associated with CME. These conditions include: recent cataract or other intraocular surgery, ocular tumors, retinal vascular occlusive disease, ocular inflammatory conditions, diabetes mellitus, macular pucker, retinitis pigmentosa, or juxtafoveal telangiectasia (4). The diagnostic test, fluorescein angiography (FA), proves helpful in distinguishing between the two disorders. Early superficial leakage, from a dilated retinal capillary bed, and late accumulation of fluid in cystoid spaces is apparent in CME (4).

In certain cases, geographic atrophy of the RPE may also appear similar to a macular hole. This occurs when the atrophy is sharply demarcated, circular, and centered foveally (4). Differentiation can again be aided by contact lens biomicroscopy, which

allows visualization of an intact retina over the area of atrophy and the absence of the surrounding cuff of fluid. Fluorescein angiography is not as beneficial in this case as both conditions show a window defect. Since many conditions may mimic a macular hole, it is vital to provide proper diagnosis so appropriate treatment can be initiated.

With the background information established, the discussion of treatment options is in order. When considering surgery, two main criteria must be taken into consideration: the amount of vision loss and whether or not there is a presence of a full thickness retinal break. Laser photocoagulation is one treatment option that has been used to flatten the localized detachment around the hole (5). While this procedure has the benefit of being noninvasive, it isn't very popular due to very limited visual improvement (5). Another more popular surgical option is the conventional vitrectomy with a gas tamponade. The purpose of the vitrectomy is to relieve all vitreomacular traction. This is done by removing the cortical vitreous including the posterior hyaloid membrane and any epiretinal membrane surrounding the hole (17). The tamponade, provided by the gas-fluid exchange, is intended to reattach the detached cuff of retinal tissues. After the surgery, the patients are required to remain in a strict facedown position that keeps the tamponade gas bubble over the macula. Many believe this step determines the success of the surgery. Successful surgery is determined by anatomic success or complete hole closure, along with visual success.

Autologous plasmin enzyme may change the way vitrectomies are performed. After anesthesia is injected, the autologous plasmin enzyme is inserted into the midvitreous cavity through the pars plana (17). This enzyme automatically separates the posterior vitreous from the retina in approximately fifteen minutes (17). In most cases a

PVD is created without suction or mechanical peeling of the posterior hyloid membrane (17). This procedure was tested on nine eyes which all went on to have successful macular hole closure (17). Eight of the nine eyes had a spontaneous PVD, with one eye needing very minimal suction (17). With no evidence of intraocular toxicity, many surgeons feel manipulation of the perihole tissue may be unnecessary, especially in Stage 3 macular hole (17). With little or no suction or mechanical peeling needed, this new enzyme may reduce the risk of a concurrent retinal detachment and decrease the trauma to the fragile tissue surrounding the macular hole.

A study has been completed for Stage 1 macular holes which compares the results of performing a prophylactic vitrectomy verses observation of the macular hole (15). The outcomes are as follows: a full thickness hole developed in 10 of 27 eyes that received the prophylactic vitrectomy as compared to 14 of 35 eyes that were observed (15). It was concluded there is no substantial benefit to performing a vitrectomy on Stage 1 macular holes. The operated eyes also showed the appearance or progression of nuclear sclerotic cataract as a common side effect of vitrectomy (in 12 of 27 eyes) up to 17 months after surgery (15).

In general, when a practitioner notices a stage 1 macular hole, the current standard of care mandates that no surgical intervention is indicated (11). Current responsibilities include closely monitoring the hole for development into a full thickness macular hole and patient education regarding the importance of amsler grid self monitoring for any changes in the macular area (11). It is also important to inform patients that according to current research, 50% of Stage 1 holes spontaneously disappear, while the other 50% either stay the same or go on to develop into Stage 2 holes (4). Evidence also shows

Stage 1 macular holes with visual acuity of 20/50 or worse are at a greater risk of progressing to full thickness Stage 2 macular holes (4). In contrast, Stage 1 macular holes with initial visual acuity of 20/40 or better have greater chances of remaining stable or spontaneously resolving (4).

While surgery has not been proven beneficial on Stage 1 macular holes, vitrectomy surgery may be necessary on more severe holes. The Bascom Palmer Eye Institute evaluated the effects of not performing vitrectomy surgery and simply monitoring Stage 2, 3 and 4 holes. This study involved 65 eyes and was conducted from January 1, 1968 to December 31, 1993. The data from the initial and final examinations are the following (2):

Initial exam	Final exam
Stage 2 --- 15 eyes (24%)	Stage 3 --- 10 eyes (16%)
Stage 3 --- 23 eyes (37%)	Stage 4 --- 53 eyes (84%)
Stage 4 --- 25 eyes (40%)	

This study also measured when the visual acuity of these patients became 20/200 or worse. The initial exam showed 35 eyes (54%) had an acuity of 20/200 or worse as compared to the final exam when 53 eyes (82%) had an acuity of 20/200 or worse (2).

This long-term study determined that unoperated Stage 2, 3, and 4 macular holes demonstrated a progression of the hole size and stage in addition to vision loss that generally stabilized at 20/200 to 20/400 (2). Another clinical trial, *The Vitrectomy for Macular Hole Study*, completed by W. R. Freeman and colleagues compared the “progression of natural history of full thickness macular holes and the role of vitrectomy surgery for full thickness macular holes” (8,7). This trial included 36 eyes that had an

early full thickness Stage 2 macular hole (8,7). Twenty-one eyes were observed and 15 had surgery, which included a pars plana vitrectomy and the peeling of the posterior cortical vitreous to create a PVD (8,7). After twelve months, the results revealed a definite distinction between the observation group and the surgery group. Fifteen of the 21 observed eyes went on to progress to a full thickness stage 3 or 4 hole while only 3 of the 15 eyes in the surgery group progressed to a Stage 3 or 4 macular hole (8,7). The visual function was also noted as being significantly better in the surgery group (8,7). It is now generally accepted the best mode of treatment for any Stage 2, 3, or 4 macular hole is a 3-port pars plana vitrectomy surgery. Yet the question remains, which gas tamponade and adjunct agent, in association with a vitrectomy, will provide the patient with the best anatomical and visual outcomes.

Most tamponades are in the form of the gas perfluoropropane (C3F8). The studies involving these materials are ongoing and often hard to validate. It has been documented that lower concentrations of C3F8, in the range of 5-10%, are not as effective as the higher concentrations of 16-20% (16). One study gave the following results comparing success rates for air and C3F8 tamponades (16):

- Air = 53% anatomical success and 20% visual success
- 16% C3F8 = 97% anatomic success and 62% visual success

Although tamponade use is in the early stage of development, its use has proven beneficial. The C3F8 gas has also been widely used and researched, with notable success, in other retinal surgeries including retinal detachments and tears (1).

There has also been a recent development in the use of silicone oil as a tamponade. Early results indicate silicone oil has a surgical success rate similar to that of

a gas tamponade (18). Patients will benefit by not having to maintain the constant, one to three week, face down position required for gas tamponades. They may return to near normal activity almost immediately (18). In addition, there are no restrictions for flying or traveling to high altitude (18). The only downside to silicone oil tamponade is increased expense of surgery as an additional procedure is needed to remove the silicone oil tamponade after four to eight weeks (18).

Adjunct therapy is one of the newest treatments out there. Various treatments are currently being investigated. One pharmacologic adjunct being tested is known as Transforming Growth Factor-B or TGF-B2. It's intended to stimulate collagen and glycoprotein synthesis and induce cellular proliferation and migration (16). A study involving 60 eyes was completed, where twenty-three received the TGF-B2 treatment in addition to the vitrectomy. Results indicated the visual acuity improved by at least two lines in 14 out of 23 eyes (61%) (16). Overall, the expanded report showed a 96% anatomic and 85% visual success with these 23 eyes (16). A larger study was done involving 90 eyes in which 30 patients were given a placebo and 58 were given the TGF-B2 treatment (16). The results, 16 of the 30 holes resolved with placebo treatment and 53 of the 58 holes resolved with the TGF-B2 (16). It appears macular holes treated with a TGF-B2 in addition to the vitrectomy are showing much better surgical outcomes.

The other adjunct therapy also being tested is the Autologous serum. Several studies have shown anatomic success range of 80-90%. One particular study involved 29 eyes with Stage 2-4 full thickness macular holes. These patients were treated with 20-30 mL of autologous serum over the macula hole followed by 16% perfluoropropane gas injection (9). Postoperative notes indicated that 28 eyes had flat macular holes with no

detection of the macular holes in 27 eyes (9). The visual acuity improved two lines or more in 22 of the eyes (9). These results indicate the use of an adjunct agent may become one of the most important things in improving visual success rates.

Another promising adjunct therapy is Autologous Platelet Concentrate. A pilot study has reported a 95% anatomic success rate (16). In addition, the visual acuity improved to 20/40 or better in 45% of the eyes and improved two lines or more in 85% of the cases (16). A Biological Tissue Adhesive that is composed of bovine thrombin and pooled human fibrinogen is also being investigated as an adjunct therapy (16). A study has shown an 80% anatomic success rate, but the visual success rate doesn't appear as impressive (16).

While this topic is quite new, macular hole surgery and research has come very far. Many adjunct therapies are in the early experimental stages, yet it would be premature to assume the best solution for macular hole surgery has been found. Both silicone oil and C3F8 tamponade treatments have comparable success rates, however, there are advantages and disadvantages of each one. Currently the silicone oil treatment in conjunction with the 3 port pars plana vitrectomy seems to be "the hot item". This is easier for the patient since there is minimal face down positioning, but two surgeries are required. The opposite is true with the C3F8, a minimum of 10-14 days of face down positioning is necessary, but only one surgery is needed. With the knowledge of this information, the doctor and patient must evaluate which procedure will be of most benefit.

After discovering a macular hole, the proper protocol for the optometrist will be the following:

- If it is a stage 1 hole with fairly good visual acuity (20/40 or better), simply monitor and co-manage with the retinal specialist. Send the patient home with an amsler grid and have the patient return to the clinic in one month or ASAP if there are any grid or visual changes.
- If a stage 2 or higher macular hole is noticed, refer to a retinal surgeon. The surgeon should be willing to perform a 3 port pars plana vitrectomy in conjunction with either silicon oil or C3F8 gas tamponade.
- It is necessary to educate the patient about their disease, explain the surgical procedure and the essentials of postoperative care. The patient must understand, to obtain a successful outcome, they must comply with the recommended postoperative face down position.
- Patient must be made aware of possible postoperative complications. These can include CME, progression of cataracts, possibility of the macular hole reopening, or the slight chance of macular hole formation in the fellow eye.

It is important to note the patient's age has less of an influence on visual improvement than the age of the macular hole (13). However, research has established that preoperative factors of good visual acuity, earlier hole stage, and younger age correlated with better postoperative visual acuity (9).

While vitrectomies occur in just about every macular hole surgery, the techniques used, along with the different types of tamponades and adjunct agents, are still evolving.

Experimentation and research will continue to be conducted until surgical procedures with better success rates, less post-operative complications, and a decrease in patient recovery time occurs. These are the goals of the surgeons. Until the "perfect" solution

arises, it is important for the optometrist to not only be able to identify a macular hole, but also determine what needs to be done at the proper time. It is essential for every optometrist to have an honest, trustworthy, working relationship with a retinologist in their area. This will make the co-management of a patient with a macular hole much easier for the both the doctors and more importantly for the patients.

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