LAMELLAR MACULAR HOLE: A COMPLICATION OF CYSTOID MACULAR EDEMA AFTER CATARACT EXTRACTION: A CLINICOPATHOLOGIC CASE REPORT*

BY *J. Donald M. Gass,* MD

CYSTOID MACULAR EDEMA IS THE MOST COMMON CAUSE OF LOSS OF CENTRAL vision after uneventful cataract extraction.[1,2] Its etiology is unknown. Most patients experience spontaneous recovery of vision. In a few, however, the edema may persist and secondary permanent complications such as lamellar macular hole formation may occur.[2] Prior to the advent of fluorescein angiography there was general agreement that it was difficult, if not impossible, in the absence of a serous macular detachment to distinguish clinically a full-thickness hole from a lamellar hole in the macula. In 1970,[3,4a] evidence was presented that fluorescein angiography might be useful to discriminate these two conditions. Biomicroscopic and angiographic findings were illustrated in one patient who appeared to have evolved an inner lamellar macular hole as a complication of aphakic cystoid macular edema.[4b] This patient subsequently has died and there was opportunity to confirm the clinical diagnosis histopathologically. The purposes of this report are to correlate the biomicroscopic, fluorescein angiographic, and histopathologic findings in this patient; to emphasize the usefulness of fluorescein angiography in the detection of inner lamellar hole formation in patients with cystoid macular edema; and to discuss the value of biomicroscopy and angiography in the differential diagnosis of various types of macular holes.

CASE REPORT

A white woman, age 51 years, was examined at the Bascom Palmer Eye Institute in June, 1961, because of photopsia in the right eye. Her past

*From the Bascom Palmer Eye Institute, Department of Ophthalmology, University of Miami School of Medicine, Miami, Florida.

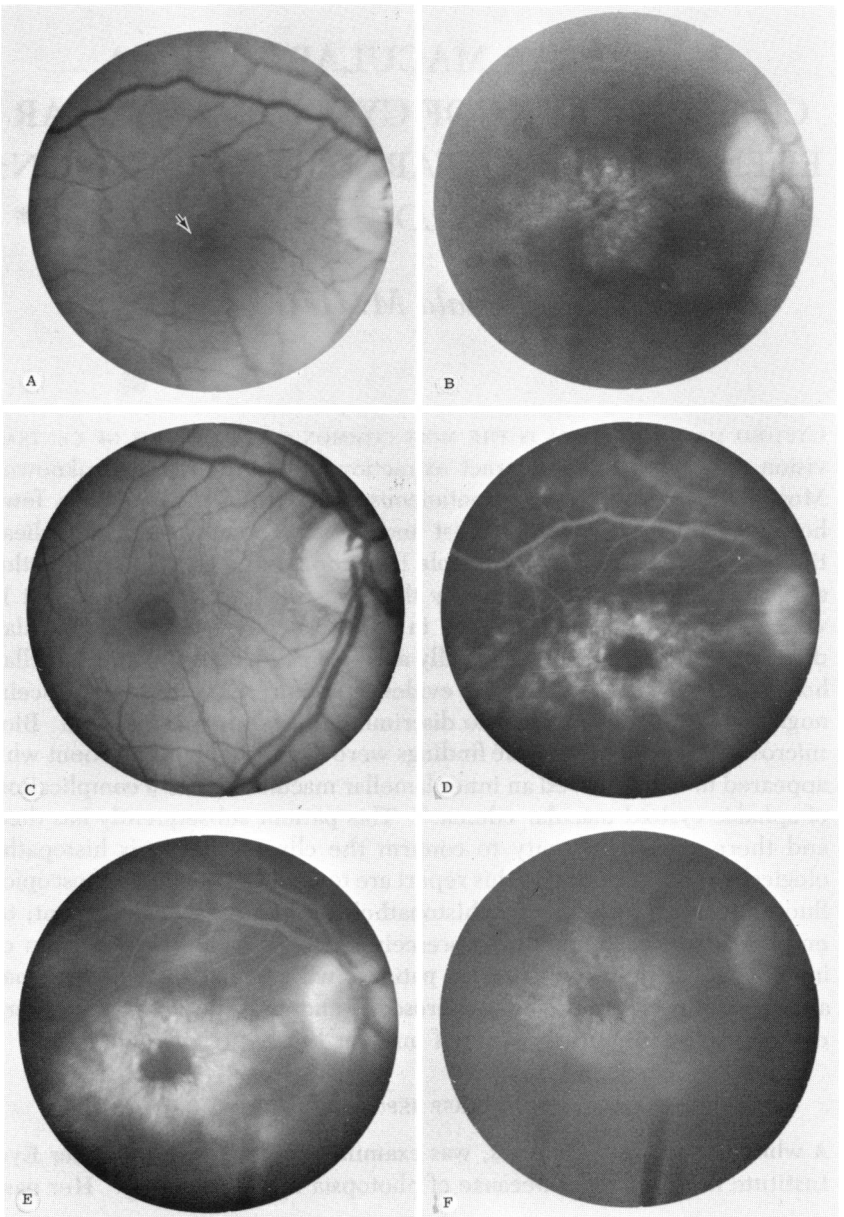

FIGURE 1

A: Right eye. May 18, 1965. Note the deep retinal yellow exudate (*arrow*) secondary to cystoid macular edema. B: One-hour angiogram. C: Same eye after development of a lamellar macular hole. D: - F: Angiogram showing evidence of cystoid macular edema surrounding the lamellar macular hole. Absence of fluorescence centrally is evidence of inner lamellar hole formation.

medical history was unremarkable except for mild hypothyroidism which was controlled medically. Her visual acuity was 20/60 in each eye. She had cataracts in each eye and a posterior vitreous separation in the right eye. The fundi were normal. On March 29, 1965, she had an uneventful round-pupil intracapsular cataract extraction from the right eye. During the second week postoperatively the vision in the right eye corrected to 20/30. The macula appeared normal. On May 18, 1965, the vision in the right eye was 20/40. Biomicroscopy and fluorescein angiography revealed cystoid macular edema in the right eye (Figure 1A, B). By September, 1965, the pupil was peaked and vitreous strands led to the cataract wound. Biomicroscopic evidence of persistent cystoid macular edema was confirmed angiographically. In December, 1965, the acuity was 20/25 and cystoid changes were no longer visible in the macula. On March 30, 1966, the macular edema had returned and visual acuity in the right eye was 20/70. Visual acuity in the left eye was less than 20/200 due to an advanced cataract. On July 18, 1966, she had an uneventful cataract extraction from the left eye. An intentional sector iridectomy was done to preserve the anterior hyaloid face. However, between the fifth and fifteenth postoperative days it ruptured spontaneously. Between the fifteenth and thirty-sixth postoperative days cystoid macular edema developed in the left eye. On the latter day visual acuity in the left eye was 20/50. By September 27, 1966, visual acuity was 20/70 in the right eye and was 20/25 in the left eye. Ophthalmoscopy of the right eye showed cystoid macular edema and a mild crinkled cellophane-like reflex on the inner retinal surface in the macula. There was no biomicroscopic evidence of cystoid edema in the left macula.

Thirty-two months after cataract extraction in the left eye the visual acuity was 20/70 in the right eye and 20/50 in the left eye. Some vitreous cells were present in both eyes. The right macula showed a slight irregular, oval-shaped defect interpreted as an inner lamellar macular hole with a faint crinkled cellophane-like reflex on the inner retinal surface surrounding the hole (Figure 1C). A second light reflex, or sheen, was present in the depth of the macular hole which suggested the presence of retinal tissue on the inner surface of the retinal pigment epithelium. There was no biomicroscopically visible cystoid spaces in the retina surrounding the hole in the right macula but there was cystoid macular edema in the left eye (Figure 2A). Fluorescein angiography revealed evidence of cystoid edema in the retina surrounding the lamellar hole in the right eye although there was no fluorescence within the area of the lamellar hole throughout the one-hour study (Figure 1D-F). The typical angiographic picture of cystoid macular edema appeared in the left eye

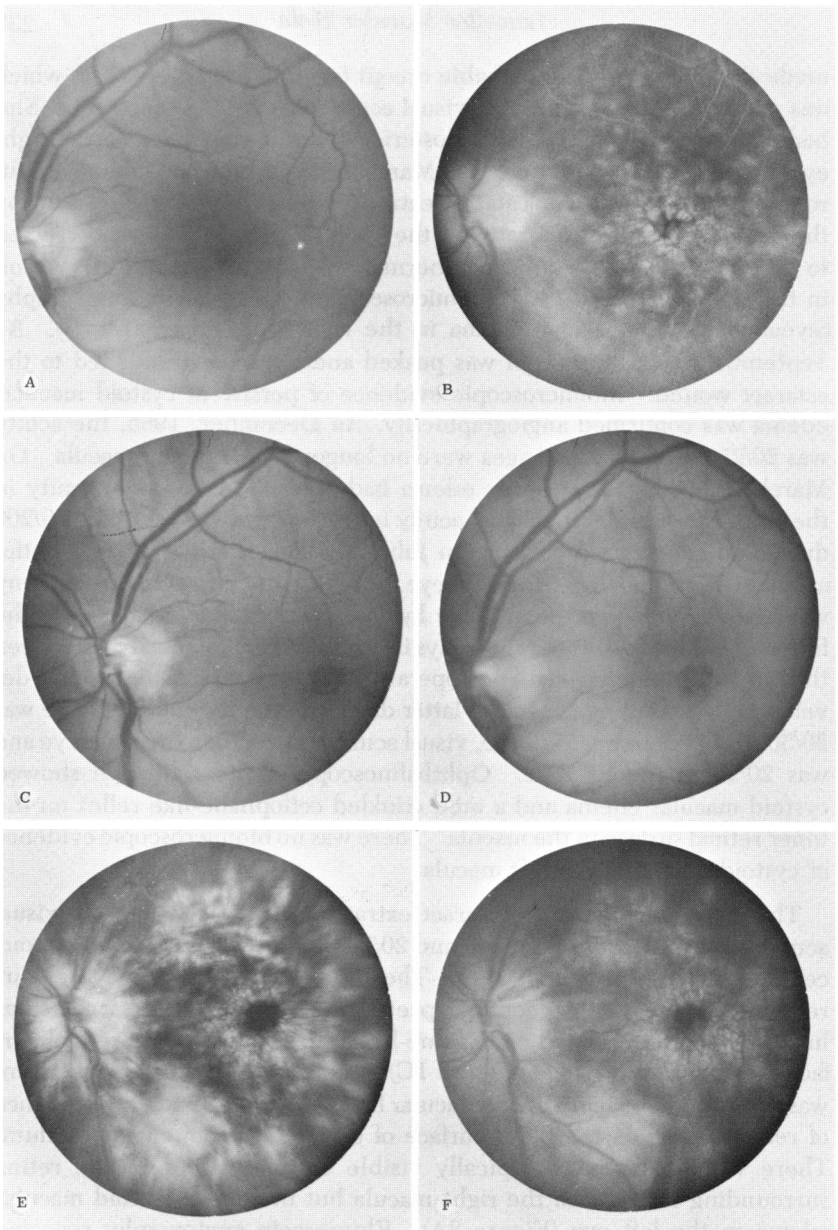

FIGURE 2

A: Left eye. January, 1969. Cystoid macular edema. B: One-hour angiogram. C: Same eye. August, 1969. Multifaceted lamellar macular hole. Septae separating the holes are not well defined. D: Same eye. July 14, 1970. The septae separating the multifaceted lamellar hole are more apparent. E: and F: Angiograms showing evidence of cystoid macular edema surrounding the lamellar hole.

(Figure 2B). Re-examination in October, 1968, revealed no changes except for the development of a cellophane-like reflex in the left macula. By August, 1969, the patient had developed evidence of lamellar hole formation in the left eye (Figure 2C). Visual acuity was 20/70 in each eye. On this occasion she gave a history of hypochromic anemia of unknown cause and congestive heart failure.

On July 14, 1970, visual acuity was 20/100 in the right eye and 20/400 in the left eye. The right fundus was unchanged. Four honeycomb lamellar defects could be seen in the inner retinal layers of the left macula (Figure 2C, D). Fluorescein angiography revealed evidence of cystoid macular edema surrounding the lamellar macular holes in both eyes (Figures 1D-F, 2E, F). No documentation of the presence or absence of vitreous cells appears in the patient's record after August, 1969. On August 9, 1970, the patient died of an acute myocardial infarction. The eyes were obtained for histopathologic study and were fixed in formalin.

On gross examination, both eyes measured 23 × 23 × 24 mm. The pupil of the right eye was displaced superiorly and there was a sector iridectomy superiorly in the left eye. The right eye was sectioned vertically. There was a patent peripheral iridotomy superiorly. The lens was absent. Vitreous strands extended from the peripheral retina and pars plana temporally through the pupil into the anterior chamber toward the cataract wound superonasally. The posterior vitreous cavity was filled with clear watery vitreous. With careful gross dissection there was no evidence of formed vitreous leading from the anterior part of the eye to the macula. A horizontal linear fold extended from the optic disc into the macular area and an oval-shaped lamellar macular hole was present. Yellow pigment was prominent in the center of the macula.

The left eye was sectioned horizontally. The lens was absent. The vitreous in the region of the pars plana and anterior vitreous was formed; posteriorly it was clear and watery. The retina between the disc and macula was thrown into a prominent horizontal fold and there was a crater in the central macular area. Serial sections were prepared through the macular areas of each eye.

MICROSCOPIC EXAMINATION — RIGHT EYE

There was a healed scar of a well-approximated peripheral corneal wound superiorly. The lens was absent. In one area superonasally, a sheet of condensed vitreous was adherent to the anterior surface of the iris and the posterior surface of the corneal scar and was continuous with fine wavy vitreous strands which extended through the pupil to the area of the pars plana and peripheral retina temporally. The structure of the

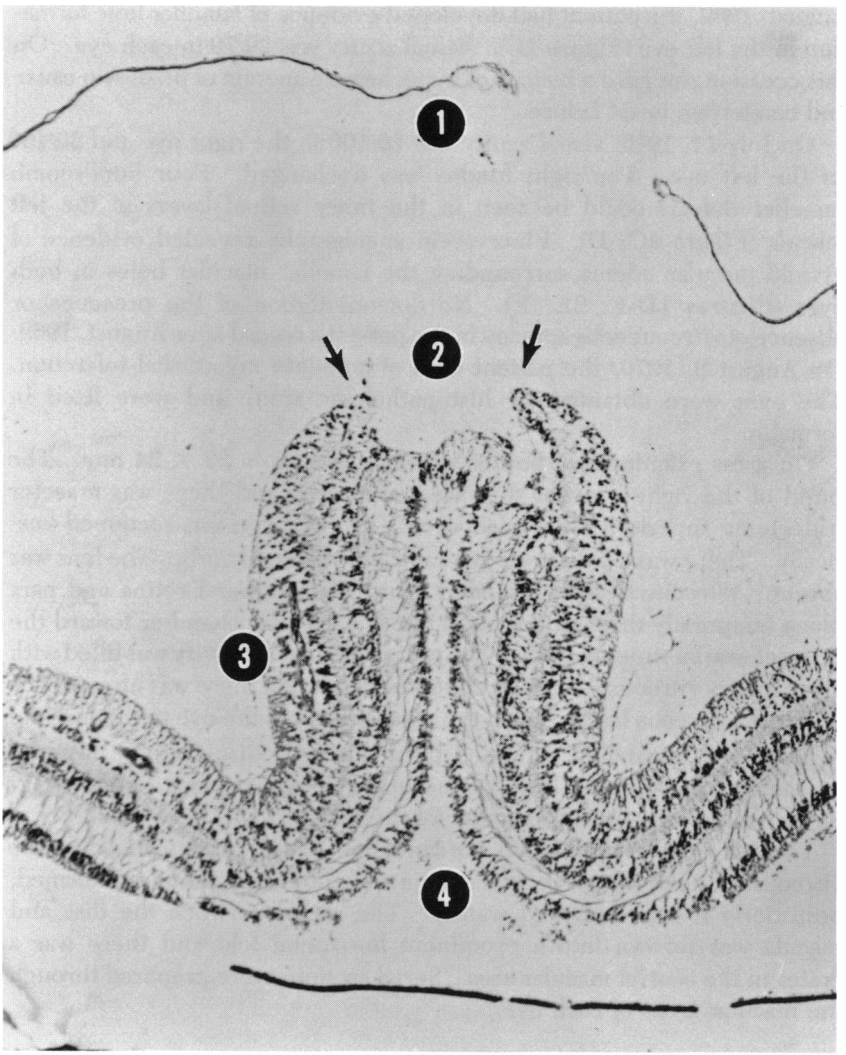

FIGURE 3
Macular area, right eye, showing (1) artifactitious detachment of the internal limiting membrane and epiretinal membrane, (2) an inner lamellar macular hole (*arrows*), (3) dilated perifoveal capillaries, (4) cystoid spaces in the inner nuclear and outer nerve fiber layers, and thinning of the outer nuclear and rod and cone layers. (PAS photomicrograph × 70)

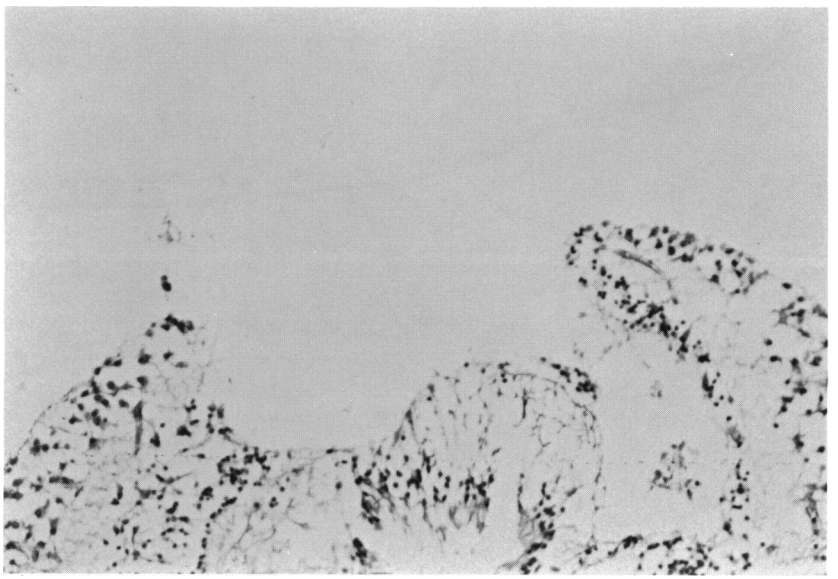

FIGURE 4
Right macula. High power view of lamellar hole. (PAS photomicrograph × 120)

anterior vitreous appeared normal. No evidence of formed vitreous appeared in the posterior two-thirds of the eye. The uvea and the vitreous were free of inflammatory cells. In the macular area the retina was thrown into a prominent fold and in many sections the internal limiting membrane was detached artifactitiously (Figures 3, 4). A lamellar hole involved the inner half of the retina in the center of the macula. Except for mild autolytic changes and a diffuse loss of some cellular elements, the rod and cone layer and outer nuclear layer were intact across the base of the lamellar hole. There was some undercutting of the edge of the hole to form a lip which consisted of ganglion cells and a small portion of the inner nuclear and plexiform layer. A monocellular membrane extended from the retinal tissue at the edge of the hole onto the inner surface of the internal limiting membrane for a distance of about one disc diameter around the circumference of the macular hole (Figure 5). No evidence of fine wrinkling of the internal limiting membrane was seen under this cellular layer. Most of the nuclei of this cellular layer were round or oval and slightly vesicular and some contained nucleoli. The cell membranes separating these cells were not clearly visible. Fibrillar material stained faintly blue with the Masson trichrome stain, but did not stain with Alcian blue. The retinal capillaries surrounding the lamellar macular hole were

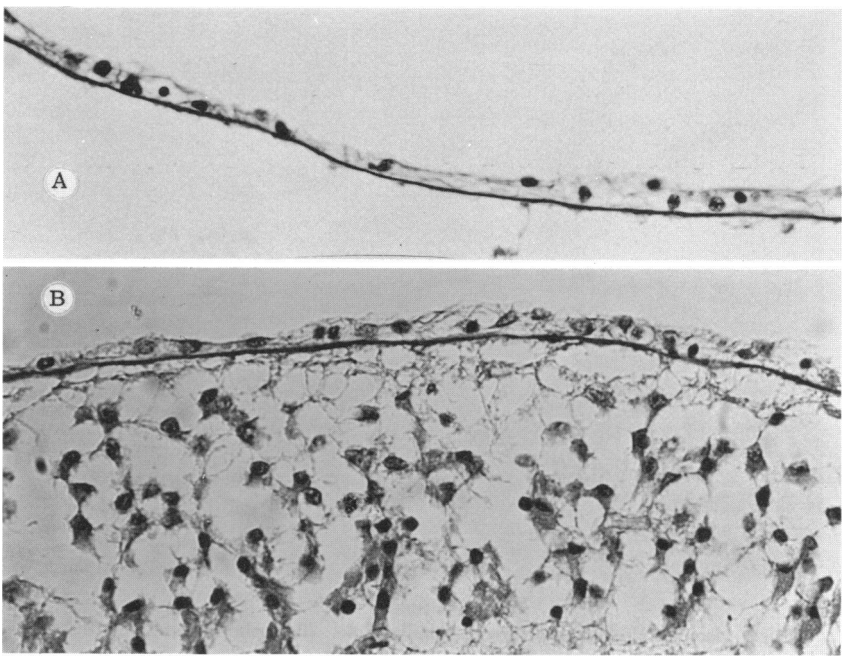

FIGURE 5
Right macula. High power view of epiretinal cellular membrane. A: Same section with artifactitious detachment of internal limiting membrane illustrated in Figure 3. B: In section nearer to the edge of the lamellar hole to show the true relationship of epiretinal cellular membrane to the retina. (PAS photomicrograph × 305)

dilated but otherwise appeared normal. There were small cystoid spaces in the outer plexiform layer as well as the inner nuclear layer surrounding the hole (Figure 6). There was evidence of loss of some of the nerve fibers comprising the nerve fiber layer of Henle. The retina outside the macular area was normal. The optic nerve, retinal pigment epithelium, Bruch's membrane, and the choroid were normal.

MICROSCOPIC EXAMINATION — LEFT EYE

The microscopic examination revealed findings similar to those in the right eye. A prominent fold crossed the macular area. The lamellar hole in the left macula was subdivided in at least four separate compartments by sloping septa composed of remnants of the outer plexiform layer (Figure 7). This accounted for the multiloculated clinical appearance of the lamellar hole in the left eye (Figure 2F). A monocellular layer similar to that described in the right eye was present on the inner surface of the internal limiting membrane surrounding the macular hole. This mem-

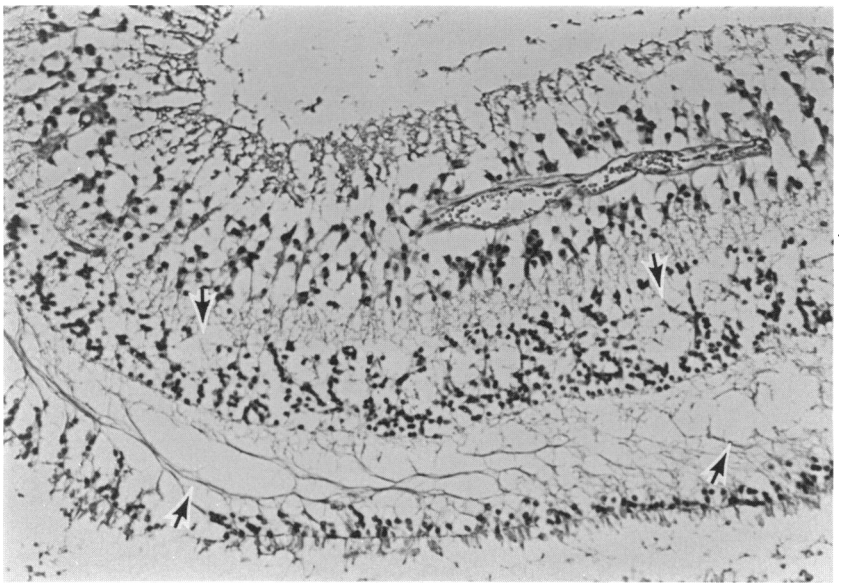

FIGURE 6
Right macula. High power view same section illustrated in Figure 3 to show dilated retinal capillaries and cystoid spaces (*arrows*) in the inner nuclear and outer plexiform layers. (PAS photomicrograph × 120)

brane extended around the overhanging lips of the hole and was continuous with the retinal tissue (Figures 7, 8). Cystoid spaces were identified within the inner nuclear and outer plexiform layers in the macular area. There were no vitreous strands extending from the macular region anteriorly. The optic nerve was normal. The histopathologic diagnoses were: (1) surgical aphakia of each eye, (2) cystoid macular edema, and (3) inner lamellar macular hole.

DISCUSSION

This histopathologic finding confirmed the biomicroscopic and fluorescein angiographic diagnosis of inner lamellar macular holes and cystoid macular edema of each eye. The rounded edges of the holes and the extension of a cellular layer from the retina proper around the edge of the holes onto the inner retinal surface clearly demonstrated that the holes were not postmortem artifacts. Figure 9 depicts diagrammatically the structural changes that occur when the inner wall of the large central cysts in cystoid macular edema rupture. The cysts collapse and the surrounding retinal tissue retracts to form an inner lamellar hole with rounded edges.

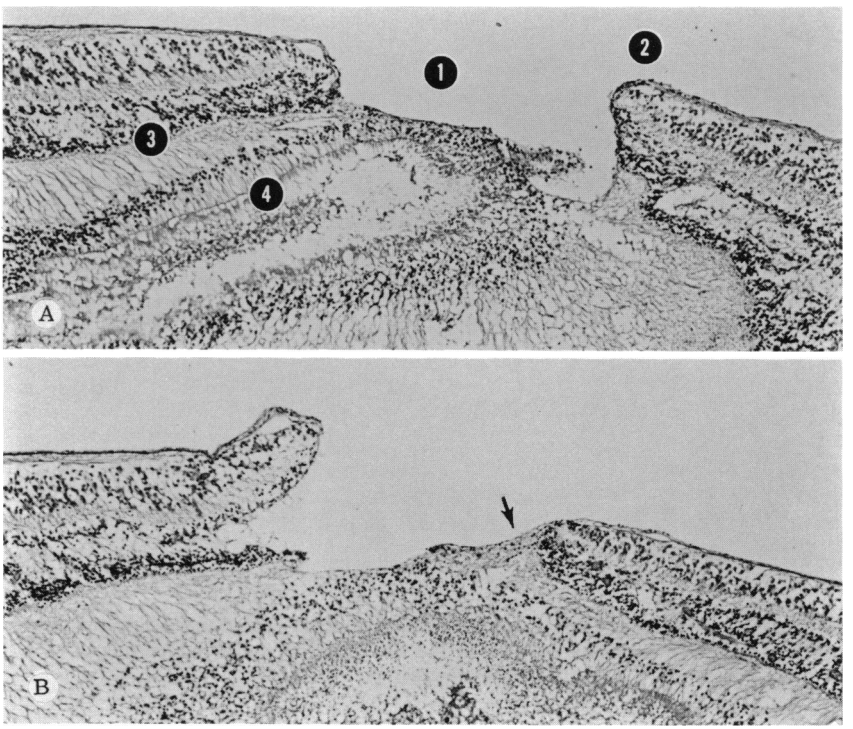

FIGURE 7

A: Macular area of left eye showing (1) lamellar macular hole, (2) epiretinal cellular membrane, (3) cystoid spaces in the inner nuclear and outer plexiform layers, and (4) thinning of the outer nuclear and rod and cone layers. The apparent widening of the inner nuclear, outer nuclear, and outer plexiform layers on the right side of the photomicrograph is caused by a tangential section through the artifactitiously folded retina. B: Section through the lamellar hole at the site of one of the sloping septae (*arrow*) which subdivided the hole (PAS photomicrograph ×50)

Some disruption of the longer, parafoveal Henle's nerve fibers compressed between the large cysts probably occurs. With retraction of the inner retinal tissue surrounding the hole, the larger round paracentral cysts become more oval or slit-like in configuration. This change in configuration probably accounts for the difficulty in detecting biomicroscopically the cystic spaces surrounding a lamellar macular hole, while angiography, on the other hand, easily demonstrates their presence. Whether or not the partial loss of receptor elements in the central macular area of the above case was caused primarily by chronic cystoid macular edema, or by hole formation cannot be determined. No apparent histopathologic explanation for the rupture of the inner cyst walls was found. The clinical

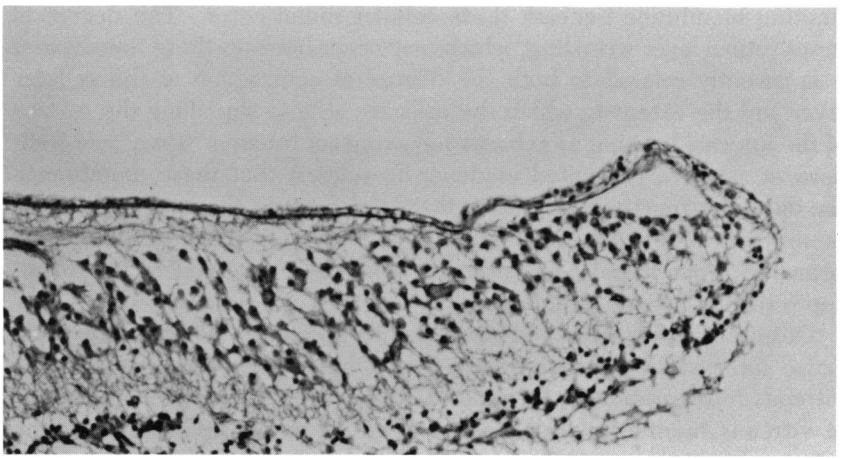

FIGURE 8
Left macula. High power view showing epiretinal cellular membrane extending around the edge of the lamellar hole. (PAS photomicrograph × 140)

observation of posterior vitreous separation prior to the development of macular holes suggest that vitreous traction probably played no role in the formation of the hole. The marked undercutting of the edges of the hole in most areas and tapering thickness of the ganglion cell layer near the edge of the hole suggest that spontaneous rupture of the inner cyst wall at the fovea occurred. In this area the inner wall is comprised of little more than the internal limiting membrane which in the fovea is so thin that it can be detected only with electron microscopy.

The histopathologic findings in both eyes confirmed that the crinkled cellophane reflex on the inner retinal surface surrounding the macular hole was caused by a cellular membrane on the inner surface of the internal limiting membrane. Similar cellular membranes have been demonstrated histopathologically by previous authors[5,6,7] as the cause for the ophthalmoscopic findings of cellophane-like crinkling of the inner retinal surface. The origin of these membranes is uncertain. The histopathologic findings in the present case suggest the possibility that they were derived from proliferation of cells from the retina around the edge of the lamellar holes or through other defects in the internal limiting membrane onto the surface of the internal limiting membrane. There was clinical evidence that these epiretinal membranes were present in the macula of both eyes following the development of cystoid macular edema but prior to the development of a lamellar hole. There was minimal clinical and no histopathologic evidence of wrinkling of the internal

limiting membrane beneath these cellular membranes. The degree of inner retinal layer wrinkling, which may occur beneath these membranes is apparently related to both the degree of contraction of the cellular layer and the extent to which the cells are able to slip along the surface of the internal limiting membrane following contraction. Foos[8] and Bellhorn et al[7] have presented evidence to suggest that these membranes are due to astrocytic proliferation through breaks in the internal limiting membrane. The often-used clinical terms, "preretinal fibrosis" and "preretinal vitreous membrane" probably should be replaced by the term, "epiretinal astrocytic membrane."

Despite careful gross and microscopic inspection of these eyes, no cause for cystoid macular edema could be found. While there was vitreous incarceration in the wound of one eye, there was no evidence of vitreous traction on the macula. There was no disturbance of the relationship of the anterior vitreous to the peripheral retina or pars plana. The uveal tract and vitreous were free of inflammation. Except for some dilatation of the capillaries in the area of the lamellar macular holes, no other abnormality of the retinal blood vessels was found. The cause of the abnormal retinal capillary permeability and cystoid macular edema in aphakia remains a mystery.

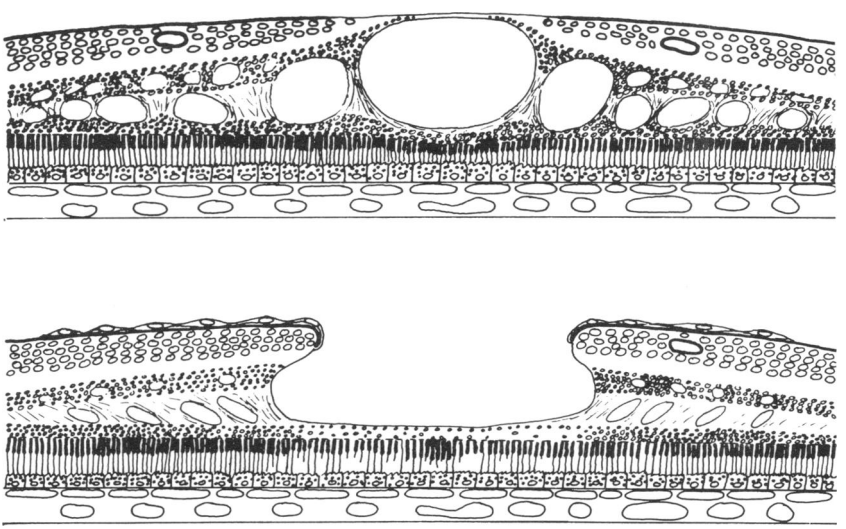

FIGURE 9

Diagrams showing the anatomic changes which occur following rupture of the inner cyst wall in cystoid macular edema. (*Above*) Cystoid macular edema. (*Below*) Lamellar macular hole, surrounding cystoid edema, and epiretinal cellular membrane.

What is the explanation for the fluorescein angiographic findings in the present case? Figure 9 illustrates diagrammatically the anatomical changes prior to and following rupture of the inner retinal wall in an aphakic patient with cystoid macular edema. Prior to the lamellar hole formation, the dye diffuses out of the leaky perifoveal retinal capillaries into the serous exudate which is responsible for the multicystoid pattern of distended extracellular spaces. The several large central cysts in the foveal area are the last to stain heavily with the dye because of their more distant location from the perifoveal capillary network. The walls of these large cystoid spaces are formed by the compressed nerve fibers of the layer of Henle. The nonfluorescent stellate, or Chinese figure, which becomes visible centrally during the later stages of angiography (Figures 1B, 2B) is caused by these compressed nerve fibers. The heavy concentration of the xanthophilic pigment in the nerve fiber layer of Henle centrally probably contributes to the nonfluorescent appearance of the walls of the cystoid spaces. After rupture of the inner cyst walls and lamellar hole formation, fluorescein continues to concentrate in the smaller perifoveal cysts but centrally is free to diffuse anteriorly into the vitreous. Thus, during the later phases of angiography a polycystic pattern of retinal staining occurs around the lamellar hole which remains nonfluorescent or hypofluorescent throughout the course of angiography. Therefore, in following cystoid macular edema in both aphakic and phakic patients, angiography can be invaluable in detecting the complication of lamellar hole formation. Failure of the area ordinarily occupied by the central cysts to stain suggests that inner lamellar hole formation has occurred and that the return of acuity to normal levels is no longer possible.

In the patient presented above, the clinical diagnosis of lamellar hole was made primarily on the basis of the following biomicroscopic features: (1) the presence of a sharply outlined, faceted area as seen with the fine slit-lamp beam in the central macular area; (2) the presence at the base of a bright sheen or reflex suggesting the presence of a layer of transparent retinal tissue; and (3) the absence of a surrounding halo of retinal detachment and the absence within the hole of small yellow deposits on the surface of the retinal pigment epithelium, both of which are often present in a full-thickness macular hole (Figure 9). The diagnosis was further supported by failure of the area of the hole to show fluorescence during either the early or late stages of fluorescein angiography.

Three diagnoses other than lamellar macular hole might have been considered to account for the oval lesion in the macula: (1) a large central macular cyst, (2) a full-thickness macular hole, and (3) a hole in a con-

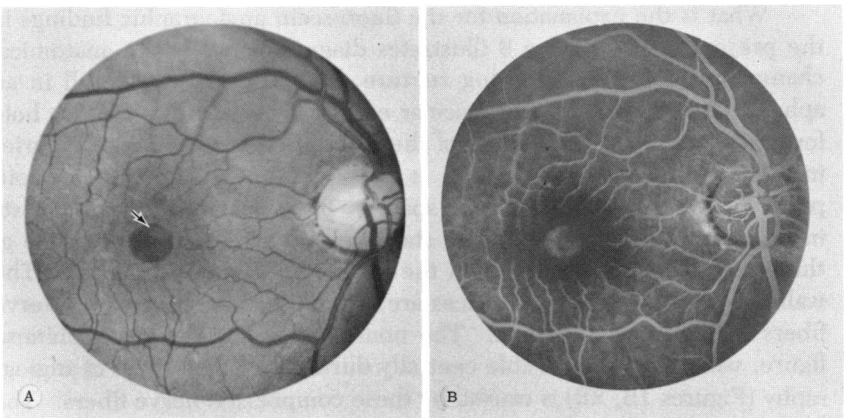

FIGURE 10

A: Full-thickness macular hole. Visual acuity was 20/70. Note the surrounding retinal halo of detachment and the small oval operculum (*arrows*). Yellowish deposits often present within the hole were absent in this patient. B: Angiogram showing early finely granular hyperfluorescence corresponding with the macular hole.

tracted perifoveal epiretinal membrane. If the oval lesion had been a solitary cyst, the inner wall of the cyst should have been visible biomicroscopically, and in the presence of the changes in retinal capillary permeability in cystoid macular edema, the dye should have stained the large cyst in the late phases of angiography. In the absence of surrounding cystoid macular edema, angiography cannot differentiate a lamellar macular hole from a solitary macular cyst. Neither should cause abnormal fluorescence in the macula.

Any one of the following findings would have been evidence favoring the diagnosis of a full-thickness macular hole: (1) a halo of serous retinal detachment surrounding the hole; (2) the presence of small yellow deposits on the surface of the pigment epithelium within the hole; (3) the presence of a small operculum suspended just in front of the macular hole; and, (4) absence of a light reflex as the slit-beam was carried across the base of the hole (Figure 10).

If the macular lesion had been a full-thickness hole, angiography should have demonstrated a discrete area of finely granular hyperfluorescence corresponding with the hole during the early phases of angiography (Figure 10).[3,4a] Figure 11 demonstrates diagrammatically that this hyperfluorescence is caused by several factors which permit increased visibility of the choroidal fluorescence. One factor is the absence of the xanthophilic pigment which is normally concentrated within the

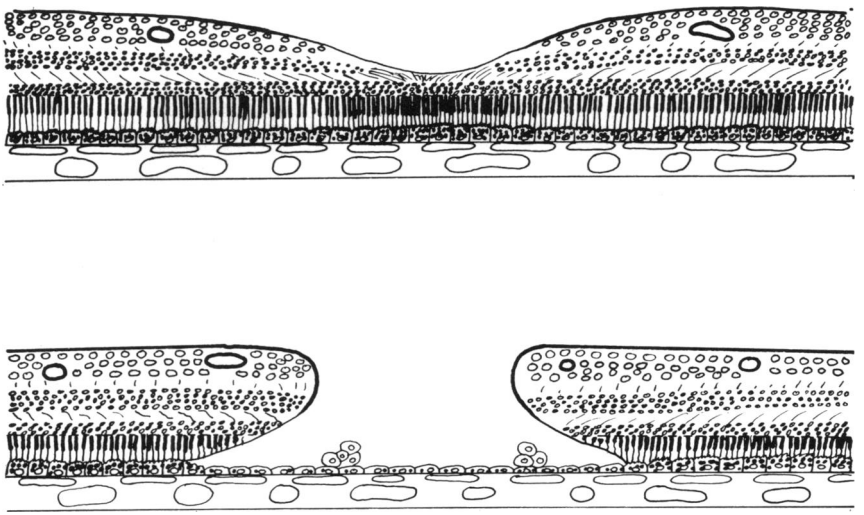

FIGURE 11

Diagram illustrating anatomical changes which occur following full-thickness macular hole formation. (*Above*) Normal macula. (*Below*) Full-thickness hole (operculum not included in illustration). Note flattening of pigment epithelium, loss of pigment, and cellular deposits (*arrow*) in the area of the hole.

outer nuclear and outer plexiform layers in the central macular area. A second important factor is the anatomic change which occurs in the pigment epithelium in the area of the hole. The pigment epithelium becomes a less effective light barrier both as the result of flattening of the cells which no longer interdigitate with the outer segments of the rods and cones and probably as the result of loss of pigment within the cells. A slight loss of retinal transparency at the edge of the hole is an additional light barrier which intensifies the relative hyperfluorescence within the confines of the hole.

The spontaneous contraction of an epiretinal membrane which surrounds but does not extend over the center of the macula may produce a biomicroscopic picture which can simulate closely a lamellar or full-thickness macular hole[4c,9] (Figures 12, 13). These patients are usually asymptomatic and have normal or nearly normal acuity. The shape of the hole in the epiretinal membrane may be round, ovoid, or tear-drop in shape. A crinkled, cellophane-like reflex indicative of an epiretinal membrane surrounds the hole. Fine retinal folds usually radiate outward from the hole. The slit-lamp beam drops abruptly into the depth of the hole. The foveal reflex is usually absent. The pigment epithelium within the hole appears normal. Features of a full-thickness hole — a halo of serous detachment, yellow deposits at the base, and opercula — are

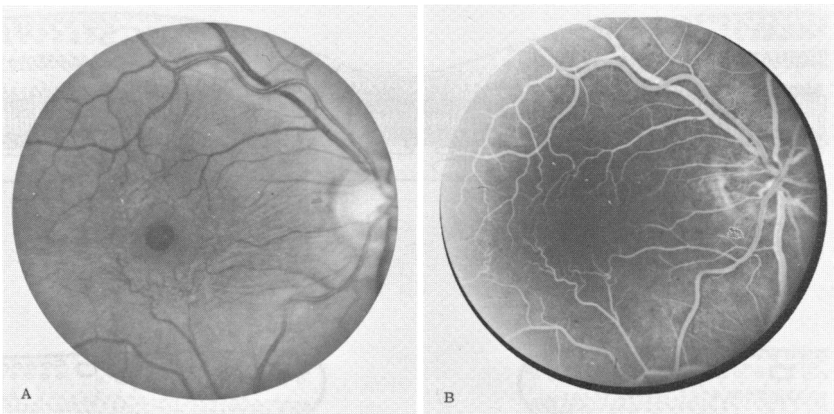

FIGURE 12

A: Hole in contracted perifoveal epiretinal membrane simulating macular hole in an asymptomatic 64-year-old woman, with 20/15 visual acuity, and normal Amsler grid, and static and kinetic perimetric findings. Note the fine crinkling of the inner retinal surface surrounding the hole and the fine retinal folds radiating outward from the macular areas. B: Angiography shows no abnormality.

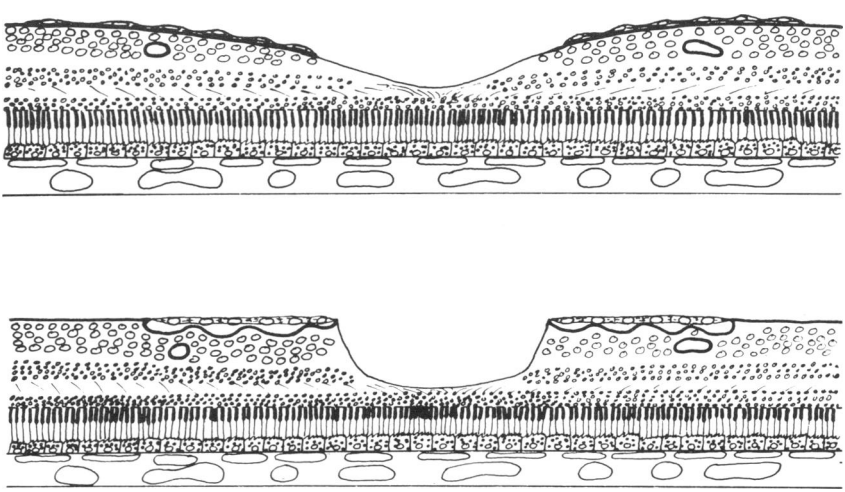

FIGURE 13

Diagram illustrating the anatomical changes which occur following the spontaneous contraction of a perifoveal epiretinal cellular membrane. (*Above*) Monocellular membrane on the inner surface of the internal limiting membrane in the perifoveal area prior to spontaneous contraction. (*Below*) Pseudomacular hole formation caused by spontaneous contraction of the epiretinal membrane. Shrinkage of the membrane causes fine irregular folds of the underlying inner retinal layers, radiating inner retinal folds peripheral to the membrane and minimal or no distortion of the outer retinal layers.

absent. In these patients, epiretinal cellular membranes, believed to be identical to that found clinically and histopathologically in the patient presented in this report, may grow onto the surface of the macula and for some unexplained reason spare the foveal area. Figure 13 demonstrates diagrammatically the anatomic changes which may occur when this membrane contracts and when it is densely adherent to the internal limiting membrane. The inner retinal surface is thrown into fine irregular folds and is displaced centrally and slightly anteriorly by the sphincteric action of the contracting surface membrane. This causes a sharply outlined concavity which superficially may simulate a full-thickness or lamellar macular hole (Figure 12). Fluorescein angiography in these patients is typically normal. In some patients with a relatively blond fundus, a very faint diffusely hyperfluorescent zone corresponding with the hole in the membrane may be evidence during the early minutes of angiography. Presumably this is caused by the barrier effect of the semitransparent epiretinal membrane which provides enough contrast to permit visualization of the faint choroidal fluorescence centrally that in the absence of this membrane would be inapparent. This faint diffuse fluorescence is usually easy to differentiate from the sharply circumscribed, more intense, finely granular pattern of fluorescence which corresponds precisely with a full-thickness macular hole. The visual prognosis in patients with this "pseudomacular hole" which is caused by a hole in an epiretinal membrane is excellent. Only rarely will the degree of macular distortion increase following its initial discovery. Since perifoveal epiretinal membranes may accompany lamellar as well as full-thickness macular holes, the clinician must rely on clinical, biomicroscopic, and angiographic criteria to differentiate a lamellar macular hole, a full-thickness macular hole, and a fenestration in the epiretinal membrane giving the impression of a macular hole.

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DISCUSSION

DR A. E. MAUMENEE. I wish to compliment Dr Gass for bringing to us another classical clinicopathologic case report. By such excellent studies as this he has contributed more to our knowledge of the pathogenesis of macular and retinal disease than anyone else in ophthalmology today. This case report typifies the superb clinical evaluation, excellent histopathologic study, and clear interpretation of the correlation of this material that is so characteristic of his work.

1. In this presentation today he has supplied further evidence that vitreous attachment to the macula is not the cause of cystoid maculopathy.
2. He has classified and given the differential diagnostic findings and pathologic changes in:
   a. preretinal membrane holes
   b. inner-lamellar retinal holes
   c. full-thickness macular retinal holes
3. He has suggested that these inner-lamellar holes are the result of a spontaneous rupture of a retinal cyst in cystoid maculopathy and that such changes might account for the irreversible visual loss in patients with the Irvine-Gass syndrome.
4. He has given supportive evidence for the retinal glial origin of preretinal macular membrane.

I can find nothing to disagree with him in these observations and can only thank him for his original clarification of many of the points which have been confusing in the past.

I would like to ask Dr Gass three questions. First, did he find any evidence of inflammatory cell infiltration in the ciliary body or in the perivascular areas in the retina? Cystoid maculopathy characteristically occurs in patients with intraocular inflammation — particularly of the anterior segment of the eye — in such entities as pars planitis, Behcet's syndrome, acute nongranulomatous iridocyclitis, acute recurrent (nodular) cyclitis, sarcoidosis and nematode endophthalmitis and it also occurs following operative procedures on the anterior segment of the eye, particularly when there has been an unusual amount of inflammatory response after cataract extraction, penetrating keratoplasty (aphakic eyes), retinal reattachments, glaucoma filtering procedures, and pars plana vitrectomy. Characteristically, those eyes that develop cystoid maculopathy have a more irritable course than the usual patient following cataract extraction

and even when there appears to be practically no evidence of inflammation, over a period of time the pupil becomes bound down to the hyaloid face of the vitreous and will not dilate indicating that there has been inflammatory reaction in the iris. In addition, periphlebitis and phlebitis were found in the macular area in the clinicopathologic case report of cystoid maculopathy published by Michels, Green, and myself in Ophthalmic Surgery (1971). A cataract extraction was done on this patient in May of 1967. When seen at the Wilmer Institute five months later he had cystoid maculopathy and was given 80 mg of systemic prednisone per day for eight days and then switched to every other day regime for four weeks. His visual acuity improved to 20/25 and remained at this level. He was last seen at Wilmer on October 31, 1969 — one month before he died.

Histologically, vitreous was attached to the wound above and adherent to the posterior surface of the iris. There was a mild inflammatory cellular infiltration in the ciliary body, a definite periphlebitis and phlebitis in the vessels near the macular area, a cystoid maculopathy and a serous detachment of the sensory retina. A similar phlebitis and periphlebitis was found in one other case of cystoid maculopathy.

Secondly, did Dr Gass mean to infer that all preretinal membranes arose from the astrocytes of the retina? Dr John Clarkson and Dr William Richard Green have reviewed the autopsy surgical material at the Wilmer Institute and found that the preretinal membranes, including those in the macular area, are composed of four types of tissue: (1) Condensed vitreous, (2) Preretinal cells or fibroblasts, (3), Retinal glial cells, and (4) Retinal pigment epithelial cells.

Finally, did Dr Gass mean to imply that the primary cause of permanent visual loss in cystoid maculopathy was due to lamellar hole formation? I have observed a number of patients who have apparently developed permanent visual loss; that is, loss of vision for four or five years or longer who do not have an evidence of lamellar holes but rather have a disturbance in the pigment epithelium in the macular area as the only manifestation of a macular lesion.

Again, I wish to congratulate Dr Gass on his splendid presentation. I hope that he will present many more of these to us in coming years.

DR RICHARD TROUTMAN. This may not be *àppropos* to this paper, but I would like to ask Doctor Gass if, in the Miami area where a number of intraocular implants have been done, he has noted a difference in the type of cystoid maculopathy he has seen or an increased incidence of cystoid maculopathy as has been reported after the use of the Copeland type of implant?

DR J. DONALD M. GASS. First, I should like to thank Doctor Maumenee for his very kind remarks. In regard to his question concerning the inflammation, you have to recall the course in this lady was five years in the right eye and approximately four years in her left eye. During the first two years of the time she had this cystoid edema, we noted vitreous cells in the eye but this became less and less

noticeable and finally in the last year there is no mention of vitreous cells at all. I wish I could say that I had noted whether they were there or not but I honestly don't know. All I can say is that they apparently were not a prominent aspect of her disease in the later stages.

We sectioned one eye vertically and one eye horizontally, but we only did serial sections through the macular area. Perhaps we should go back and section the whole eye to find out if there is a focus of inflammation somewhere in the eye. There is no question that inflammatory cells in the vitreous is a very common finding in patients with cystoid edema; but you do see patients with vivid cystoid edema and not an inflammatory cell in the eye. While I agree that inflammation is important there is a strange absence of inflammatory cells clinically in some of these patients.

I wanted to clarify that the histopathologic section I showed initially did show a serous detachment of the macula. This was not our patient. Actually there was no serous detachment of the macula in our case.

In regard to the question ar all preretinal membranes astrocytic in origin, up until recently I rather liked the idea that most of these preretinal membranes were condensed vitreous. That appealed to me but there is some evidence that at least some of these are astrocytic in type. Some people, particularly Doctor Machemer, feels strongly that these are cellular membranes. They are not mainly fibrocellular. The answer is I doubt seriously that all these membranes are due to the same thing.

In regard to the lamellar macular hole being the prime cause of visual loss, I'm not certain that this is true; although I would say that if you see a patient who has loss of vision after cataract extraction and you can't explain it on the basis of what you can see with the slit lamp, it is conceivable that, that patient indeed went through a period of time where he had a ruptured inner wall of the cyst. After the cystoid edema has disappeared the lamellar hole may be difficult to appreciate. I have never been impressed that seroud detachment of the macula is a very prominent aspect of cystoid macular edema, and I rather doubt that this is the cause often of permanent loss of vision in the macula; but I really don't know the answer.

I have not noticed any peculiar type of cystoid macular edema associated with intraocular lenses. I do not know the answer as to whether cystoid macular edema is more common in these patients. A controlled prospective study to answer this question is underway in Miami.