Clinicopathologic Features of Surgically Excised Choroidal Neovascular Membranes

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Purpose: The purpose of this study is a descriptive correlation of the clinical, fluorescein angiographic, and pathologic features in a large series of patients who underwent surgical removal of choroidal neovascular membranes.

Methods: The patients' clinical data were recorded for each surgically removed choroidal neovascular membrane received in the authors' laboratory. Fluorescein angiographic characteristics of the membranes, including well-demarcated versus poorly demarcated preoperative appearance, postoperative choroidal atrophy, and membrane recurrence, were recorded whenever possible. The pathologic features of the membranes, including cellular and extracellular constituents, were determined on light and electron microscopic examination.

Results: A total of 123 membranes were studied. Underlying diseases in decreasing order of frequency were age-related macular degeneration, ocular histoplasmosis syndrome, myopia, idiopathic and pattern dystrophy. The cellular and extracellular constituents of the membranes were similar, regardless of underlying disease, with the exception of basal laminar deposit, seen almost exclusively in age-related macular degeneration. Well-demarcated membrane components were localized with a central subretinal pigment epithelium fibrovascular core. Poorly demarcated membranes were represented by a subneurosensory retinal (breakthrough) component, although most of these membranes had associated retinal pigment epithelium. Fragments of Bruch's membrane were common in specimens from patients with postoperative choroidal atrophy, and there was generally a lack of vascular channels in membranes that led to recurrence.

Conclusions: This study suggests that choroidal neovascular membranes represent a stereotypic, nonspecific response, regardless of underlying disease. Most membranes are subretinal pigment epithelium, and what is recognized angiographically as a subneurosensory retinal component contains associated retinal pigment epithelium in most instances. Fragments of Bruch's membrane in the specimen correlate with postoperative choroidal atrophy. Lack of vascular channels in the surgical specimen may correlate with a risk for postoperative membrane recurrence.

Ophthalmology 1994;101:1099–1111

Modern vitreoretinal surgical techniques enable removal of submacular tissue.[1] There recently have been several

Originally received: September 20, 1993.
Revision accepted: January 11, 1994.

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Presented at the American Academy of Ophthalmology Annual Meeting, Chicago, November 1993.

Supported in part by a departmental grant from Research to Prevent Blindness, Inc, New York, New York, Knights Templar Foundation, Springfield, Illinois, and National Institutes of Health departmental core grant EY06360, Bethesda, Maryland.

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clinical reports describing surgical removal of choroidal neovascular membranes from patients with age-related macular degeneration[2-4] and the ocular histoplasmosis syndrome.[3,4] The histopathologic features of surgically excised choroidal neovascular membranes from small numbers of patients with age-related macular degeneration,[5,6] the ocular histoplasmosis syndrome,[7] and idiopathic disease[8] have been described. This type of surgery provides tissue for histopathologic examination and enables clinical correlation, including those with fluorescein angiographic findings at a relatively early point in the evolution of the membrane, rather than in late stages as studied in eyes obtained postmortem.[9,10]

Preoperative fluorescein angiographies of these membranes have shown classic[4,11-13] and occult[4,11-13] patterns. For the purpose of this study, membranes were classified as being either well or poorly demarcated. There has been postoperative angiographic evidence of choroidal (choriocapillaris) atrophy after surgery, although it is unknown if this is due to removal of a specific tissue, such as fragments of Bruch's membrane, retinal pigment epithelium, and/or choroid, or whether the atrophy was present before surgery. Occasionally, the choroidal neovascular membrane recurs after surgical removal[3] and a question arises regarding the presence or absence of any cellular constituent in the originally excised membrane that might correlate with recurrence.

We undertook a retrospective study of the histopathologic features of a large series of surgically removed choroidal neovascular membranes to compare the relative frequencies of the cellular and extracellular constituents with previous small series from our laboratory. We previously reported the histologic features for only 20 membranes[5,7,8] and compared the histologic and fluorescein angiographic features in only five membranes.[14] We compared the histologic and fluorescein angiographic features for poorly demarcated membranes, postoperative choroidal "atrophy," and postoperative membrane recurrence in specimens from our laboratory for the first time. In addition to membranes secondary to age-related macular degeneration, ocular histoplasmosis syndrome, and idiopathic disease, we report for the first time features of membranes secondary to myopia and pattern dystrophy. We compared the histopathologic findings in the membranes with the patient's underlying disease, preoperative well-demarcated versus poorly demarcated fluorescein angiographic appearance, postoperative fluorescein evidence of choroidal atrophy, and recurrence. We did not attempt to correlate the visual outcome with fluorescein angiographic appearance or underlying disease in this descriptive, clinicopathologic study.

Materials and Methods

Surgically excised choroidal neovascular membranes accessioned in the L. F. Montgomery Ophthalmic Pathology Laboratory, Emory Eye Center, from January 1991 through September 1993, were studied. For each membrane, the patient's underlying disease, age, sex, and operated eye were recorded. The preoperative (well-demarcated versus poorly demarcated) and postoperative (intact or atrophied choroid) fluorescein angiographic interpretation was listed for each patient whose angiogram was available. Well-demarcated membranes were defined as having a "bull's eye" appearance, and poorly demarcated membranes were defined as having a scalloped "net-like" appearance in the early phases of the fluorescein angiography. The classification was for clinicopathologic correlation purposes and the Macular Photocoagulation Study classification of classic versus occult was not used.[13] Preoperative fluorescein angiograms were usually within 1 week of surgery, and postoperative fluorescein angiograms were usually 1 to 2 months after surgery. Any clinical recurrences demonstrated by fluorescein angiography were noted.

The membranes were removed via previously described surgical techniques.[2,15] The membranes were placed in 10% neutral-buffered formalin or 2.5% gluteraldehyde and processed for routine light microscopic or transmission electron microscopic examination, respectively. For "routine" light microscopy, the membranes were dehydrated through increasing concentrations of alcohol, cleared with xylene, and embedded on edge in paraffin. In addition, 5-μm-thick sections through the centers of the membranes were stained with hematoxylin–eosin and periodic acid-Schiff. Surgical artifacts were negligible due to delicate handling of the specimens. For transmission electron microscopic examination, the specimens were postfixed with 0.1 mol/l of cacodylate buffer and 1% osmium tetroxide. After standard dehydration, the membranes were embedded on edge in epoxy resin, and semithin (0.1-μm) sections were cut and stained with toluidine blue. Thin sections were cut and stained with uranyl acetate–lead citrate. Previously reported criteria were used for ultrastructural identification of cellular and extracellular constituents of the membranes.[16,17] We classified the histologic appearance of the membranes independent of clinical information. All sections were examined. The overall configuration for each membrane was recorded, including whether the membrane displayed breakthrough into the subneurosensory retinal space. A subset of five well-demarcated membranes was topographically studied by submitting the core and rim as separate surgical specimens.[14] Specific topographic components of poorly demarcated membranes that were not evaluated as separate components could not be identified at the time of surgery.[18] Membranes that were associated with postoperative recurrence were studied regarding the presence or absence of specific components.

Results

Clinical Characteristics

The clinical characteristics including preoperative and postoperative fluorescein angiographic findings are summarized in Table 1. There were 123 patients studied, and the underlying diseases in decreasing order of frequency were age-related macular degeneration (Figs 1 and 2),

Table 1. Clinical and Fluorescein Angiographic Features of 123 Surgically Excised Choroidal Neovascular Membranes

	AMD (n = 90)	OHS (n = 18)	Myopia (n = 7)	Idiopathic Disease (n = 6)	Pattern Dystrophy (n = 2)
Average age (yrs)	75	46	47	34	61
Sex					
M	42	7	7	2	1
F	48	11		4	1
Eye					
OD	33	9	4	3	1
OS	57	9	3	3	1
Preoperative FA					
Well demarcated	22	8	6	1	
Poorly demarcated	28		1		
Postoperative FA					
Choroidal atrophy	9	1	1		
Recurrence	4	4	2	2	

AMD = age-related macular degeneration; OHS = ocular histoplasmosis syndrome; OD = right eye; OS = left eye; FA = fluorescein angiogram.

ocular histoplasmosis syndrome (Fig 3), myopia, idiopathic disease, and pattern dystrophy. The average ages of the patients ranged from 34 years for idiopathic disease to 75 years for age-related macular degeneration. There were approximately the same number of men (n = 59) as women (n = 64) in the study. The right and left eyes were operated on equally, except in patients with age-related macular degeneration, in whom the left eye was operated on more frequently. A preoperative angiographic determination of membrane configuration was made in 66 patients, 37 of whom had well-demarcated and 29 of whom had poorly demarcated membranes. All but one of the available angiograms of the membranes from patients with ocular histoplasmosis syndrome, myopia, and idiopathic disease were well demarcated, although there were more poorly demarcated than well-demarcated membranes in patients with age-related macular degeneration. There was postoperative fluorescein angiographic evidence of choroidal atrophy in 11 patients (Fig 4). There were 12 membranes excised that later recurred. This recurrence rate may have been underestimated, because postoperative fluorescein angiograms were evaluated in only approximately half of the patients in this study.

Pathologic Findings

The histopathologic features of the excised membranes are summarized in Table 2. All 123 membranes were examined by light microscopy, either the "routine" light microscopy sections or the toluidine blue-stained sections, and 78 membranes were examined by transmission electron microscopy. After examination of approximately the first 50 membranes by transmission electron microscopy, most components were identified by light microscopic examination alone. The light microscopic and ultrastructural features of the membranes were compared. The major cellular and extracellular components (retinal pigment epithelium, vascular endothelium, fibrocytes, macrophages, and photoreceptors) and extracellular components (collagen, basal laminar deposit, and fibrin) were identified correctly by light microscopy in all of the compared cases (see Discussion section). Other components were identified correctly on light microscopy in the last ten patients examined, indicating a "learning curve." The most prominent cellular components of the membranes in decreasing order of frequency were retinal pigment epithelium (Fig 5), vascular endothelium (Fig 6), fibrocytes, macrophages, and photoreceptors. The most prominent extracellular components in the membranes in decreasing order of frequency were collagen, fibrin, basal laminar deposit, and fragments of Bruch's membrane (Fig 7). Basal laminar deposit was seen in 51 age-related macular degeneration membranes and only 1 membrane from another disease, myopia. There were fragments of choroid identified in four membranes (Fig 4), and curiously, three age-related macular degeneration membranes displayed associated foreign-body giant cells (Fig 8).[19]

Clinicopathologic Features of Membrane Types

The clinicopathologic features of the membranes according to preoperative and postoperative fluorescein angiographic appearance are listed in Table 3. Preoperative fluorescein angiograms showed all membranes to be classic and included well- and poorly demarcated varieties. Well-demarcated membranes[14] had a central core of nonscalloped hyperfluorescence surrounded by inner hypofluorescent and outer faintly fluorescent rims (Fig 1). The core, inner, and outer rims were composed of fibrovascular tissue, hypertrophied retinal pigment

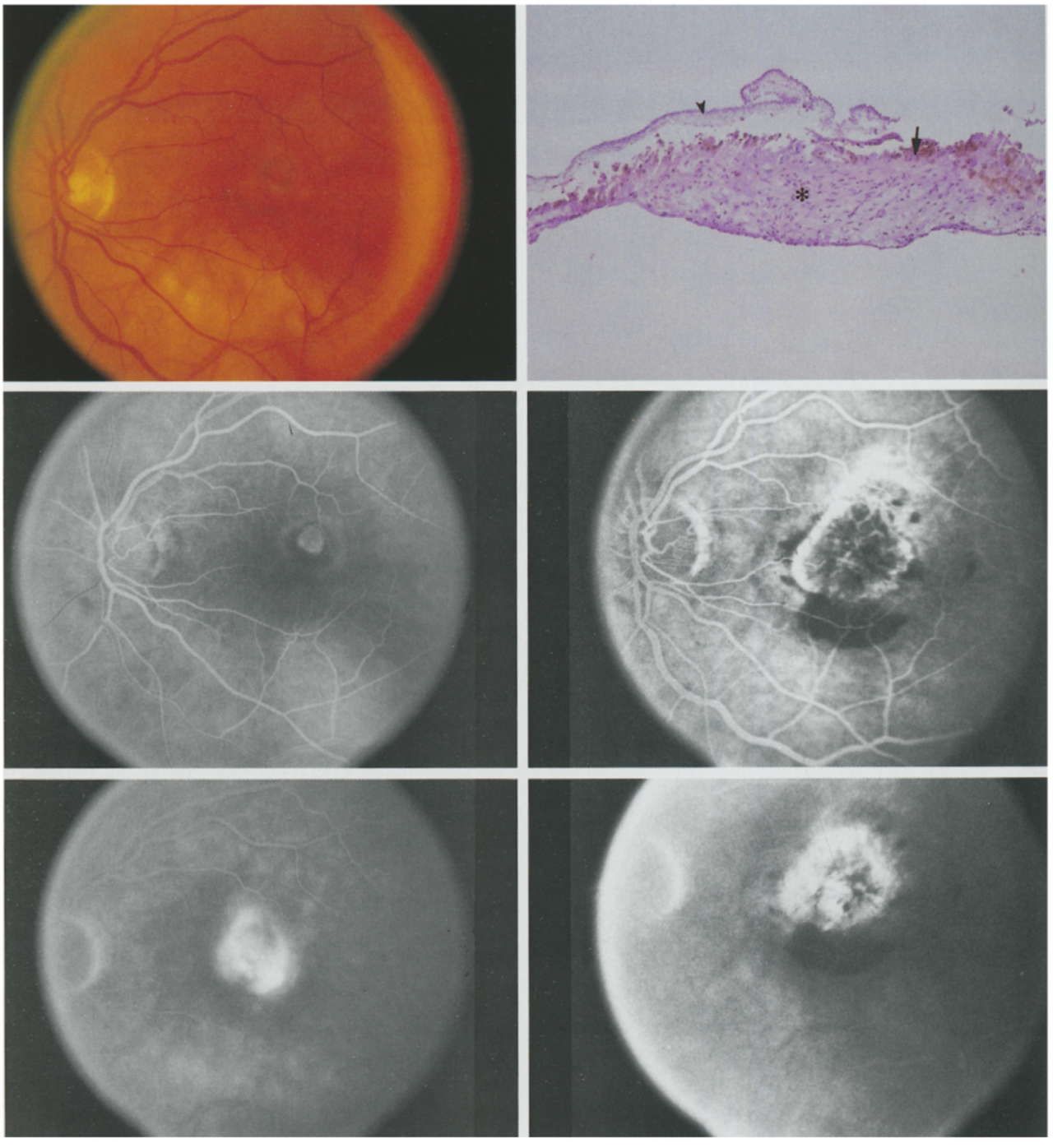

Figure 1. The funduscopic **(top left)** and fluorescein angiographic features **(center left)** in the left eye of this 73-year-old woman with age-related macular degeneration show a well-demarcated extrafoveal choroidal neovascular membrane with a "bull's eye" appearance. The membrane was treated with laser photocoagulation and recurred 3 weeks later under the fovea **(bottom left).** The excised membrane (asterisk) **(top right)** lies external to the retinal pigment epithelium (arrow) (courtesy of *Ophthalmol Clin North Am 1993;6:359–74*). Photoreceptor segments (arrowhead) are present in the specimen (hematoxylin–eosin; original magnification, ×25). Early **(center right)** and late **(bottom right)** phases of the 6-week postoperative fluorescein angiogram show a poorly demarcated vascular net with scalloped edges, representing a recurrent (persistent) membrane.

epithelium, and fibrin, respectively (Fig 9).[14] Poorly demarcated membranes displayed angiographic vascular nets with scalloped edges that exhibited late-phase leakage, obscuring the border (Fig 2). There is overlap of interpretation of poorly demarcated and poorly defined (occult) membranes as defined by the Macular Photocoagulation Study.[13] These poorly demarcated membranes were composed of evenly dispersed fibrovascular tissue, usually associated with retinal pigment epithelium.[18] Breakthrough, a histologic interpretation,

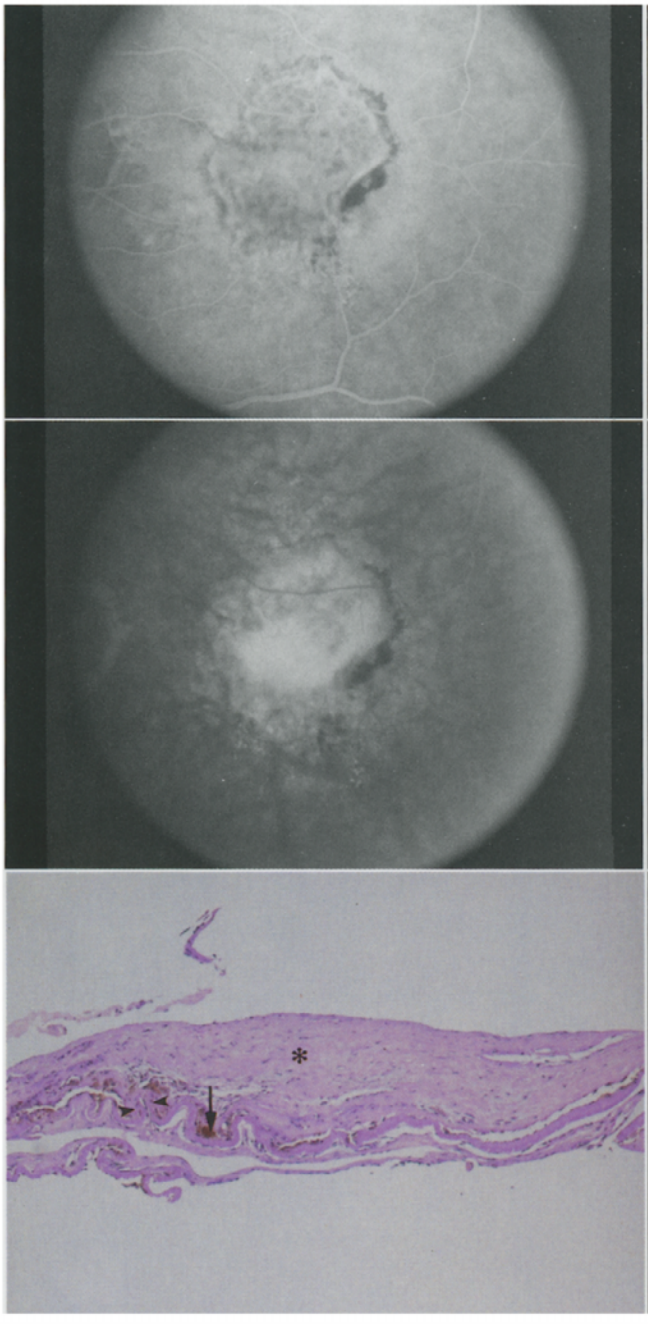

Figure 2. The early **(top)** and late **(center)** phases of the fluorescein angiogram in the left eye of this 71-year-old woman with age-related macular degeneration show a large, poorly demarcated choroidal neovascular membrane that displays late-phase leakage. The surgically excised membrane **(bottom)** is composed of fibrovascular tissue (asterisk) internal to the retinal pigment epithelium (arrow) and a subjacent eosinophilic band of diffusely thickened inner aspect of Bruch's membrane. A point of "breakthrough" (between arrowheads) is noted (hematoxylin–eosin; original magnification, ×25).

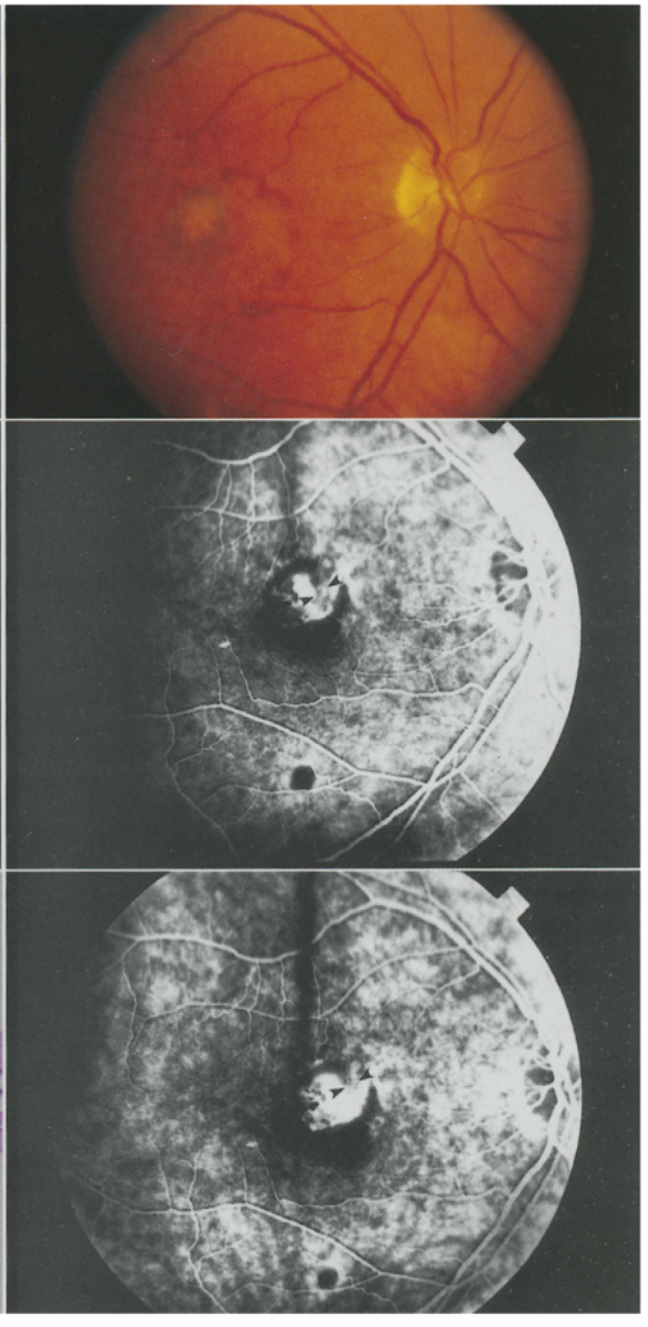

Figure 3. The fundus **(top)**, early **(center)**, and late **(bottom)** fluorescein angiographic appearance of the right eye of this 48-year-old woman with the ocular histoplasmosis syndrome shows a well-demarcated choroidal neovascular membrane with evidence of a poorly demarcated (breakthrough) subneurosensory retinal component (between arrowheads).

was seen in 15 membranes and consisted of subneurosensory retinal fibrovascular tissue internal to the level of the retinal pigment epithelium (Fig 2). Breakthrough occurred in approximately one in ten membranes, regardless of underlying disease. Eight of nine breakthrough membranes with interpretable angiograms displayed a poorly demarcated appearance. The remaining breakthrough was incipient and occurred in a well-demarcated membrane with an early poorly demarcated component (Fig 3). Postoperative fluorescein angio-

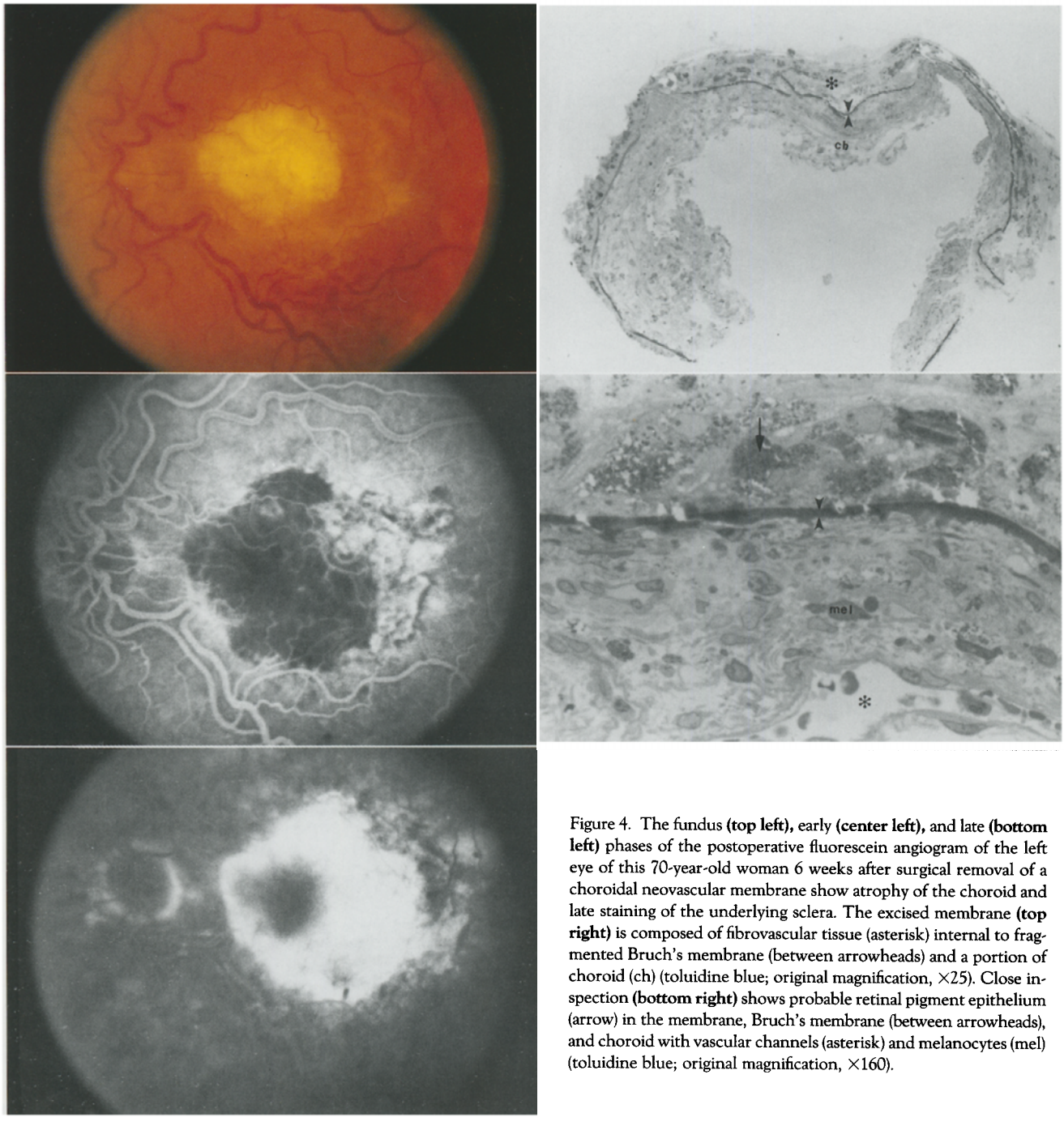

Figure 4. The fundus **(top left),** early **(center left),** and late **(bottom left)** phases of the postoperative fluorescein angiogram of the left eye of this 70-year-old woman 6 weeks after surgical removal of a choroidal neovascular membrane show atrophy of the choroid and late staining of the underlying sclera. The excised membrane **(top right)** is composed of fibrovascular tissue (asterisk) internal to fragmented Bruch's membrane (between arrowheads) and a portion of choroid (ch) (toluidine blue; original magnification, ×25). Close inspection **(bottom right)** shows probable retinal pigment epithelium (arrow) in the membrane, Bruch's membrane (between arrowheads), and choroid with vascular channels (asterisk) and melanocytes (mel) (toluidine blue; original magnification, ×160).

grams included choroidal atrophy and membrane recurrence. Choroidal atrophy was present in 11 patients, 5 of whom had a fragment of Bruch's membrane and/or choroid in the surgical specimen (Fig 4). Nine of the 11 patients with choroidal atrophy contained retinal pigment epithelium in the membrane. Choroidal atrophy appeared as a hypofluorescent "punched-out" lesion at the site of surgery, evident at approximately 6 weeks postoperatively. There were 12 recurrent membranes with fluorescein angiographic evidence of hyperfluorescence increasing with time in the angiogram at the site of or immediately adjacent to the surgery site. The recurrences tended to be poorly demarcated and located under the fovea. There was no evidence of vascular channels in 5 of the 12 original surgically excised membranes that later recurred (Fig 1).

Table 2. Pathologic Features of 123 Surgically Excised Choroidal Neovascular Membranes

	AMD (n = 90)	OHS (n = 18)	Myopia (n = 7)	Idiopathic Disease (n = 6)	Pattern Dystrophy (n = 2)
RPE	75	16	5	6	1
Vascular endothelium	76	12	3	3	1
Fibrocyte	41	9	5	3	1
Macrophage	41	10	4	2	1
Photoreceptor	34	8	2	3	
Erythrocyte	22	4	2	2	
Lymphocyte	22	4			
Myofibroblast	7	1			
PMN	1				
Ghost erythrocyte	3				
FBGC	3				
Melanocyte	1	1			
Plama cell	1	1			
Pericyte		1		1	
Collagen	55	10	4	5	2
Fibrin	32	7	2		
BLD	51		1		
Fragment of Bruch's membrane	21	1	1		
Choroid	3	1			
Breakthrough*	12	2		1	

AMD = age-related macular degeneration; OHS = ocular histoplasmosis syndrome; RPE = retinal pigment epithelium; PMN = polymorphonuclear leukocyte; FBGC = foreign body giant cell; BLD = basal laminar deposit.

* Subneurosensory retinal component.

Discussion

The data generated in this study may be categorized according to disease or membrane type. We first analyzed the data according to underlying disease.

The vast majority of membranes, regardless of underlying disease, were composed of retinal pigment epithelium and vascular endothelium. Most of the membranes contained fibrocytes and collagen. This confirms previous small series from our laboratory for membranes from patients with age-related macular degeneration,[5] ocular histoplasmosis syndrome,[7] and idiopathic disease.[8] We show for the first time that choroidal neovascular membranes from patients with myopia and pattern dystrophy are composed of similar constituents. The number of membranes in our study with vascular channels may have been underestimated because not all membranes were examined by electron microscopy, and immunohistochemical localization of vascular endothelium was not used. Similarly, vascular pericytes may have been underestimated.

We found that, with experience, cells including retinal pigment epithelium, vascular endothelium, fibrocytes, photoreceptors, macrophages, inflammatory cells, melanocytes, and extracellular material, including fragments of Bruch's membrane, basal laminar deposit, fibrin, and collagen, could be identified on "routine" light microscopy. We confirmed this by comparing the light microscopic appearance of what we suspected to be these components with corresponding cells and material examined by transmission electron microscopy and immunohistochemical staining.[20] For example, retinal pigment epithelium formed monolayers or tubuloacinar structures, maintained polarity, and often displayed intracytoplasmic golden brown lancet-shaped pigment granules (Fig 5). Vascular channels lined by endothelium were composed of tubules lined internally by low, flat cells, and often contained erythrocytes in the lumen (Fig 6). Fibrocytes had spindle-shaped, tapered nuclei and were associated with collagen. Fibrin consisted of fine, eosinophilic fibrillogranular material. Basal laminar deposit was composed of linear streaks of variably granular eosinophilic material, often located between the retinal pigment epithelium and inner aspect of Bruch's membrane (Fig 7). A limitation of interpretation by light microscopy alone is that some cells, such as myofibrocytes, fibrous astrocytes, and hyperplastic retinal pigment epithelium, may be spindle-shaped, simulating fibrocytes. These former cell types may have been underrepresented in our results.

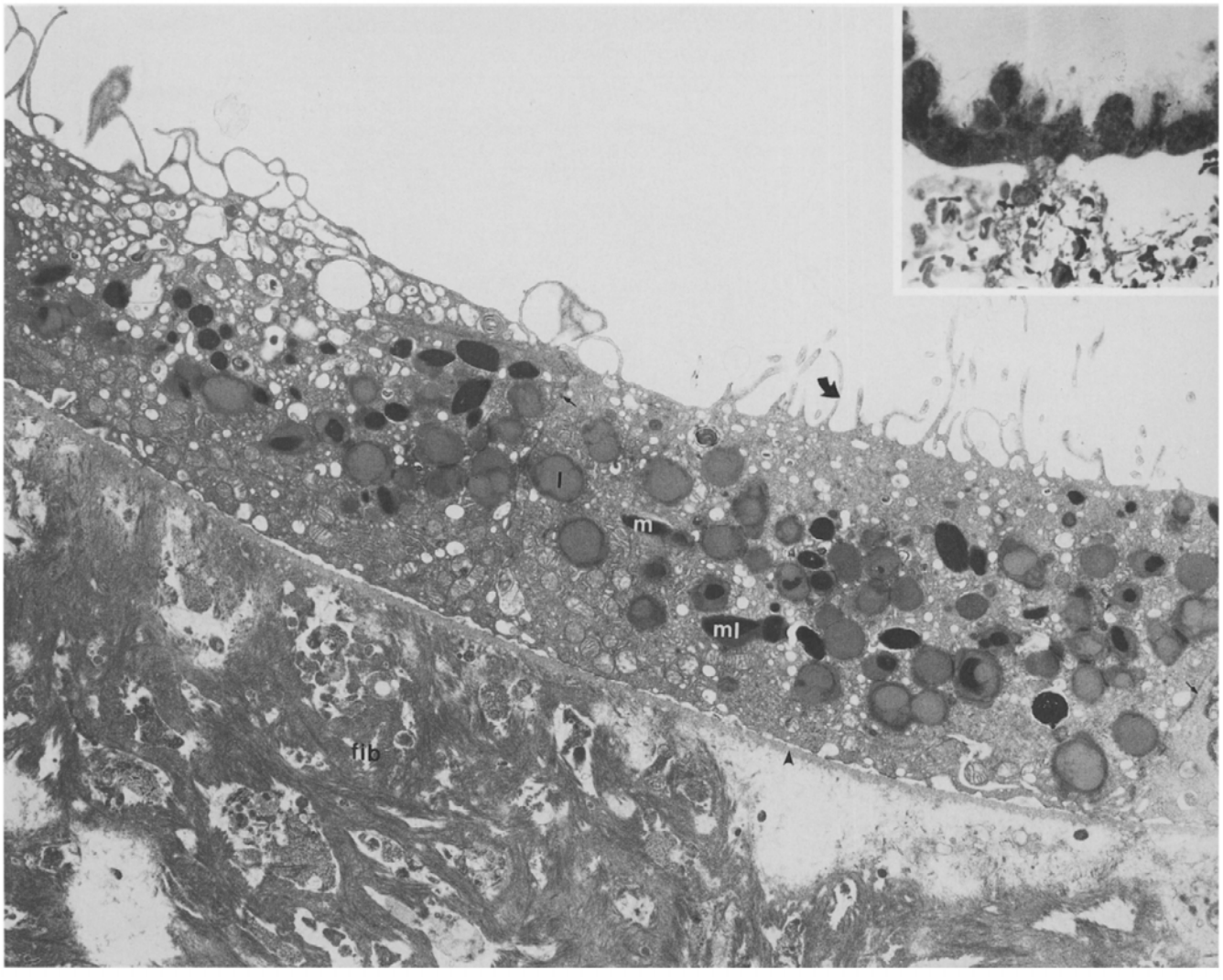

Figure 5. Retinal pigment epithelium in a surgically excised choroidal neovascular membrane is composed of a layer of cuboidal cells with surface microvillous processes (curved arrow) and intercellular junctions (arrows). The cells contain intracytoplasmic lipofuscin (l), lancet-shaped melanin (m), and melanolipofuscin (ml) granules. Basal lamina (arrowhead) and fibrin (fib) are present at the base of the cells (original magnification, ×8410; *inset*, original magnification, ×160).

We did not distinguish basal laminar deposit from basal linear deposit in this study. Basal laminar deposit is internal to and basal linear deposit is external to the basement membrane of the retinal pigment epithelium.[21] In our experience, location between the two deposits often overlaps and it may be difficult to distinguish between them on light microscopic examination; therefore, we combined basal laminar and basal linear deposit and classified them both as basal laminar deposit. The importance of recognizing basal laminar deposit in the membranes is that our data indicate that this material is seen almost exclusively in membranes secondary to age-related macular degeneration. If we saw basal laminar deposit in the membrane, we were able to predict with reasonable accuracy that the patient's underlying disease was age-related macular degeneration.

Curiously, we saw three membranes that contained foreign-body giant cells (Fig 8). Again, this finding was seen only in membranes from patients with age-related macular degeneration.[19] Foreign-body giant cells have been observed in membranes associated with age-related macular degeneration in whole eyes examined postmortem,[19] and the significance of this finding is unknown. Other than basal laminar deposit and foreign-body giant cells, the cellular and extracellular components of the membranes were similar, regardless of the underlying disease, consistent with the concept that choroidal neovascular membranes represent a stereotypic, nonspecific wound repair-like response to a specific stimulus.[20]

The data also were categorized according to specific membrane type. All membranes with interpretable fluorescein angiograms in this study were classic, either well or poorly demarcated. Well-demarcated membranes had a "bull's eye" fluorescein angiographic appearance[11,18] and comprised a little fewer than half of the age-related macular disease membranes, although they almost exclusively

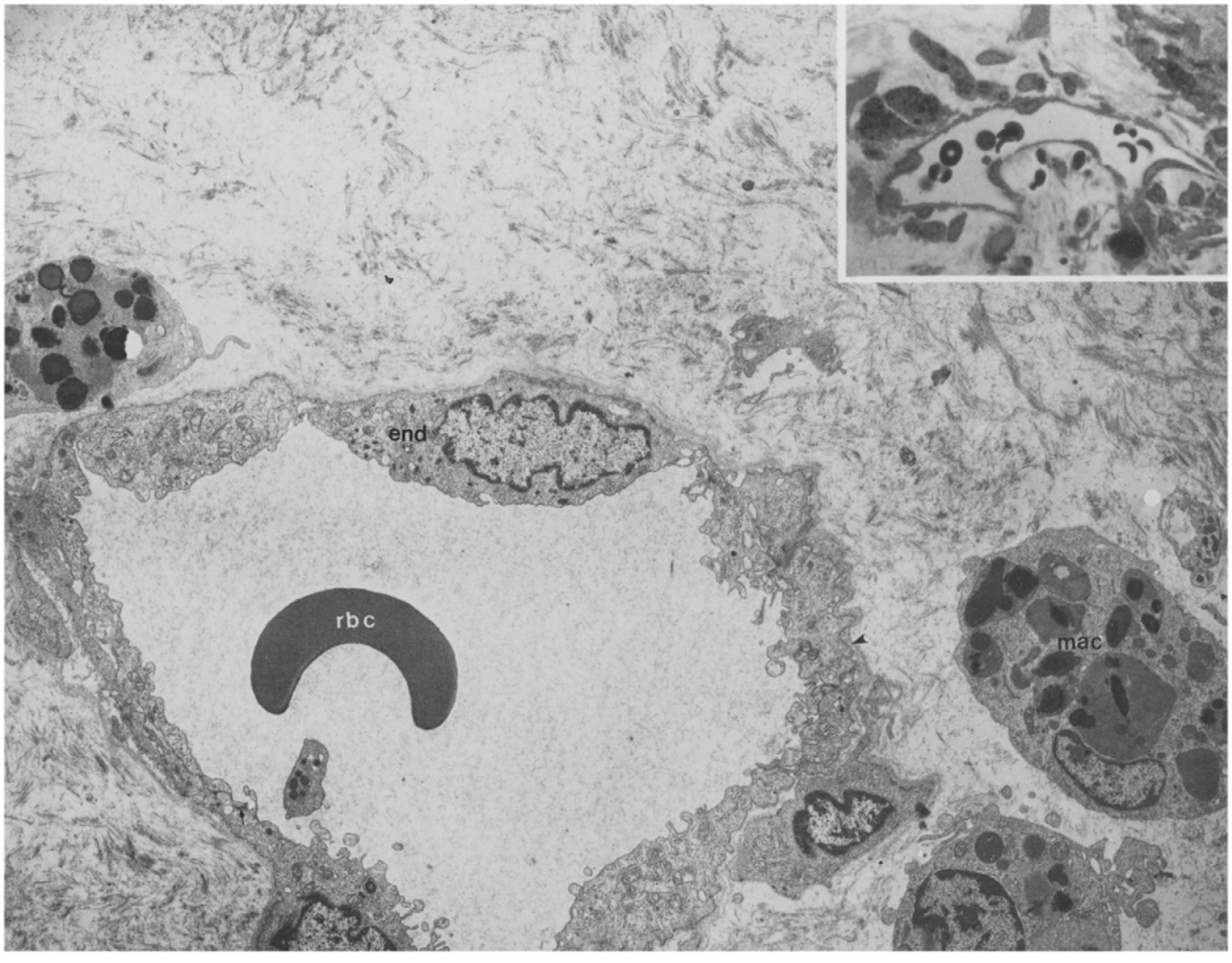

Figure 6. A vascular channel in a surgically excised membrane is surrounded by loosely arranged collagen and fibrin, lined by endothelium (end), and contains an erythrocyte (rbc). The endothelium displays a basal lamina (arrowhead) and intercellular junctions (arrow). Several pigment-containing macrophages (mac) are present in the membrane (original magnification, ×5510; *inset*, original magnification, ×160).

comprised the ocular histoplasmosis, myopia, and idiopathic membranes. Specific components of the well-demarcated membranes were examined, and the membranes were found to contain a central nonscalloped hyperfluorescent core composed of fibrovascular tissue surrounded by rims of hypertrophied retinal pigment epithelium and subretinal fibrin,[14] corresponding to the "bull's eye" appearance (Fig 10). The core or center has been interpreted on clinical examination to be a fibrovascular membrane occurring below the retinal pigment epithelium, causing the angiographic "hot spot" (Fig 1). This hot spot was confirmed on pathologic examination to be the central fibrovascular core internally surfaced by retinal pigment epithelium (Fig 9). The outer concentric rim around the center of the bull's eye does not contain a fibrovascular component. The finding of a lack of a vascular component in the outer rim of well-demarcated membranes was confirmed by a recent study (Bynoe, unpublished data; presented at the 1993 ARVO Annual Meeting).

Slightly more than half of the age-related macular degeneration membranes with available fluorescein angiograms were poorly demarcated, represented by scalloped vascular nets with late-phase leakage obscuring the border (Fig 2). These poorly demarcated membranes have been interpreted on clinical examination to be true subneurosensory membranes, not surfaced by retinal pigment epithelium. In our study, there were 15 histopathologic breakthrough (subneurosensory retina) membranes. Of these 15 breakthrough membranes, 14 had associated retinal pigment epithelium, generally underlying the breakthrough component (Fig 2). It is important to note that when a surgeon removes a subneurosensory retinal (breakthrough) membrane, retinal pigment epithelium also is removed in almost all cases. It is interesting that eight of nine histopathologic breakthrough membranes with interpretable preoperative fluorescein angiograms were poorly demarcated, thus confirming the clinical impression that poorly demarcated membranes are in the

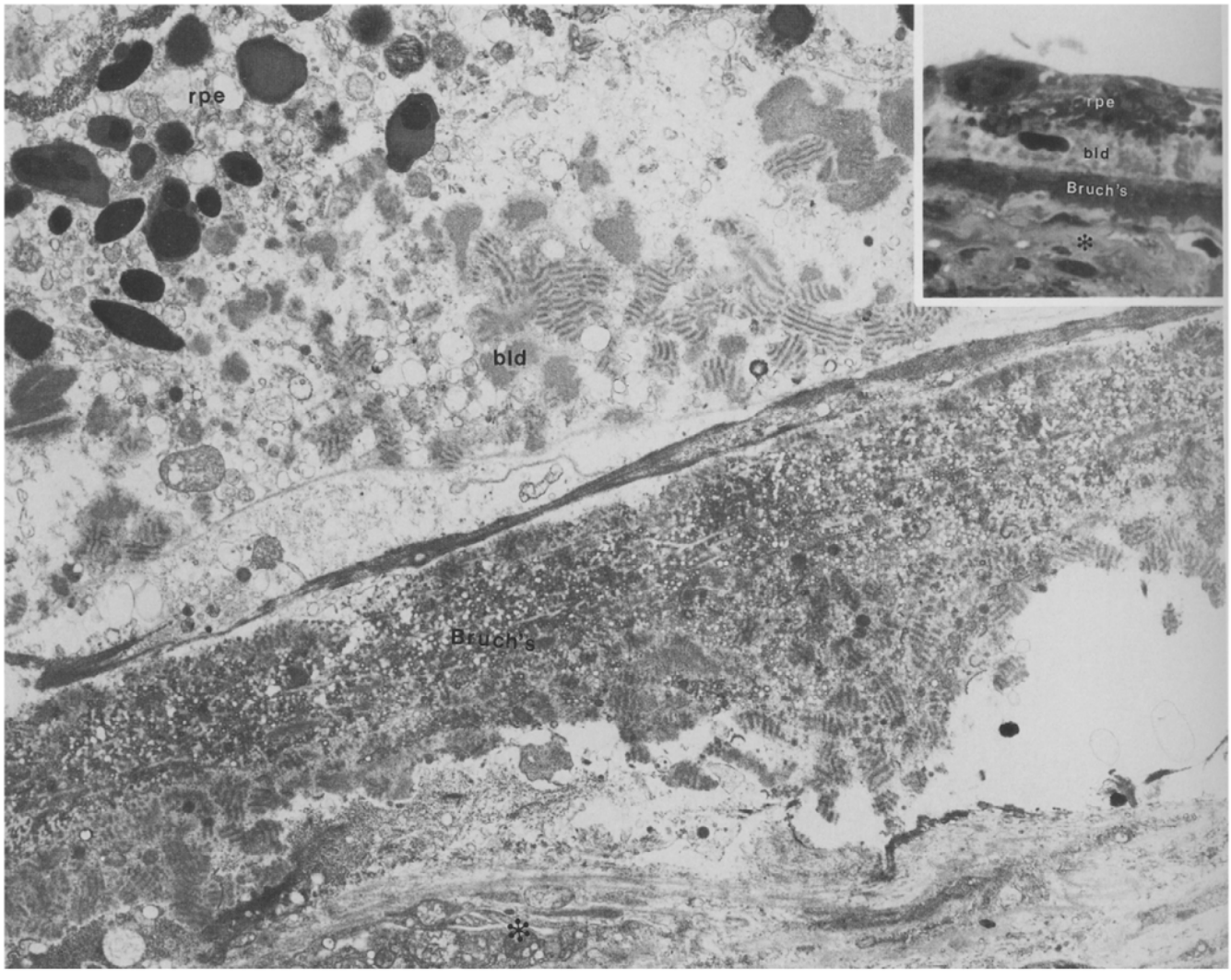

Figure 7. Basal laminar deposit (bld) lies between the retinal pigment epithelium (rpe) and the inner aspect of Bruch's membrane in this choroidal neovascular membrane excised from a patient with age-related macular degeneration. Wide-spaced collagen is in the basal laminar deposit and scarred choroid versus a component of the choroidal neovascular membrane (asterisk) are present within Bruch's membrane (original magnification, ×10,440; *inset*, original magnification, ×400).

subneurosensory retinal space (Fig 11). The ninth breakthrough membrane had a small, incipient subneurosensory retinal component, and was angiographically well demarcated with an early poorly demarcated component (Fig 3). That membrane may represent a sequential link between well-demarcated and poorly demarcated membranes. Additionally, preoperative well-demarcated membranes that recurred often displayed postoperative poorly demarcated features (Fig 1). The significance of this is that well-demarcated membranes might evolve into poorly demarcated membranes or have a poorly demarcated (subneurosensory retinal) component. A limitation of our study regarding membrane type is that retinal pigment epithelium conceivably might line the external surface of the membrane alone. A subneurosensory retinal membrane might histologically simulate a subretinal pigment epithelial membrane, and the number of subneurosensory retinal membranes in our study may have been underestimated. Two dimensional reconstruction of serial sections may provide better evidence of definitive membrane localization.

An angiographic feature that surgeons have noted in some patients after removing choroidal neovascular membranes is apparent atrophy, or absence of the choriocapillaris and possibly larger choroidal vessels. The question arises as to whether portions of the choroid, retinal pigment epithelium, or Bruch's membrane were surgically removed, thereby causing this appearance. We were able to identify this appearance of angiographic postoperative choroidal atrophy in 11 patients. Retinal pigment epithelium was present in nine of the membranes, reflecting the fact that retinal pigment epithelium is present in most surgically excised membranes, regardless of whether there is postoperative choroidal atrophy. Fragments of Bruch's membrane were present in five of the membranes, one of which contained a fragment of choroid (Fig 4).

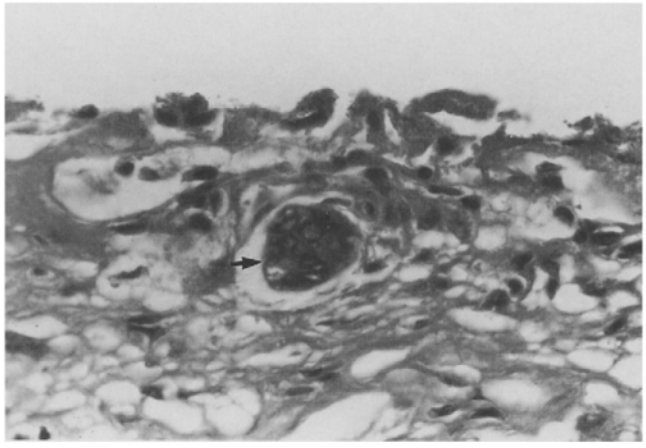

Figure 8. A foreign-body giant cell (arrow) is present in a surgically excised choroidal neovascular membrane (hematoxylin–eosin; original magnification, ×160).

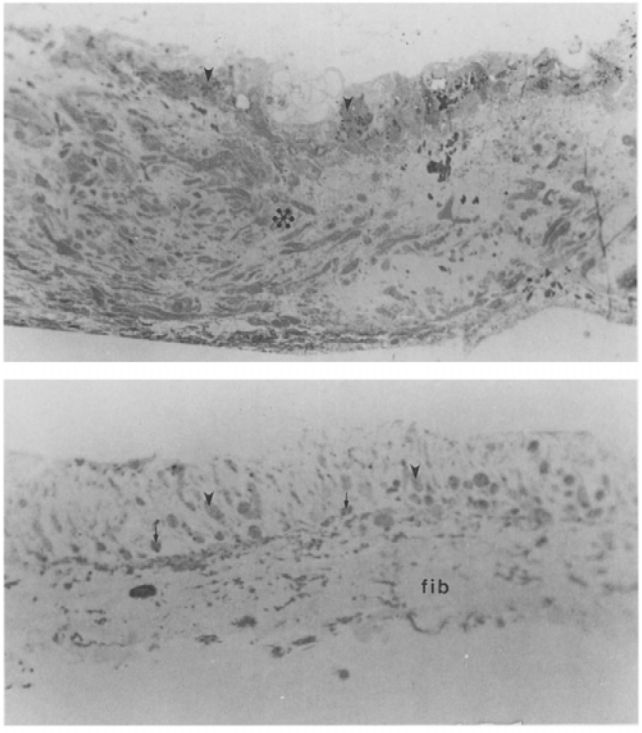

Figure 9. The surgical specimen from the core **(top)** of a well-demarcated choroidal neovascular membrane is composed of fibrovascular tissue (asterisk) surfaced by retinal pigment epithelium (arrowheads). The rim of the membrane (bottom) consists of photoreceptor segments (arrowheads), macrophages (arrows), nonspecific proteinaceous material, and fibrin (fib) (toluidine blue: **top,** original magnification, ×63; **bottom,** original magnification, ×160) (from reference 14) (originally published in Ophthalmology 1993;100:415–22).

Conversely, there were fragments of choroid in three other surgically excised membranes and fragments of Bruch's membrane in many other membranes that did not display postoperative angiographic choroidal atrophy. The appearance of Bruch's membrane and lack of choroid in surgically excised membranes from patients with postoperative angiographic evidence of choroidal atrophy has been observed by others (Nasir, unpublished data; Pollack, unpublished data; presented at 1993 ARVO Annual Meeting). The pathogenesis of this angiographic phenomenon is unclear, although it is possible that removal of the Bruch's membrane scaffold may cause atrophy and prevent fibrovascular regrowth in the area of the choriocapillaris (Fig 12). It is unknown why this angiographic appearance does not occur more frequently, because Bruch's membrane or choroid was removed in a number of patients who did not display postoperative angiographic evidence of choroidal atrophy. It is possible that in some instances removal of or damage to the choroid may lead to granulation tissue proliferation and revascularization, thus filling in the choroidal defect.

Another interesting issue is that of recurrence of membranes after surgical excision. We found that most of the components in surgically excised membranes that later recurred contained constituents found in most other membranes, with the exception of a lack of vascular channels in approximately half of the membranes that recurred. The absence of vascular channels was confirmed even after examination of multiple sections and electron microscopic examination of tissue through the centers of the membranes. This was considered unusual because

Table 3. Clinicopathologic Features of 123 Surgically Excised Choroidal Neovascular Membranes

Membrane Type	Disease				FA Findings	Pathology
	AMD	*OHS*	*Myopia*	*Idiopathic*		
Well demarcated (n = 37)	22	8	6	1	"Bull's eye" appearance	Fibrovascular core surrounded by rim
Poorly demarcated (n = 29)	28	0	0	1	Scalloped net with late obscuration	Fibrovascular membrane with breakthrough
Choroidal atrophy (n = 11)	9	1	1		"Punched-out" appearance	Fragment of Bruch's membrane and/or choroid
Recurrence (n = 12)	4	4	2	2	Increased late fluorescence	Lack of vascular channels in original membrane

AMD = age-related macular degeneration; OHS = ocular histoplasmosis syndrome; FA = fluorescein angiography.

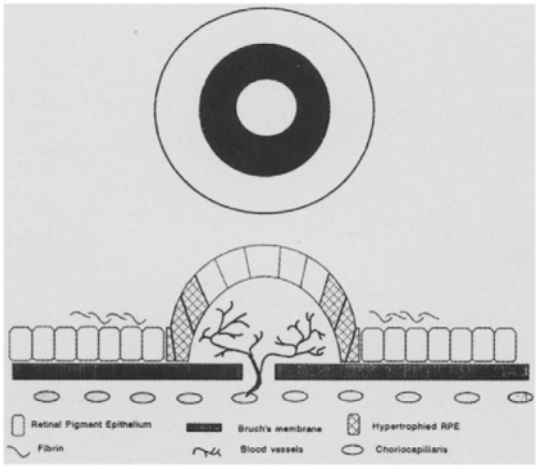

Figure 10. The diagrammatic late-phase fluorescein angiographic appearance of a well-demarcated membrane shows a "bull's eye" appearance corresponding to the diagrammatic histopathology shown below. The central hyperfluorescence, inner rim of blocked fluorescence, and outer rim of faint fluorescence correspond to subretinal pigment epithelium neovascularization, retinal pigment epithelial hypertrophy or hyperplasia, and subneurosensory retinal fibrin, respectively.

only a small minority of other membranes lacked detectable vascular channels. The lack of detectable vascular channels may have been due to sampling error and/or lack of immunohistochemical localization of vascular endothelium. Alternatively, it is possible that the vascular component of the membrane was removed inadequately at surgery, leading to recurrence, similar to cases of membrane persistence after attempted laser ablation.[10] Although conclusions regarding outcome events such as recurrence cannot be drawn from this study, we hypothesize

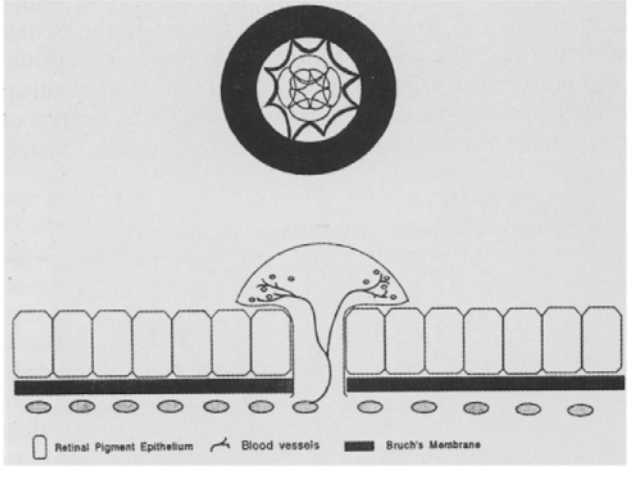

Figure 11. The diagrammatic late-phase fluorescein angiographic appearance of a poorly demarcated membrane at the top shows a "net" with a scalloped border corresponding to the diagrammatic histopathology shown below. The net is composed of a subneurosensory retinal (breakthrough) component of the membrane surrounded by material exuded from the vessels.

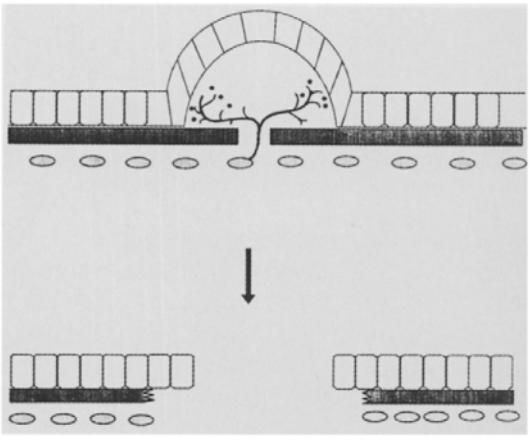

Figure 12. Choroidal atrophy after surgical removal of a choroidal neovascular membrane may occur after removal of retinal pigment epithelium, Bruch's membrane, and possibly choroid without subsequent granulation tissue proliferation.

that recurrence actually may represent incomplete removal, and the proper designation should be "persistence" rather than recurrence. Additionally, most recurrent (persistent) membranes after removal of a well-demarcated membrane were poorly demarcated. This descriptive finding suggests that surgery might disrupt the retinal pigment epithelium, allowing the membrane access into the subneurosensory retinal space (Fig 13).

Results of histologic examination of surgically removed choroidal neovascular membranes, at least on light microscopy, help explain fluorescein angiographic features. Another important reason to examine these membranes histologically is that occasionally a membrane will belie an underlying malignant melanoma mistaken for a disciform scar (Sassani, unpublished data).

The membranes studied in this series, although the largest histopathologic study of surgically excised choroidal neovascular membranes to date, represent a selected

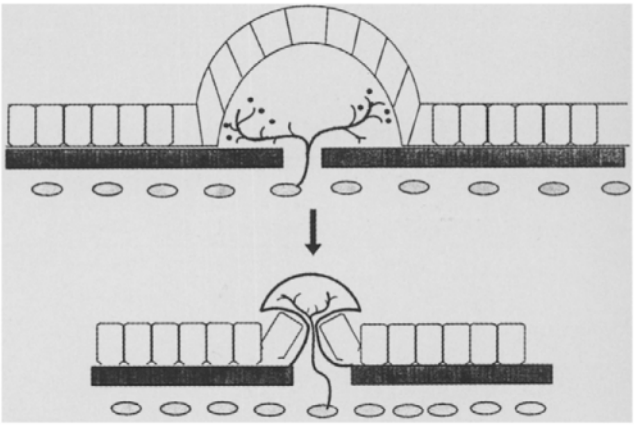

Figure 13. Postoperative recurrence (persistence) of a choroidal neovascular membrane may be due to inadequate removal of the vascular component of the membrane. The recurrent (persistent) membrane usually exhibits breakthrough into the subneurosensory retinal space.

sample that may not be generalized to all patients with the underlying diseases described herein. This is true because multiple surgeons removed the membranes, a variety of factors led the patients to seek ophthalmic consultation, and there were clinical differences between unoperated membranes and operated membranes for each individual surgeon. A valid statistical analysis of the results cannot be made because of the limited number of sections examined for each membrane and the possibility of sampling error. The purpose of this study was to describe the pathologic features of the membranes and compare the pathologic features with the fluorescein angiographic findings.

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