A LONG-TERM FOLLOW-UP STUDY OF CYSTOID MACULAR EDEMA IN APHAKIC AND PSEUDOPHAKIC EYES*

BY *C. P. Wilkinson,* MD

INTRODUCTION

CYSTOID MACULAR EDEMA OCCURS TRANSIENTLY IN AS MANY AS 60% OF EYES FOLLOWING cataract surgery.[1] Although this affects vision modestly and disappears spontaneously in the vast majority of cases, it is one of the most significant causes of reduced central vision following lens extraction. Major developments in the field of cataract surgery in the past decade have included the introduction of phacoemulsification techniques, modifications of older methods of extracapsular surgery, and a dramatic increase in the use of intraocular lenses. Although many authors have compared the incidence of macular edema following routine intracapsular surgery with that which occurs after extracapsular procedures and after a variety of implantation techniques, relatively little information concerning the natural course of the macular edema that occurs in the latter two groups of eyes has appeared in the literature. The purpose of this paper is to present long-term follow-up information regarding symptomatic cystoid macular edema that occurred in aphakic and pseudophakic eyes following intracapsular and extracapsular cataract extractions.

HISTORICAL REVIEW

A syndrome of visual loss caused by macular changes associated with the spontaneous rupture of the anterior hyaloid face following uncomplicated intracapsular cataract extraction was described by Irvine in 1953.[2] This report was the first to identify macular dysfunction as the cause of the reduced vision associated with changes in the anterior vitreous, which also had been observed by others.[3,4] Subsequent authors[5-9] provided further documentation of macular lesions causing visual loss following

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cataract surgery, and others[8-10] presented evidence that alterations in the optic nerve were occasionally responsible for this diminished vision. The precise nature of the macular and optic nerve changes associated with reduced visual acuity following cataract extraction was not described until 1966, when Gass and Norton[11] detailed the classic clinical and angiographic findings associated with this syndrome. The cystoid appearance of intraretinal fluid surrounding the fovea had been identified histopathologically[12] and clinically[13-15] many years prior to Irvine's article. Although the term "macular edema" was mentioned in his paper, Irvine's apparent primary intent was to describe vitreous changes, and the associated macular lesions were not precisely defined. Similarly, although subsequent authors[6-9] used the term "macular edema" in titles or texts of articles discussing this syndrome, they did not recognize that the typical macular lesion was due solely to intraretinal fluid. Gass and Norton[11] were the first to identify the characteristic cystoid appearance of macular edema as the usual cause of reduced vision following cataract surgery, and they documented the apparent pathogenesis of these macular changes angiographically by demonstrating that alterations in the permeability of the capillaries surrounding the macula allowed serum to leak into the extracellular spaces of the retina and optic nerve head. Although previous authors[6,8] had described isolated cases of macular edema unassociated with abnormalities in the anterior vitreous, approximately half the cases presented by Gass and Norton did not exhibit the changes in this area that were described by Irvine.

The cause of the macular edema that follows cataract extraction was debated long before the clinical pathophysiology of the disorder was described. In his original description of the syndrome, Irvine[2] mentioned the likelihood of vitreous traction upon the macula as the cause of visual loss, but he specifically noted that the macular changes might be secondary to iritis and inflammation. Chandler[5] interpreted the maculopathy as a response to inflammation. Nicholls[6,7] hypothesized that changes in the blood flow of the retinal and choroidal circulations were responsible for the central retinal changes, and Welch and Cooper[8] described vasomotor instability of the choroid as the probable cause of fluid accumulation in the macular area. Hypotony had been recognized as a cause of macular edema prior to Irvine's description,[16] but the previously mentioned authors ruled out this problem as a cause of the typical syndrome following cataract surgery. The role of vitreous traction upon the macula as a cause of the edema received renewed support in articles by Tolentino and Schepens[17] and by Reese et al.[18] These authors described fine strands of vitreous running from a detached posterior vitreous face to the macular

area, and they stated that the traction that these caused was responsible for macular edema following cataract extraction. Gass and Norton,[11] Maumenee,[19] and Jaffe[20] also described cases in which macular changes were due to vitreous traction in phakic and aphakic eyes, but they pointed out the significant differences in such eyes compared with more typical cases of macular edema following cataract surgery. Most observers have been unable to detect posterior vitreoretinal adhesions in the vast majority of these eyes, and at the present time inflammation is regarded as the primary cause of macular edema following cataract extraction.[21] It has long been recognized that this edema is frequently associated with signs and symptoms of intraocular inflammation,[2,3,11] and similar macular changes have been described in a variety of types of uveitis.[22-24] Macular edema occurs following other types of eye surgery in phakic as well as aphakic eyes,[25-28] particularly if the vitreous has been manipulated.[29,30] Iris fluorescein angiograms performed upon aphakic eyes with macular edema have revealed abnormal leakage of iris vessels as well as perifoveal capillaries,[31,32] indicating that a diffuse inflammatory process may be responsible for the permeability changes that cause swelling of the central retina. Finally, histopathologic studies[33-35] of eyes with macular edema following cataract surgery have demonstrated significant numbers of inflammatory cells in the iris, ciliary body, and retina. The precise mechanisms by which inflammation produces the retinal vascular permeability changes that cause macular edema remain unknown, although the roles of prostaglandins[36,37] and other substances[38] involved in inflammatory responses have recently received considerable interest in the literature.

Some aphakic and pseudophakic eyes with severe macular edema do not exhibit significant signs or symptoms of inflammation, and there are probably other factors that contribute to this postoperative complication. Certain authors[39-41] have hypothesized that structural differences in eyes following removal of the lens are responsible for subsequent macular edema. The term "endophthalmodonesis" refers to the relative mobility of certain intraocular structures, such as iris and vitreous, compared with relatively immobile portions, such as the cornea and sclera. Binkhorst[39] has hypothesized that a loss of the "stabilizing factor" of the lens-zonule barrier following cataract surgery causes increased endophthalmodonesis, which results in abnormal flow patterns that cause macular edema. Others[40,41] have theorized that the removal of the lens allows potentially toxic substances normally confined to the anterior chamber of the eye to gain access to the macular vessels, and the posterior lens capsule[40] or the anterior hyaloid face[41] are believed to function as possible barriers to the posterior migration of such substances. As is the case with the apparent

role of inflammation, precise explanations of the mechanisms by which structural changes following cataract surgery produce macular edema remain unknown. Topical epinephrine predisposes some aphakic eyes to develop macular edema,[42,43] although the etiologic factors of this relationship are unknown at this time. Additional factors that have been implicated in contributing statistically to the incidence of macular edema include the use of hyaluronidase,[44,45] the practice of preoperative digital massage,[46] and light toxicity due to the use of the operating microscope.[47] Prospective controlled studies using angiographic techniques will be required to document the importance of these possibilities.

Experimental studies[48] regarding the causes of macular edema following cataract surgery have demonstrated that a disruption of the blood-retina barrier at the levels of the retinal capillaries and retinal pigment epithelium can be produced by removing lenses of primates. These changes occurred much more frequently in the macular area than in the periphery of the retina, and the eyes with the most significant alterations were eyes in which vitreous was deliberately lost at the time of the surgical procedure. None of the eyes with electron microscopic evidence of a disruption of the blood-retina barrier demonstrated fluorescein angiographic evidence of macular edema, but this model is the best that has been produced to date. A recent study[49] of the effects of intraocular lens implantation in primate eyes failed to produce any signs of cystoid macular edema. Studies[50] demonstrating that topical epinephrine reaches the retina in aphakic animal eyes in a significantly greater concentration than in similar phakic eyes lend support to the possibilities of certain anterior segment substances reaching the macular area in increased amounts following lens removal. It is hoped that future experimental studies will provide new insights into the complex causation of macular edema following cataract and other forms of intraocular surgery.

The value of the treatment of the macular edema that follows cataract surgery remains unknown. Anti-inflammatory agents have been the treatment of choice for the past two decades, and some eyes respond well to topical, periocular, and systemic corticosteroid therapy, although the results are often unpredictable. Although recent reports have demonstrated that pretreatment with topical[36] or systemic[51] indomethacin may reduce the incidence of macular edema following cataract surgery, the realistic value of this drug in preventing and treating this complication is controversial. Other anti-inflammatory drugs such as aspirin, ibuprofen, and fenoprofen have been used with occasional apparent success, but their documented value in the therapy of postoperative macular edema remains unknown.

Figures regarding the incidence of macular edema following cataract surgery have varied considerably because of differences in the techniques of detecting these retinal changes. All early publications were retrospective in nature, and the incidence was determined by assessing patients with disappointing postoperative visions. More recent prospective studies using fluorescein angiograms have demonstrated a more significant incidence of this syndrome, although the majority of eyes with angiographic evidence of macular edema have demonstrated a visual acuity better than 20/40.[52] A complete discussion of publications regarding the incidence of macular edema following various forms of cataract surgery with and without implantation is beyond the scope of this paper.

The prognosis for aphakic eyes with cystoid macular edema following cataract extraction is good because of the tendency for the problem to resolve spontaneously. Gass and Norton[53] reported on 64 aphakic eyes that had been observed for at least one year following the development of macular edema. Intracapsular surgery had been performed in 97% (62) of these cases, and a spontaneous resolution of the edema occurred in 72% (45) of the eyes. Macular changes resolved within one year in 65% of the eyes in which edema ultimately disappeared. In eyes without vitreous adhesions to the cataract wound, 78% resolved in an average of 25 weeks. Resolution of edema was less satisfactory in eyes with these adhesions, but it occurred in 60% of cases in an average of 65 weeks. Vision was 20/40 or better in all eyes in this report in which edema resolved, and a return to 20/25 vision or better occurred in 72% of cases. Jacobson and Dellaporta[54] published a retrospective study involving a group of 28 aphakic eyes with cystoid macular edema that had been documented angiographically. Seventy-one percent (20) of the eyes experienced a spontaneous resolution of the macular edema and an improvement in vision to at least 20/30. Ninety percent of the cases that resolved did so within one year. Prospective studies have demonstrated an even greater incidence of clearing, because most cases of cystoid macular edema are mild with visions better than 20/40, and most patients with minimal swelling and good vision are not referred for retinal evaluations that lead to their being included in follow-up studies of macular edema. Hitchings et al[55] repeated angiograms at six months in 29 patients who had demonstrated fluorescein leakage six weeks following cataract surgery. The edema had disappeared in 55% (16) of these eyes, and the mean visual acuity of those that demonstrated leakage had improved from 6/9 to 6/7.5. Thirty-three of the original eyes were subsequently studied two years following their initial angiograms, and macular edema was observed in only 12% (4) of the cases.[56] Vision was 20/30 or better in all eyes.

The natural course of the cystoid macular edema that occurs in aphakic eyes following extracapsular surgery and in pseudophakic eyes associated with all forms of cataract extraction has received relatively little attention in the literature in spite of the fact that many reports regarding the incidence of this complication in these eyes have been published.[52,57,58] Follow-up data on Fung's prospective study[59] regarding aphakic eyes in which phacoemulsification had been performed has demonstrated that the vast majority of these eyes have experienced a resolution of their edema and a return of vision to excellent levels (written communication, Sept. 1980). In a retrospective study of pseudophakic eyes following extracapsular procedures, Winslow et al[60] noted that 54% (19) of the 35 eyes that had angiographic evidence of macular edema six weeks following surgery had cleared within one year. Only 15% (3) of the 20 eyes with an intact posterior capsule and macular edema at six weeks continued to exhibit fluorescein leakage at 12 months, but 87% (13) of the 15 cases with an open capsule continued to have edema at this time. Vision had improved to 20/40 or better in all eyes in which edema resolved except those with media problems or senile macular degeneration. The prospective study of cystoid macular edema in aphakic and pseudophakic eyes conducted by the Miami study group[52] discussed the incidence of edema at certain time periods rather than the outcomes of cases of edema that were discovered at the initial observation. In a recent retrospective study of clinical pseudophakic macular edema, Stern et al[61] suggested that pseudophakic eyes in which iris fixation had been employed had a poorer prognosis than aphakic cases following intracapsular surgery. Recurrences were observed in 76% (38) of the 50 pseudophakic eyes with macular edema in their series. Forty-four percent (22) of the 50 eyes in this series did not recover vision better than 20/40 during the duration of this study, in which eyes were followed up from one to six years. Although no prospective studies comparing the natural course of aphakic and pseudophakic macular edema in comparable groups of eyes have been published, a comparison of the prospective data provided by Hitchings[56] and Winslow et al[60] suggests that there may be a difference in the outcomes in these groups of eyes, at least if the posterior lens capsule is not intact. The report of Stern et al[61] also suggests that intraocular lenses may be associated with a more severe form of macular edema than occurs in comparable aphakic eyes.

This follow-up study was initiated to evaluate the possible effects of intraocular lenses upon the natural course of cystoid macular edema following intracapsular and extracapsular cataract extractions.

MATERIALS AND METHODS

One hundred fifty-four angiograms of good quality, which demonstrated cystoid macular edema in aphakic or pseudophakic eyes, were performed upon patients referred to senior staff members of our institution between June 1975 and December 1979. Each angiographic study was preceded by a complete eye examination, which included measurements of the best corrected vision and intraocular pressure, a slit-lamp evaluation of the anterior and posterior segments, and indirect ophthalmoscopic examinations. The charts of each of these patients were reviewed by the author, and 61 eyes of 61 patients were eliminated from further investigation because of associated anterior and posterior segment factors (Table I) that hindered a study of the natural course of typical cystoid macular edema occurring in aphakic and pseudophakic eyes. Cases that were complicated only by vitreous incarceration in the cataract wound were not excluded from this follow-up evaluation. Following the elimination of 61 cases, the series to be studied further consisted of 93 eyes of 83 patients. Forty-seven eyes were aphakic and forty-six were pseudophakic. All patients were asked to return for follow-up examinations. Two patients had died without an adequate documentation of the course of their macular edema, and one patient could not be located; the four eyes of these three patients were

TABLE I: CASES OF APHAKIC AND PSEUDOPHAKIC MACULAR EDEMA ELIMINATED FROM FOLLOW-UP STUDY

ASSOCIATED PROBLEM	NO. OF EYES
Complicated anterior segment surgery	25
Keratoplasty, anterior reconstruction (17)	
Vitrectomy for chronic cystoid macular edema in aphakic eye (6)	
Vitrectomy for other aphakic problems (2)	
Rhegmatogenous retinal detachment	12
Retinal vascular disease	8
Background diabetic retinopathy (5)	
Branch vein occlusion (2)	
Branch artery occlusions (1)	
Other macular disease	8
Senile macular degeneration (3)	
Senile macular hole (3)	
Severe preretinal membrane (2)	
Anterior segment pathologic conditions	7
Bullous keratopathy (5)	
Uveitis, rubeosis (2)	
Uveitis prior to cataract surgery	1
Total	61

lost to follow-up. Information obtained a minimum of one year after the initial examination and angiogram was available for 89 eyes, including 44 of the 47 potential aphakic eyes and 45 of the potential 46 pseudophakic cases. Follow-up studies were performed at our institution for 34 aphakic and 37 pseudophakic eyes, whereas data on ten aphakic and eight pseudophakic cases were obtained from referring ophthalmologists. Follow-up data included a determination of the best corrected vision and a description of the cornea, anterior chamber, vitreous structures, and macula. Fluorescein angiograms were performed upon all patients returning to our institution except those who were allergic to fluorescein dye or who refused to participate in this stage of the examination. Follow-up angiographic studies were available for 25 of the 34 aphakic eyes and for 29 of the 37 pseudophakic cases that were reexamined at our institution. The maculas of all eyes in which repeat angiograms were not performed could be clearly visualized and accurately described. The follow-up period in this study ranged from one to more than four years and averaged slightly greater than two years (Table II).

TABLE II: LENGTH OF FOLLOW-UP PERIOD

TIME	NO. OF EYES		
	TOTAL	APHAKIC	PSEUDOPHAKIC
1–2 yr	22	6	16
2–3 yr	21	14	7
3–4 yr	26	12	14
4+ yr	20	12	8
Total	89	44	45

RESULTS

The ages of the 80 patients in this study ranged from 43 to 89 years and averaged 68 years (Table III). Forty percent (32) of the patients were men, and this figure was approximately the same in both pseudophakic and aphakic patients. Ninety-seven percent (78) of the patients were white. A history of significant hypertension or arteriosclerotic cardiovascular disease was elicited in 35% (28) of these cases, and there were no differences in the incidence of these problems in patients with pseudophakic eyes compared with those in the aphakic group. Two patients in this series had a history of mild serum glucose elevation, and one of these was under treatment with oral hypoglycemic agents, but neither patient

TABLE III: AGES OF PATIENTS

AGE	NO. OF PATIENTS		
	TOTAL	APHAKIC	PSEUDOPHAKIC
40–49	1	1	0
50–59	15	8	7
60–69	18	7	11
70–79	42	21	21
80+	4	0	4
Total	80	37	43

demonstrated angiographic evidence of diabetic retinopathy. No patients were receiving topical epinephrine compounds at the time their macular edema was diagnosed or during the duration of the study. The right eye was involved in 39 cases, the left eye in 32 instances, and both eyes in 9 patients. Seven of the patients with bilateral edema were aphakic in both eyes, and two had bilateral implants. Intracapsular surgical procedures had been performed in 33 of the 44 aphakic eyes and in 18 of the 45 pseudophakic eyes (Table IV). Phacoemulsification procedures were performed in all of the remaining aphakic eyes and in 22 of the pseudophakic cases (Table IV). Other types of extracapsular surgical procedures had been performed in the remaining five pseudophakic eyes. In the intracapsular group of 18 pseudophakic cases, a Copeland implant had been placed in ten, a Binkhorst lens in seven, and a Choyce implant in a single case (Table IV). Two-loop Binkhorst or Platina lenses were employed in 23 of the 27 pseudophakic eyes in which extracapsular surgery had been performed (Table IV). A Shearing posterior chamber lens was used in two of these eyes, and a Choyce lens and a Copeland implant had been employed in single instances. Although small platinum clips were present in many of the Platina implants, no metal loop implants had been placed in any of the pseudophakic eyes in this series. In only one eye in this

TABLE IV: TYPE OF CATARACT SURGERY AND IMPLANT

GROUP	INTRACAPSULAR	EXTRACAPSULAR
Aphakic (44)	75% (33)	25% (11)
Pseudophakic (45)	40% (18)	60% (27)
Copeland implant	10	1
Binhorst 4-loop	7	0
Platina, Binkhorst 2-loop	0	23
Choyce	1	1
Shearing	0	2

study of macular edema was this complication associated with an intact posterior capsule, and this occurred in a pseudophakic eye. In a single aphakic eye, macular edema and visual loss did not occur until after a return of vision to 20/25 following a discission two years after the cataract extraction, and the "time following surgery" at which vision deteriorated was dated from the time of the second procedure. In three pseudophakic eyes, macular edema was observed following secondary operations, and the "time of the apparent onset" of edema was dated from these latter procedures, since excellent vision occurred after the surgeries prior to subsequent visual loss. In two of these eyes, secondary Choyce implants had been performed, one 30 years following an extracapsular procedure and one two years following an intracapsular operation. A secondary capsulotomy performed two years following extracapsular surgery had been employed in the third case. In a fourth pseudophakic eye, a McCannal suture was required to fixate a Platina implant 12 days following phacoemulsification. No vitreous loss occurred in any of these secondary procedures. However, a history of vitreous loss at the time of cataract surgery was obtained in 12 of the cases in the total group, and eight of these instances occurred in eyes that remained aphakic. The status of the second eye in cases with unilateral macular edema is listed in Table V.

TABLE V: STATUS OF SECOND EYE IN CASES WITH MONOCULAR CYSTOID MACULAR EDEMA (CME)

STATUS	NO. OF EYES		
	TOTAL	APHAKIC	PSEUDOPHAKIC
"Normal"	10	4	6
Cataract	28	7	21
Aphakic, no CME	15	12	3
Aphakic, history of CME	4	3	1
Intraocular lens, no CME	7	0	7
Intraocular lens, history of CME	2	0	2
Other pathology	5	4	1
Total	71	30	41

Most eyes achieved relatively good vision following surgery, prior to the onset of their macular edema, and a tabulation of the best recorded visual acuities prior to visual loss is listed in Table VI. Eighty-four percent (37) of the 44 aphakic eyes achieved 20/40 or better prior to the onset of diminished visual acuity, whereas 76% (34) of the 45 pseudophakic cases attained this level. The type of cataract surgery performed had no appar-

TABLE VI: BEST RECORDED VISIONS PRIOR TO ONSET OF EDEMA

	NO. OF EYES			
	APHAKIC		PSEUDOPHAKIC	
VISION	ICCE*	ECCE*	ICCE	ECCE
20/20	9	6	4	6
20/25–20/30	15	2	9	7
20/40	3	2	2	6
20/50–20/70	3	0	2	6
20/80–20/100	3	1	1	2
Total	33	11	18	27

*ICCE = intracapsular cataract extraction; ECCE = extracapsular cataract extraction.

ent effect upon these visual acuities. The times of the onset of reduced vision and macular edema following cataract extraction are listed in Table VII. A great majority of patients noted a loss of vision within the first six months following surgery, and this was particularly marked in the pseudophakic group, in which 89% (40) of the patients noted reduced vision within this period. The time of visual loss appeared to be unrelated to the type of cataract surgery performed in each group. The times at which patients were initially examined at our institution are listed in Table VIII, and the visual acuities obtained at that time are listed in Table IX. There was a tendency for the pseudophakic eyes to have lower visual acuities than the aphakic, particularly if implantation had been associated with extracapsular surgery.

Fifteen of the 44 aphakic eyes demonstrated vitreous adhesions to the cataract incision site, whereas similar changes were observed in only four

TABLE VII: TIME OF VISUAL LOSS FOLLOWING SURGERY

	NO. OF EYES			
	APHAKIC		PSEUDOPHAKIC	
TIME	ICCE*	ECCE*	ICCE	ECCE
Never good	4	1	3	5
1–3 mo	7	3	2	4
3–6 mo	12	5	12	14
6–12 mo	2	2	1	3
1–2 yr	3	0	0	1
2+ yr	2	0	0	0
?	3	0	0	0
Total	33	11	18	27

*ICCE = intracapsular cataract extraction; ECCE = extracapsular cataract extraction.

TABLE VIII: TIME OF EXAMINATION AND ANGIOGRAM AFTER SURGERY

	NO. OF EYES			
	APHAKIC		PSEUDOPHAKIC	
TIME	ICCE*	ECCE*	ICCE	ECCE
1–3 mo	1	1	1	4
3–6 mo	9	6	6	7
6–12 mo	13	1	9	12
1–2 yr	5	3	2	4
2+ yr	5	0	0	0
Total	33	11	18	27

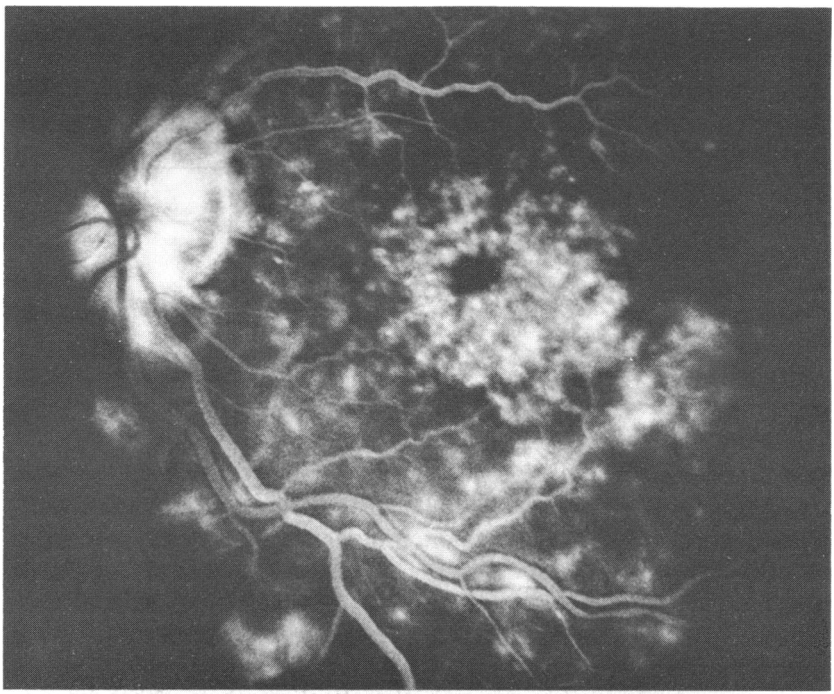
*ICCE = intracapsular cataract extraction; ECCE = extracapsular cataract extraction.

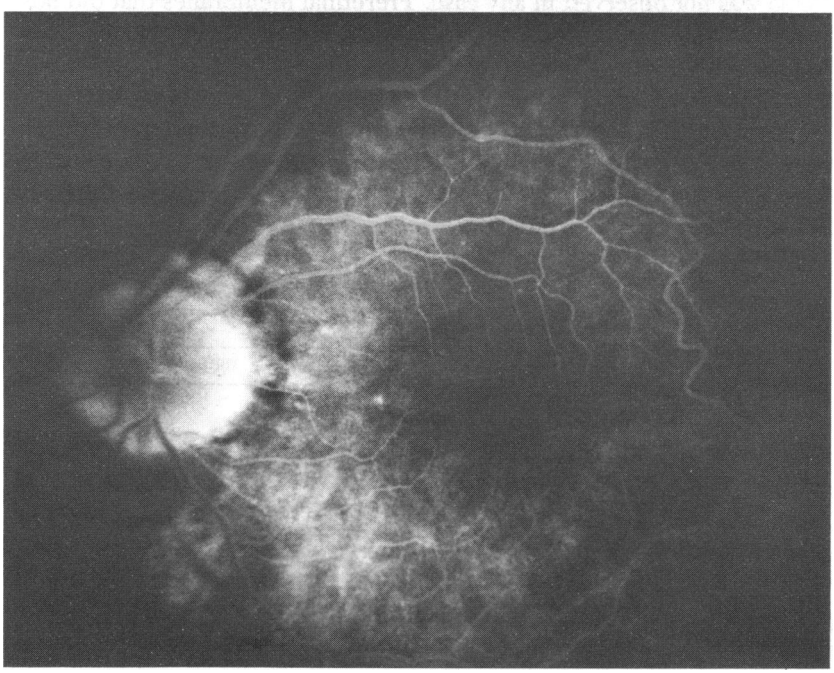
of the 45 pseudophakic cases. A history of documented vitreous loss at the time of cataract surgery was obtained in eight of these aphakic and one of the pseudophakic eyes. A significant anterior chamber cellular reaction was rarely observed in either group. The vast majority of eyes exhibited significant liquification of the vitreous gel, and most had occasional inflammatory cells in the vitreous cavity. A posterior vitreous detachment was documented in the majority of eyes. Direct vitreous traction upon the macula was not observed in any case. Preretinal membranes that did not cause distortion of the retinal surface were observed in approximately 8% of each of the groups of eyes, but cases with preretinal traction were not included in this study. An intraocular pressure less than 10 mm Hg was not observed in this series. In four eyes applanation tensions were greater than 22 mm Hg, but the intraocular pressures never exceeded 30 mm Hg. Three eyes had been placed on miotic therapy following cataract extraction, but epinephrine compounds were used in no eyes.

TABLE IX: VISUAL ACUITIES AT TIME OF INITIAL EXAMINATION

	NO. OF EYES			
	APHAKIC		PSEUDOPHAKIC	
VISION	ICCE*	ECCE*	ICCE	ECCE
20/30	2	1	1	0
20/40	2	1	0	2
20/50–20/70	11	3	8	8
20/80–20/100	9	1	2	2
20/200	9	5	7	13
20/400	0	0	0	2
Total	33	11	18	27

*ICCE = intracapsular cataract extraction; ECCE = extracapsular cataract extraction.



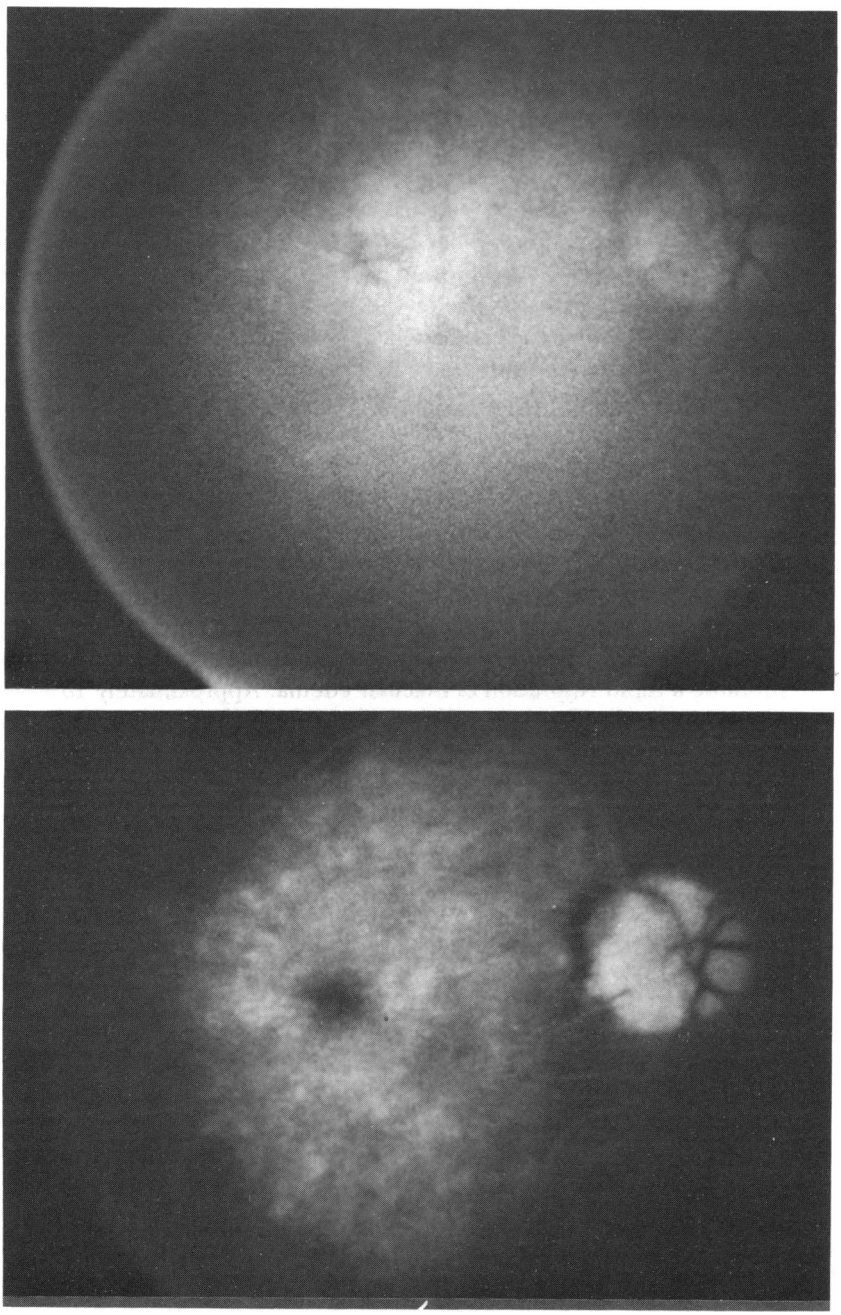


The vast majority of cases exhibited extensive fluorescein leakage of the classic form into the macula, and a typical petaloid configuration surrounding the fovea was observed in 88% (78) of cases. In the remaining eyes, unequivocal leakage occurred, but a classic stellate configuration of 360° was not observed. Leakage occurred from optic nerve head capillaries in 42% (37) of eyes. The resolution or persistence of macular edema during the follow-up period was usually documented with fluorescein angiography. In eyes in which clearing occurred, the angiograms returned to normal (Fig 1) or exhibited only mild retinal pigment epithelial changes associated with drusen in the macular area. In eyes in which improved vision was associated with persistent edema, fluorescein angiograms usually demonstrated a reduction in leakage (Fig 2). Similarly, in eyes with persistent edema in which vision deteriorated, angiography frequently revealed increased leakage of fluorescein (Fig 3). However, a consistent relationship between changes in vision and the extent of leakage was not observed in all cases (Fig 4). Macular holes did not develop in any of the eyes in this series. Virtually all cases had been treated with anti-inflammatory agents by their referring ophthalmologists, but in no case was such therapy considered adequate by the patient. Approximately two-thirds of the cases were treated with oral anti-inflammatory agents following referral to our institution, but such therapy was never observed to promote a rapid resolution of macular edema. Approximately 15% (13) of patients noted subjective improvement on systemic cortisone, ibuprofen, or fenoprofen, but objective evidence of a dramatic therapeutic effect was not observed.

A complete resolution of the macular edema was observed in 29 (66%) of the 44 aphakic eyes in this series (Table X). Clearing occurred within one year in 16 (55%) of the eyes that cleared during the period of this study (Table XI), and 25 (86%) cleared within two years. Fifteen of the 44 aphakic eyes had vitreous adhesions to the cataract incision, and only six (40%) of these cleared during the duration of this study (Table X). This figure is considerably less than the 79% rate of clearing that was observed in the 29 aphakic eyes without such vitreous changes (Table X). Two of the six eyes with vitreous adhesions that cleared did so within one year,

FIGURE 1

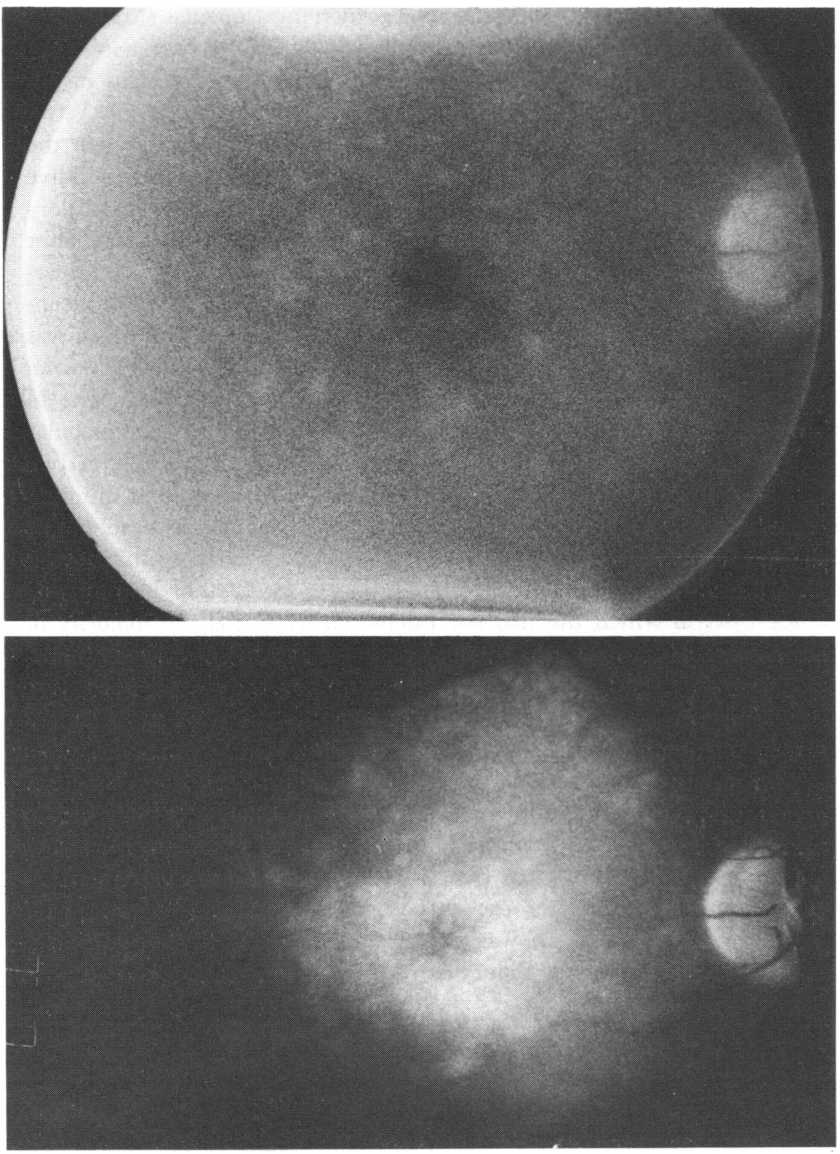
Late-stage fluorescein angiograms of pseudophakic left eye of 72-year-old woman who had undergone extracapsular cataract surgery combined with Platina implant in March 1976. Top, December 1976; visual acuity was 20/200 and severe cystoid macular edema was present. Bottom, November 1980; visual acuity was 20/25 and edema had resolved.



and five of the six experienced a resolution of macular edema within two years of their initial angiograms. There was a tendency for more resolution of macular edema in aphakic eyes in which intracapsular surgery had been performed than in the smaller number in which the edema followed extracapsular procedures (Table X). Twenty-four of the 33 eyes in the former group cleared compared with five of 11 cases in the latter. Vitreous adhesions to the wound appeared to be more significant than the history of extracapsular procedures, however, as clearing occurred in five of eight eyes without vitreous adhesions following extracapsular surgery (Table X). Only six of 12 eyes with vitreous adhesions occurring after intracapsular procedures experienced a resolution of edema, and no clearing occurred in the three eyes with vitreous adhesions following extracapsular surgery (Table X). Resolution following extracapsular surgery was somewhat slower than after intracapsular procedures (Table XI). Two of the five eyes in the former group cleared within one year, whereas 14 (58%) of the 24 eyes in the latter experienced a resolution of the macular edema within this period. Similar differences were observed after two years of follow-up. There were no differences in the ages or in the incidence of hypertension or arteriosclerotic cardiovascular disease in patients in whom edema cleared compared with those who exhibited persistent macular edema. Visual acuities returned to 20/40 or better in all aphakic eyes in which the macular edema cleared, and the majority of eyes achieved 20/30 vision or better (Table XII). There were no differences in the visual acuities following resolution of edema in the intracapsular vs the extracapsular groups or in eyes with and without vitreous adhesions. The visual acuities in the aphakic eyes with persistent edema ranged from 20/40 to 20/200 (Table XIII), and there were no significant causes of reduced vision other than these macular changes. There was a tendency for eyes with persistent edema following extracapsular surgery to have visions slightly better than occurred in similar cases following intracapsular procedures; the presence of vitreous adhesions in eyes with persistent edema, however, was not associated with lower visions than occurred in similar cases without such adhesions.

FIGURE 2

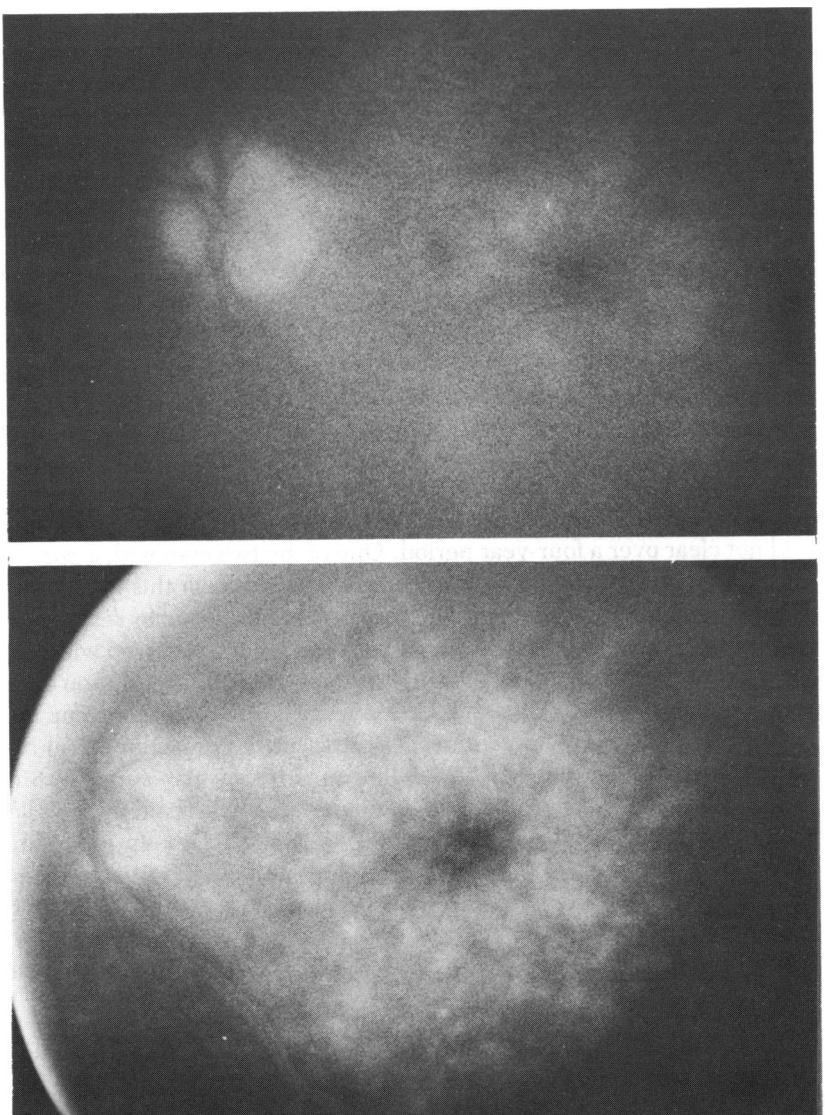
Late-stage fluorescein angiograms of pseudophakic right eye of 78-year-old woman who had had intracapsular cataract extraction combined with Copeland implant in November 1975. Top, June 1976; visual acuity was 20/200 and severe macular edema was present. Bottom, July 1980; visual acuity was 20/60 and less leakage of fluorescein was observed.



In the pseudophakic group of eyes, macular edema completely resolved in 18 (40%) of the 45 cases (Table XIV). Resolution occurred in 15 (56%) of the 27 eyes in which extracapsular surgery had been employed, but it was observed in only three (17%) of the 18 eyes in which intracapsular procedures had been performed. Four of the eyes in the latter group had vitreous adhesions to the wound, and none of these experienced clearing. If these cases are not considered statistically, resolution of edema following intracapsular surgery occurred in three (21%) of the remaining 14 cases (Table XIV). In 17 of the 18 pseudophakic eyes in which intracapsular surgery had been performed, the implants were associated with iris fixation (Table IV). If the two eyes with Copeland implants and the single eye with a Binkhorst implant in which vitreous was incarcerated in the wound are eliminated from further consideration, the clearing associated with this type of fixation remained low, as only one of eight eyes with Copeland implants and two of six with Binkhorst lenses experienced a resolution of the macular edema. Most eyes in the pseudophakic-extracapsular group contained two-loop Binkhorst or Platina implants (Table IV), and none had vitreous adhesions. The single eye in which capsular fixation was combined with iris fixation and a Copeland implant did not clear over a four-year period. One of the two eyes with a posterior chamber Shearing lens resolved, as did the one case in this group with a Choyce implant. The duration of macular changes prior to resolution in the pseudophakic eyes is listed in Table XV. Clearing occurred within one year in nine of the 18 eyes that ultimately demonstrated resolution during the follow-up period. There was a tendency for clearing to occur more slowly in pseudophakic eyes in which extracapsular procedures had been performed than in those which followed intracapsular surgery. Since longer follow-up periods might allow more eyes to clear, all eyes without vitreous adhesions and with at least two years of follow-up information were evaluated separately. Rates of resolution of edema were similar in these eyes when they were compared with the rates of clearing in the entire series (Table XVI). There were no differences in the incidence of hypertension or arteriosclerotic cardiovascular diseases in pseudophakic

FIGURE 3

Late-stage fluorescein angiograms of aphakic right eye of 43-year-old man who had undergone phacoemulsification procedure in March 1976. Top, April 1976; visual acuity was 20/30 and mild macular edema was present. Bottom, June 1980; visual acuity was 20/200 and severe macular edema was observed.



patients in which edema cleared when they were compared with those with persistent macular changes and visual loss. In all pseudophakic eyes in which edema cleared, visual acuities returned to 20/40 or better (Table XVII), and the vast majority achieved 20/30 or better. Visual acuities in the pseudophakic eyes with persistent macular edema are listed in Table XVIII. Visual loss was due to chronic macular edema in all cases. There was a tendency for pseudophakic eyes with persistent edema following extracapsular surgery to have visual acuities somewhat worse than those that followed intracapsular procedures.

The 18 eyes that had been reexamined by the referring ophthalmologists and the 17 eyes that were reexamined at our institution and did not received follow-up fluorescein angiograms were evaluated separately (Table XIX) to rule out the possibility that false diagnoses could distort the data. In the majority of these eyes, edema had resolved and vision had improved to 20/30 or better. In most of the remaining eyes, severe edema persisted and was associated with visual acuities of 20/200 or less. In two of these 35 eyes, persistent edema associated with less significant visual loss was observed.

DISCUSSION

The 89 eyes in this study were primarily evaluated to compare the natural course of symptomatic cystoid macular edema in aphakic eyes with that in comparable pseudophakic cases. The characteristics of the eyes in this review were similar to those published in the study of Gass and Norton.[11] The majority obtained relatively good visual acuity following surgery, and vision usually deteriorated four weeks to six months after cataract extraction with or without intraocular lens implantation. The visual acuities associated with the macular edema ranged from 20/30 to 20/200 in both aphakic and pseudophakic eyes, regardless of the type of cataract surgery that had been performed.

The natural course of the macular edema in the aphakic eyes in this series approximated that described previously in retrospective studies.[53,54] Sixty-six percent (29) experienced a complete resolution of edema, and vision improved to 20/40 or better in all cases that cleared. The

FIGURE 4

Late-stage fluorescein angiograms of pseudophakic left eye of 80-year-old woman who had had intracapsular cataract extraction combined with Binkhorst four-loop implantation in June 1978. Top, June 1979; visual acuity was 20/200 and significant macular edema was present. Bottom, November 1980; visual acuity had improved to 20/60 although extensive leakage of fluorescein persisted, and little change in media had occurred.

TABLE X: CLEARING OF EDEMA IN APHAKIC EYES

	TOTAL		NO VITREOUS ADHESIONS		VITREOUS ADHESIONS	
	NO. EYES	NO. CLEAR	NO. EYES	NO. CLEAR	NO. EYES	NO. CLEAR
Total	44	29	29	23	15	6
ICCE*	33	24	21	18	12	6
ECCE*	11	5	8	5	3	0

*ICCE = intracapsular cataract extraction; ECCE = extracapsular cataract extraction.

TABLE XI: TIME OF CLEARING OF EDEMA IN APHAKIC EYES

	NO. OF EYES		
TIME	TOTAL (29)	ICCE* (24)	ECCE* (5)
Less than 6 mo	7	5	2
6–12 mo	9	9	0
12–18 mo	5	4	1
18–24 mo	4	4	0
2–3 yr	3	1	2
?	1	1	0

*ICCE = intracapsular cataract extraction; ECCE = extracapsular cataract extraction.

TABLE XII: VISUAL ACUITIES IN APHAKIC EYES IN WHICH EDEMA CLEARED

	NO. OF EYES		
VISUAL ACUITY	TOTAL (29)	ICCE* (24)	ECCE* (5)
20/20	9	7	2
20/25–20/30	17	14	3
20/40	3	3	0

*ICCE = intracapsular cataract extraction; ECCE = extracapsular cataract extraction.

TABLE XIII: VISUAL ACUITIES IN APHAKIC EYES WITH PERSISTENT EDEMA

	NO. OF EYES		
VISUAL ACUITY	TOTAL (15)	ICCE* (9)	ECCE* (6)
20/40	1	0	1
20/50–20/70	3	1	2
20/80–20/100	0	0	0
20/200	7	5	2
20/400	4	3	1

*ICCE = intracapsular cataract extraction; ECCE = extracapsular cataract extraction.

times required for resolution in these aphakic eyes ranged from three months to three years. Clearing occurred within one year in 55% (16) of those that cleared, and this speed of resolution is somewhat slower than that published previously.[53,54] Macular edema cleared in 79% (23) of the total group of aphakic eyes without vitreous adhesions to the cataract wound and in 86% (18) of eyes following intracapsular surgery without such adhesions. These figures further support the findings of previous authors that the majority of aphakic eyes that have cystoid macular edema without vitreous adhesions following cataract surgery will experience a resolution of the problem and achieve excellent vision, even if they are relatively severe cases that have been referred for retinal evaluations. Vitreous adhesions to the cataract incision profoundly reduced the likelihood of resolution of edema in both the intracapsular and extracapsular groups. Only 40% (6) of the aphakic eyes with these adhesions demonstrated clearing, and this figure is lower than that previously published[53] regarding similar cases.

The precise reasons for the relationship between these vitreous changes and a relatively poor prognosis for the associated macular edema remain unknown. As mentioned previously, inflammation is regarded as the most important cause of macular edema, and eyes with vitreous incarceration in the surgical incision are frequently associated with increased inflammatory signs and symptoms. Traction forces between the wound, iris, vitreous base, ciliary body, and peripheral retina may cause increased irritability and inflammation in these eyes, but a more precise explanation must await future research in this area. The relatively small number of aphakic eyes in which extracapsular surgery had been performed cleared somewhat less frequently than those in which intracapsular surgery had been employed, and the three eyes with vitreous adhesions in the former group did not clear, in spite of their being followed up for more than three years. However, the differences between clearing in aphakic eyes without vitreous adhesions following extracapsular and intracapsular procedures were not significant. A tendency for delayed resolution of edema was observed in aphakic eyes following extracapsular surgery, as two of the five eyes that cleared required more than two years to do so. Although none of the aphakic eyes in which extracapsular surgery had been performed exhibited significant amounts of residual peripheral lens cortex, small amounts of this material may have contributed to increased inflammation and a slightly increased incidence of persistent macular edema. Regardless of the presence of vitreous adhesions or a history of extracapsular surgery, vision improved to 20/40 or better in all

TABLE XIV: CLEARING OF EDEMA IN PSEUDOPHAKIC EYES

	TOTAL		NO VITREOUS ADHESIONS		VITREOUS ADHESIONS	
	NO. EYES	NO. CLEAR	NO. EYES	NO. CLEAR	NO. EYES	NO. CLEAR
Total	45	18	41	18	4	0
ICCE*	18	3	14	3	4	0
ECCE*	27	15	27	15	0	0

*ICCE = intracapsular cataract extraction; ECCE = extracapsular cataract extraction.

TABLE XV: TIME OF CLEARING OF EDEMA IN PSEUDOPHAKIC EYES

	NO. OF EYES		
TIME	TOTAL (18)	ICCE* (3)	ECCE* (15)
Less than 6 mo	7	1	6
6–12 mo	2	1	1
12–18 mo	3	1	2
18–24 mo	2	0	2
2–3 yr	3	0	3
?	1	0	1

*ICCE = intracapsular cataract extraction; ECCE = extracapsular cataract extraction.

TABLE XVI: CLEARING OF MACULAR EDEMA IN EYES WITHOUT VITREOUS ADHESIONS

	APHAKIC		PSEUDOPHAKIC	
GROUP	NO. EYES	NO. CLEAR	NO. EYES	NO. CLEAR
All eyes in study				
ICCE*	21	18	14	3
ECCE*	8	5	27	15
Eyes with at least 2 yr of follow-up				
ICCE	16	13	8	1
ECCE	8	5	18	12

*ICCE = intracapsular cataract extraction; ECCE = extracapsular cataract extraction.

TABLE XVII: VISUAL ACUITIES IN PSEUDOPHAKIC EYES IN WHICH EDEMA CLEARED

	NO. OF EYES		
VISUAL ACUITY	TOTAL (18)	ICCE* (3)	ECCE* (15)
20/20	6	1	5
20/25–20/30	11	2	9
20/40	1	0	1

*ICCE = intracapsular cataract extraction; ECCE = extracapsular cataract extraction.

aphakic eyes in which edema cleared, even if more than two years were required for this to occur.

The natural course of the cystoid macular edema in the pseudophakic group of eyes was considerably less satisfactory than that which occurred in the aphakic cases, as only 40% (18) of the former group experienced a resolution of their edema during the course of this study. Clearing occurred within one year in half of the eyes that resolved. None of the four pseudophakic eyes with vitreous adhesions cleared, again demonstrating the adverse effects of this anterior segment complication. A review of figures regarding the resolution of edema in aphakic and pseudophakic eyes without vitreous adhesions demonstrated that 79% (23) of the former group resolved compared with 44% (18) of the latter (Table XVI). Important differences also existed between pseudophakic eyes in which intracapsular surgery had been combined with iris fixation and those in which capsular fixation followed extracapsular procedures. Excluding cases with vitreous incarceration, only 21% (3) of the intracapsular group cleared compared with 56% (15) of the extracapsular series.

When the apparent effect of a single variable such as the presence of an intraocular lens is studied in a retrospective fashion, it is critical that other factors that could introduce bias into the comparison be eliminated. The groups under consideration should be as similar in all respects as possible other than the single characteristic or variable under investigation. The pseudophakic and aphakic groups of patients in this study were similar in most respects, as were the intracapsular and extracapsular groups of pseudophakic eyes. All the patients were comparable in terms of age, sex, and the incidence of hypertension and arteriosclerotic cardiovascular disease. They were all products of the same referral sources during similar time periods, and comparable techniques for intracapsular and extracapsular surgery were employed by the same referring ophthalmologists, regardless of an intention to perform implantation following lens removal. It has been a practice at our institution to perform fluorescein angiography upon all patients referred with a diagnosis of cystoid macular edema following cataract surgery, because angiograms improve our ability to rule out other problems that may be contributing to visual loss. Thus, fluorescein studies have been performed on virtually all aphakic and pseudophakic patients referred with a possibility of macular edema, and patients in neither the aphakic nor pseudophakic group were selected for angiography because they represented unusually severe cases. Although retrospective studies are never as ideal as prospective, for the purposes of a statistical evaluation, the aphakic and pseudophakic groups of eyes in this study were relatively well-matched, as were the intracapsular and extra-

TABLE XVIII: VISUAL ACUITIES IN PSEUDOPHAKIC EYES WITH PERSISTENT EDEMA

VISUAL ACUITY	NO. OF EYES		
	TOTAL (27)	ICCE* (15)	ECCE* (12)
20/30	1	1	0
20/40	2	1	1
20/50–20/70	7	6	1
20/80–20/100	1	1	0
20/200	7	3	4
20/400	9	3	6

*ICCE = intracapsular cataract extraction; ECCE = extracapsular cataract extraction.

TABLE XIX: STATUS OF EYES WITHOUT FOLLOW-UP FLUORESCEIN ANGIOGRAMS

STATUS	NO. OF EYES	
	APHAKIC (19)	PSEUDOPHAKIC (16)
No cystoid macular edema (CME), vision = 20/30 or better	15	9
CME, vision = 20/200 or less	4	5
CME, vision = 20/70 and 20/100	0	2

capsular subdivisions in both groups. A chi-square statistical analysis of the figures regarding the resolution of edema in these eyes without vitreous adhesions (Table XVI) revealed that the 79% figure in aphakic eyes is significantly greater than the 44% rate regarding pseudophakic cases ($P < 0.001$). Similarly, the 86% rate of clearing of edema in aphakic eyes in which intracapsular surgery had been performed is significantly greater than the 21% that occurred in eyes following intracapsular surgery in which implants with iris fixation had been employed ($P < 0.01$). The 56% rate of clearing in pseudophakic eyes following extracapsular surgery is significantly greater than the 21% figure noted in the pseudophakic cases following intracapsular procedures, although the level of significance is less than that noted previously ($P < 0.05$). A significant difference also existed between the 79% rate of resolution in the total group of aphakic eyes and the 56% figure in pseudophakic eyes following extracapsular surgery ($P < 0.05$). No significant difference in the resolution of edema was observed when the eight extracapsular aphakic eyes were compared with the 27 extracapsular pseudophakic cases, as 63% (5) of the

former group and 56% (15) in the latter experienced a resolution of edema.

The speed of clearing in aphakic and pseudophakic eyes following intracapsular surgery was approximately the same, as most eyes that resolved did so within two years. Similarly, aphakic and pseudophakic eyes that followed extracapsular procedures exhibited a similar rate of clearing over a two-year period. In both the aphakic and pseudophakic groups of eyes, clearing tended to be somewhat slower in eyes following extracapsular surgery than after intracapsular procedures, although the difference was not statistically significant. Information obtained about eyes without vitreous adhesions that had been followed up for more than two years revealed figures of clearing comparable to those that occurred in the group as a whole (Table XVI), further substantiating the fact that pseudophakic eyes, particularly those with iris fixation, exhibit a relatively low rate of resolution of macular edema. As was the case with aphakic eyes, vision improved to 20/40 or better in all eyes in which the edema disappeared.

The reasons that the pseudophakic eyes did not clear with the frequency expected of similar aphakic cases is unknown, but all the theories regarding the causes of this complication should be considered. Inflammation occurs after all forms of eye surgery, and although the mediators of this response are poorly understood, it is possible that the presence of an intraocular lens augments the inflammatory response initiated by the surgery.[38] A longer procedure involving more manipulation of the iris occurs during lens implantation, and this may result in increased inflammation postoperatively. Eyes with iris-fixated implants experienced the lowest rate of resolution in this series, and this may be due to continued trauma to the iris from persistent friction forces between this tissue and the surface of the implant or its haptics. Studies[32] on pseudophakic and aphakic eyes with macular edema have demonstrated more significant dilatation and permeability of the iris vessels in the former group. Perhaps some of the mechanical factors which result in increased inflammation and more severe macular edema in these pseudophakic cases are similar to those associated with the relatively poor outcome observed in aphakic eyes with vitreous adhesions. The intraocular inflammatory response may be stimulated further by certain toxic[38] or antigenic[32] properties of implants. The phenomenon of endophthalmodonesis (or pseudophacodonesis) may also theoretically contribute to the relatively severe course of the macular edema that occurred in eyes in which iris fixation had been employed, because significantly more movement of the iris and

implant was observed in these cases than in those associated with capsular fixation.

The increasing popularity of intraocular lenses during the past decade has been largely due to observations that the addition of the procedure of implantation to that of cataract extraction has resulted in few significant differences in the incidence and severity of complications. Cystoid macular edema has long been recognized as a major cause of reduced visual acuity following cataract surgery, and although the incidence of this problem following lens implantation has been debated, it appears unlikely that the presence of an intraocular lens would reduce the likelihood of these macular changes developing in a given eye. Regardless of the precise incidence of macular edema following intraocular lens implantation, this study has demonstrated that the natural course of this complication in eyes with the types of implants employed in this series was significantly worse than that observed in comparable aphakic cases, particularly if the implants were associated with iris fixation. It is hoped that future prospective studies of consecutive pseudophakic cases will furnish more precise incidence figures regarding transient and chronic macular edema and will provide better explanations of the relationships between these changes and the various intraocular lenses and implantation techniques that have been employed.

SUMMARY

Forty-four aphakic and 45 pseudophakic eyes with typical cystoid macular edema following cataract surgery were reevaluated one to four years following their initial fluorescein angiograms in an effort to compare the natural courses of the macular lesions in the two groups of eyes. Both aphakic and pseudophakic eyes in which the edema was associated with vitreous adhesions to the cataract wound experienced a lower rate of resolution than comparable cases without such adhesions. Macular edema cleared significantly more frequently in aphakic eyes than in pseudophakic cases. Pseudophakic eyes in which iris fixation had been employed had a particularly poor prognosis, which was significantly worse than the natural course observed in pseudophakic eyes associated with capsular fixation. The latter group of eyes cleared significantly less frequently than did the group of aphakic eyes without vitreous adhesions. The reasons that the natural course of cystoid macular edema in pseudophakic eyes is relatively poor are unknown, but chronic inflammation may play a significant role in the pathogenesis of this important complication.

REFERENCES

1. Meredith TA, Kenyon KR, Singerman LJ, et al: Perifoveal vascular leakage and macular edema after intracapsular cataract extraction. *Br J Ophthalmol* 60:765-769, 1976.
2. Irvine SR: A newly defined vitreous syndrome following cataract surgery. *Am J Ophthalmol* 36:599-619, 1953.
3. Hughes WF Jr, Owens WC: Postoperative complications of cataract extraction. *Arch Ophthalmol* 38:577-595, 1947.
4. Kirsch RE, Steinman W: Spontaneous rupture of the hyaloid membrane following intracapsular cataract surgery. *Am J Ophthalmol* 37:657-665, 1954.
5. Chandler PA: Complications after cataract extraction: Clinical aspects. *Trans Am Acad Ophthalmol Otolaryngol* 58:382-396, 1954.
6. Nicholls JVV: Macular edema in association with cataract extraction. *Am J Ophthalmol* 37:665-674, 1954.
7. ———: Concurrence of macular edema with cataract extraction. *Arch Ophthalmol* 55:595-604, 1956.
8. Welch RB, Cooper JC: Macular edema, papilledema, and optic atrophy after cataract extraction. *Arch Ophthalmol* 59:665-675, 1958.
9. Gartner S: Optic neuritis and macular edema following cataract extraction. *EENT Monthly* 43:45-49, 1964.
10. Reese AB, Carroll FD: Optic neuritis following cataract extraction. *Trans Am Acad Ophthalmol Otolaryngol* 62:765-768, 1958.
11. Gass JDM, Norton EWD: Cystoid macular edema and papilledema following cataract extraction. *Arch Ophthalmol* 76:646-661, 1966.
12. Duke-Elder S, Dobree JH: Diseases of the retina, in Duke-Elder S (ed): *System of Ophthalmology*. St Louis, CV Mosby Co, 1967, vol 10, p 546.
13. Vogt A: Weitere ophthalmoskopische Beobachtungen im rotfreien Licht; echte Netzhautfaltchen. Cystische Degeneration der Macula lutea. *Klin Monatsbl Augenheilkd* 61:379-392, 1918.
14. Friedenwald JS: Clinical studies in slit-lamp ophthalmoscopy. *Arch Ophthalmol* 1:574-582, 1929.
15. Bangerter A: Zur Diagnose, Differentialdiagnose und Therapie des cystoiden Maculaodems (Maculacysten). *Ophthalmologica* 109:102-122, 1945.
16. Dunnington JH, Regan EF: Late fistulization of operative wounds, diagnosis and treatment. *Trans Am Ophthalmol Soc* 47:63-70, 1949.
17. Tolentino FI, Schepens CL: Edema of the posterior pole after cataract extraction: A biomicroscopic study. *Arch Ophthalmol* 74:781-786, 1965.
18. Reese AB, Jones IS, Cooper WC: Macular changes secondary to vitreous traction. *Trans Am Ophthalmol Soc* 54:123-134, 1966.
19. Maumenee AE: Further advances in the study of the macula. *Arch Ophthalmol* 78:151-165, 1967.
20. Jaffe NS: Vitreous traction at the posterior pole of the fundus due to alterations in the vitreous posterior. *Trans Am Acad Ophthalmol Otolaryngol* 71:642-651, 1967.
21. Irvine AR: Cystoid maculopathy. *Surv Ophthalmol* 21:1-17, 1976.
22. Welch RB, Maumenee AE: Peripheral posterior segment inflammation, vitreous opacification, and edema of the posterior pole. Pars planitis. *Arch Ophthalmol* 64:540-549, 1960.
23. Maumenee AE: Clinical entities in "uveitis": An approach to the study of intraocular inflammation. *Trans Am Acad Ophthalmol Otolaryngol* 74:473-504, 1970.
24. Smith RE, Godfrey WA, Kimura SJ: Chronic cyclitis: I. Course and visual prognosis. *Trans Am Acad Ophthalmol Otolaryngol* 77:OP-761-OP-768, 1973.
25. Ryan SJ: Cystoid maculopathy in phakic retinal detachment procedures. *Am J Ophthalmol* 76:519-522, 1973.
26. West CE, Fitzgerald RC, Sewell JH: Cystoid macular edema following aphakic keratoplasty. *Am J Ophthalmol* 75:77-81, 1973.

27. Kimball RW, Morse PH, Benson WE: Cystoid macular edema after cryotherapy. *Am J Ophthalmol* 86:572-573, 1978.
28. Lobes LA, Grand MG: Incidence of cystoid macular edema after retinal detachment repair. *Arch Ophthalmol* 98:1230-1232, 1980.
29. Wilkinson CP, Rowsey JJ: Closed vitrectomy for the vitreous touch syndrome. *Am J Ophthalmol* 90:304-308, 1980.
30. Kramer SG: Cystoid macular edema in penetrating keratoplasty. *Ophthalmology* 88: 782-787, 1981.
31. Kottow M, Hendrickson P: Iris angiography and cystoid macular edema after cataract extraction. *Arch Ophthalmol* 93:487-493, 1975.
32. Easty D, Dallas N, O'Malley R: Aphakic macular edema following prosthetic lens implantation. *Br J Ophthalmol* 61:321-326, 1977.
33. Michels RG, Green WR, Maumenee AE: Cystoid macular edema following cataract extraction (the Irvine-Gass syndrome): A case studied clinically and histopathologically. *Ophthalmol Surg* 2:217-221, 1971.
34. Norton AL, Brown WJ, Carlson M, et al: Pathogenesis of aphakic macular edema. *Am J Ophthalmol* 80:96-101, 1975.
35. Martin NF, Green WR, Martin LW: Retinal phlebitis in the Irvine-Gass syndrome. *Am J Ophthalmol* 83:377-386, 1977.
36. Miyake K: Prophylaxis of aphakic cystoid macular edema using topical indomethacin. *Am Intraoc Implant Soc J* 6:174-179, 1978.
37. Yanuzzi LA, Klein RM, Wallyn RH, et al: Ineffectiveness of indomethacin in the treatment of chronic cystoid macular edema. *Am J Ophthalmol* 84:517-519, 1977.
38. Obstbaum SA, Galin MA: Cystoid macular edema and ocular inflammation: The corneo-retinal inflammatory syndrome. *Trans Ophthalmol Soc UK* 99:187-191, 1979.
39. Binkhorst CD: Corneal and retinal complications after cataract surgery: The mechanical aspects of endophthalmodonesis. *Ophthalmology* 87:609-617, 1980.
40. Worst J: Extracapsular surgery and lens implantation, part 4: Some anatomical and pathophysiological implications. *Am Intraoc Implant Soc J* 4:7-14, 1978.
41. Ozaki L: Permeability of the posterior lens capsule in connection with intraocular lens implant surgery, in *Proceedings of the 22nd International Congress of Ophthalmology*. Amsterdam, Excerpta Medica, 1979, pp 1407-1410.
42. Kolker AE, Becker B: Epinephrine maculopathy. *Arch Ophthalmol* 79:552-562, 1968.
43. Michels RG, Maumenee AE: Cystoid macular edema associated with topically applied epinephrine in aphakic eyes. *Am J Ophthalmol* 80:379-380, 1975.
44. Roper DL, Nisbet RM: Effect of hyaluronidase on the incidence of cystoid macular edema. *Ann Ophthalmol* 10:1673-1678, 1978.
45. Welch RC, Welch J: The vitreous face after cataract surgery: The Second report on cataract surgery. Miami, Miami Educational Press, 1971, pp 106-107.
46. Hesse RJ, Schimek RA, Terry P: Visual recovery after ocular compression and cataract surgery. *Audio-Digest Ophthalmol* 14:1, 1976.
47. Henry MM, Henry LM, Henry LM: A possible cause of chronic cystic maculopathy. *Ann Ophthalmol* 9:455-457, 1977.
48. Tso MO: Experimental macular edema after lens extraction. *Invest Ophthalmol Vis Sci* 16:381-392, 1977.
49. Irvine AR: Extracapsular cataract extraction and pseudophakos implantation in primates: A clinicopathologic study. *Trans Am Ophthalmol Soc* 78:780-807, 1980.
50. Kramer SG: Considerations on epinephrine therapy in glaucoma. *Ann Ophthalmol* 10:1077-1078, 1978.
51. Klein RM, Katzin HM, Yanuzzi LA: The effect of indomethacin pre-treatment on aphakic cystoid macular edema. *Am J Ophthalmol* 87:487-489, 1979.
52. Miami Study Group: Cystoid macular edema in aphakic and pseudophakic eyes. *Am J Ophthalmol* 88:45-48, 1979.
53. Gass JDM, Norton EWD: Follow-up study of cystoid macular edema following cataract extraction. *Trans Am Acad Ophthalmol Otolaryngol* 73:665-681, 1969.

54. Jacobson DR, Dellaporta A: Natural history of cystoid macular edema after cataract extraction. *Am J Ophthalmol* 77:445-447, 1974.
55. Hitchings RA, Chisholm IH, Bird AC: Aphakic macular edema: Incidence and pathogenesis. *Invest Ophthalmol* 14:68-71, 1975.
56. Hitchings RA: Aphakic macular edema: A two year follow-up study. *Br J Ophthalmol* 61:628-630, 1977.
57. Emery JM, Little JH: Phacoemulsification and aspiration of cataracts. St Louis, CV Mosby Co, 1979, pp 270-273.
58. Berrocal JAR: Incidence of cystoid macular edema after different cataract operations. *Mod Probl Ophthalmol* 18:518-520, 1977.
59. Fung WE: Phacoemulsification. *Ophthalmology* 85:OP-46-OP-51, 1978.
60. Winslow RL, Taylor BC, Harris WS: A one-year follow-up of cystoid macular edema following intraocular lens implantation. *Ophthalmology* 85:190-196, 1978.
61. Stern AL, Taylor DM, Dalburg LA, et al: Pseudophakic macular edema: Long-term follow-up. *Ophthalmology*, to be published.