CME Monograph

CATARACT AND REFRACTIVE CASES JAMBALAYA

EXPERTS' RECIPES *for* PREVENTING *and* MANAGING COMPLICATIONS

Highlights From a CME Symposium

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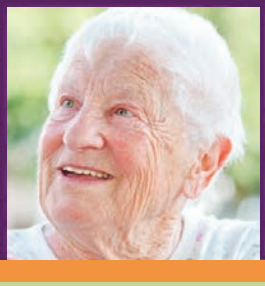

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Content Source
This continuing medical education (CME) activity captures content from a CME symposium held on November 18, 2013, in New Orleans, Louisiana.

Activity Description
Although significant advances in cataract and refractive surgery have occurred recently, there are still many challenges facing today's ophthalmic surgeons. Inflammation-mediated complications continue to adversely affect clinical outcomes. This monograph addresses management and prevention of common complications associated with cataract and refractive surgery cases. An expert faculty panel, comprising cataract surgeons and a retina specialist, has provided perspectives on a variety of topics, including identification of preoperative risk factors in patients undergoing cataract and refractive procedures as well as the optimal approaches to management of a variety of complicated clinical scenarios. Combination procedures, high-risk patient management, vitreous loss, and approaches to the incorporation of new technological and pharmaceutical options are all addressed by our panel, with the goal of improving patient outcomes.

Target Audience
This educational activity is intended for cataract and refractive surgeons and comprehensive ophthalmologists.

Learning Objectives
Upon completion of this activity, participants will be better able to:

- Discuss the potential paradigm shift in the timing of cataract surgery based on Physician Quality Reporting System outcomes, patient demand, complications, and satisfaction for surgeons and their patients considering cataract surgery
- Identify preoperative risk factors in patients undergoing cataract surgery and apply appropriate therapies (preoperative, intraoperative, and postoperative) to minimize complications
- Discuss the role of inflammation control in patients choosing procedures such as femtosecond cataract surgery and those involving advanced technology IOLs
- Evaluate the anti-inflammatory agents used in cataract surgery on efficacy, safety, and patient comfort
- Apply appropriate perioperative therapies for inflammation prevention in patients receiving advanced technology IOLs, combination procedures (such as cataract/corneal transplant), and complicated cataract procedures

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INTRODUCTION

Studies have estimated that by the year 2020, approximately 10% of the US population will have cataracts. This translates to more than 30 million people, and the burgeoning population of patients with cataracts will certainly put an incredible demand on the medical system to increase the number of procedures performed.[1] Given this increase in demand, prompt diagnosis and referral to cataract surgeons will be imperative.

Postoperative visual acuities of 20/40 are no longer acceptable, given patients' current desire to preserve their lifestyles. Patient dissatisfaction in the postoperative period is primarily attributable to missed refractive targets or unacceptable vision in the early postoperative period. The latter is commonly due to cystoid macular edema (CME) and other preventable inflammation-mediated causes.[2-4] Commonly prescribed medications used during the postoperative period are approved for pain and inflammation control, but they are used off-label in the United States to prevent CME as well.

Some patients also may experience unacceptable levels of postoperative discomfort; we must reduce postoperative pain as a key measure of patient satisfaction.[2-4] Continuing to improve patient outcomes—reducing postoperative complications while continuing to provide excellent visual outcomes—will become even more important in the next few years as meeting quality measures becomes more important. The Physician Quality Reporting System includes assessment of 20 unique Medicare Part B fee-for-service patients that will determine surgeons' reimbursement rates. Those payments will be predicated on the quality of the work we do, as determined by measuring visual acuity, complications, and patient satisfaction with the surgery. In this monograph, our expert panel will present interesting cases from their practices and provide readers with practical insights for preventing and managing inflammation-related complications associated with ophthalmic surgeries.

—Stephen S. Lane, MD

Factors Influencing Postoperative Inflammation

Certain factors can adversely influence the amount of postoperative inflammation after cataract surgery. Cataract density[5] can be associated with poor refractive outcomes and errors in axial length measurements,[6] and has been reported to increase potential complications.[5] Further, patients with darker irides are more prone to develop inflammation. Patients also will be at a higher risk for postoperative inflammation if they have a history of:

- Uveitis
- Iritis
- Rheumatoid arthritis
- Diabetes

Cystoid Macular Edema

Cystoid macular edema remains the most common cause of postoperative decreased vision after uneventful cataract surgery.[7] Clinical CME occurs in approximately 1% to 2% of patients.[8] The incidence of subclinical CME is between 10% and 20% and can be detected with either fluorescein angiography (FA) or optical coherence tomography (OCT).[8-10] Optical coherence tomography has become an excellent tool for evaluating the macula before surgery to identify higher-risk patients. Patients with obvious retinopathy, or dot-blot hemorrhages or dilated vessels or other signs of vasculopathy, have a higher risk of developing CME.

The incidence increases with any intraoperative complication,[11] particularly vitreous loss. Studies have shown that the incidence of CME is substantially increased in cases of diabetes and uveitis.[9,12]

Numerous factors can cause CME, including any retinal vascular disease or epiretinal membrane formation. We need to exclude the presence of macular disorders and ensure a healthy macula, especially in patients scheduled for premium lens surgery. Any residual lens material in the eye also can lead to postoperative inflammation, so in that situation you are dealing with a potentially high-risk patient.

Use of NSAIDs in Cataract Surgery

There is a growing trend to address this potential complication through the preoperative use of nonsteroidal anti-inflammatory drugs (NSAIDs) as well as by longer postoperative courses of these medications.[13-18] Several NSAIDs are approved in the United States for the

treatment of postoperative pain and inflammation associated with cataract surgery, including bromfenac, diclofenac, ketorolac, and nepafenac (dosing regimens vary from once daily to 4 times daily).[19] Although the use of NSAIDs for the prevention of CME is considered off-label in the United States, several studies have shown the efficacy of NSAID use for this purpose,[20-22] and nepafenac has CE (European Conformity) marking for that indication in Europe.[4]

There remains the potential for corneal complications with the use of topical NSAIDs, but problems such as corneal melts and toxicities are rare and have generally been attributed to older generic NSAID formulations.[23] Current formulations such as bromfenac, ketorolac, and nepafenac are reported to have extremely low incidences of adverse events. In one study, Singh and colleagues documented that use of nepafenac did not result in any corneal erosions, even after 90 days of use.[21]

Use of Steroids in Cataract Surgery

Ophthalmic steroids are typically classified as either ketone or steroid. Of the ketone steroids, difluprednate has been shown to have higher potency than prednisolone acetate, which is often used after intraocular surgery.[24] Loteprednol, an ester steroid, is less potent than many ketone steroids. However, when compared with prednisolone acetate, loteprednol can provide an equivalent degree of postoperative inflammation control for patients undergoing routine cataract surgery.[25-27]

Combination Therapy Studies

Few studies have evaluated the combined use of steroids and NSAIDs in the treatment of CME. Wittpenn and colleagues showed that using combination therapy improved contrast sensitivity,[18] relative to steroids alone, and Flach reported that there is some synergistic effect as well.[28]

Panel Discussion and Introductory Perspectives on Perioperative Treatment in the Routine Patient

Dr Lane: What is your treatment regimen for routine cataract patients? Does it alter if the patient is scheduled for an advanced technology lens?

Dr Donnenfeld: We know from evidence-based medicine[3,18] that 5% of patients will develop CME if you do not use an NSAID, and use only a corticosteroid. In our practice, even 5 cases of CME per every 100 patients would overwhelm us, so we start with NSAIDs 3 days preoperatively and continue for 1 month postoperatively; we usually stop corticosteroids at 3 weeks postoperatively. We have found that patients have increased contrast sensitivity, higher acceptance, less glare and halo when an NSAID is used with a diffractive multifocal intraocular lens (IOL).[29] For my premium lens patients, especially those who are receiving a multifocal IOL, it is also imperative that the retina be perfect.

Dr Holland: I prefer to start NSAIDs the day before cataract surgery. For our multifocal lens patients, I am certainly much more aggressive about trying to diagnose early CME or any kind of visual issue in the postoperative period than I would be with patients receiving standard IOLs. I will frequently use OCT to assess for retinal thickening, and I am much more aggressive about treating that because even when the CME is resolved, the loss of contrast sensitivity associated with a multifocal lens has been exacerbated by the CME and patients are not happy with their vision.

Dr Lane: Yes, these premium lens patients who have mild CME that resolves tend to notice a difference between the eye that previously had CME and the eye that never developed CME, even though the patient is 20/20 OU. The CME has caused irreparable damage to the photoreceptors.

Dr Holland: Most CME can be treated and resolved, and vision will improve, but once CME has occurred, the retina is never "normal" again. Resolved CME does not result in the same quality of vision as that in an eye that never had CME. The analogy in corneal transplantation is that *treated* endothelial rejection is not the same thing as *prevented* endothelial rejection. There will be endothelial damage and cell loss with cases of rejection.

The following case studies illustrate how inflammation prevention and control can help prevent some potential complications after cataract surgery, and, if those complications do occur, how to best manage them.

CASE FOCUS

Cataract Surgery and the High-Risk Patient With Diabetes

Keith A. Warren, MD

A 77-year-old woman with a preoperative history of bilateral moderate nonproliferative diabetic retinopathy underwent uneventful cataract surgery, without being pretreated with an NSAID. Prior to her surgery, her best corrected visual acuity (BCVA) was 20/100. The anti-inflammatory regimen postoperatively in this case was prednisolone acetate 4 times a day for a week, NSAIDs once daily for 1 week.

By the first postoperative day, her BCVA markedly improved to 20/40. At week 1, she improved a little more, to 20/30. She was sent home, and she finished her steroid regimen.

After a lengthy period of approximately 10 weeks, she came in with a complaint of a decrease in visual acuity, with a BCVA of 20/100.

Fluorescein angiography was done to examine circulatory status, and OCT was also performed **(Figure 1)**. At this point, our treatment options included aggressive topical treatment, intravitreal injections with either steroid or an anti-VEGF agent, or some combination thereof.[30-32]

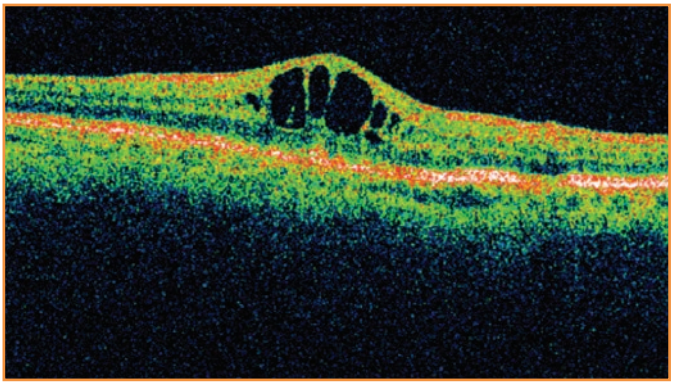

Figure 1. OCT image of a patient with diabetic retinopathy who now has edema.
Photo Courtesy of Keith A. Warren, MD

Panel Discussion: Diagnosis and Treatment Strategies for the Patient With Diabetes and CME

Dr Warren: Considering this patient already had background diabetic retinopathy, would you have pretreated her? If so, what would you have used?

Dr Lane: I certainly would have pretreated. This patient is at a higher risk for CME, so I would begin her on NSAIDs 3 days preoperatively, and would be much more aggressive in the early postoperative period by treating with difluprednate, at least 4 times daily and perhaps up to 6 times daily. This is a patient whom I would keep on NSAIDs for 6 to 8 weeks postoperatively.

Dr Holland: What we need to understand better is how long to pretreat patients with diabetes and how to continue to treat them postoperatively. The duration of postoperative treatment may wind up being much longer than the approved 2-week postoperative indications. Singh and colleagues have looked at the issue of prolonged postoperative treatment in patients with diabetic retinopathy, and the data supported the use of nepafenac for up to 90 days postoperatively to prevent CME.[20] They also incorporated the use of a topical steroid for 2 weeks or longer as part of the postoperative protocol.

Dr Warren: How would you manage this eye if it presented to you at 10 weeks with the edema? What would you have done first?

Dr Holland: I would have used a combination of a topical NSAID and a corticosteroid, eg, difluprednate and nepafenac. I would want to see the patient again in a few weeks.

Dr Donnenfeld: I would recommend using the strongest NSAID and the strongest steroid in this patient. I think we clinical ophthalmologists can actually manage these patients for the first few weeks before considering referral to a retina specialist colleague. If you have OCT imaging technology available in your office, you should be examining the macula. If the macula looks as if it is improving over time, you can manage the patient yourself. If the macula is not improving, refer to a retina specialist.

Dr Lane: When examining the OCT findings, how do you know if this is Irvine-Gass or diabetic macular edema (DME), or a combination of both? Is there anything, either from a clinical examination or from the OCT itself, that would tip you one way or the other as a retina specialist? What should we be looking at, and should we try to differentiate among the different choices?

Dr Warren: In this case, I would prefer to use FA because in a patient who has comorbidity such as diabetes, you must discern between a vasculopathy-related edema and an inflammatory-related edema. Optical coherence tomography will only show me the swelling; it is not going to show me the etiology of that swelling.

Dr Lane: That is why I would want my retina colleagues to weigh in sooner rather than later. I would refer early on.

Dr Warren: The indications for cataract surgery in patients with diabetes or retinal vein occlusion are to improve iatrogenic vision loss following anti-vascular endothelial growth factor (VEGF) therapy and/or intravitreal steroids, and to improve visualization of the fundus. I refer those patients to my anterior segment colleagues for cataract surgery.

Pretreating with an NSAID as well as with preoperative or intraoperative corticosteroids may reduce the incidence of CME in these high-risk patients.[3,20,33-35] The treatment algorithm is complicated, so consider referral to a retina specialist.

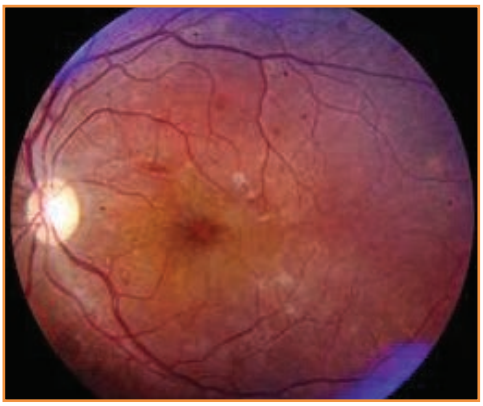

Figure 2. Funduscopic examination findings.
Photo Courtesy of Keith A. Warren, MD

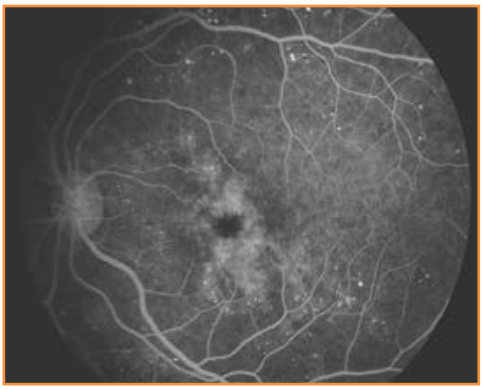

Figure 3. Fluorescein angiography findings.
Photo Courtesy of Keith A. Warren, MD

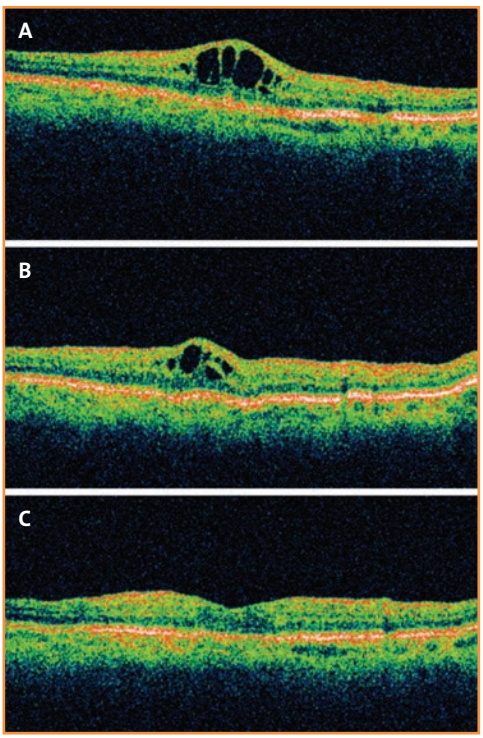

Figure 4. OCT progression: A) initial, B) 4 weeks, C) 8 weeks.
Photos Courtesy of Keith A. Warren, MD

Dr. Lane: Does anyone ever consider the use of intravitreal anti-VEGF injection at the time of cataract surgery for high-risk patients?

Dr. Warren: Intravitreal anti-VEGF injections are most commonly reserved for patients with active DME or proliferative disease. In patients with active DME, cataract surgery is not recommended until the DME has been controlled, which usually necessitates a minimum of 3 months of treatment. Ideally, the eye should be as quiet as possible for 3 months before surgery. In patients with diabetes who do not have DME, but do have background diabetic changes, the recommendation is for pretreatment 3 to 7 days prior to surgery with an NSAID.[36] As a rule, intravitreal anti-VEGF treatment is used to treat active disease and not as a prophylactic measure against the development of CME. I believe that patients with proliferative diabetic eye disease should be treated with an anti-VEGF agent, then have their cataract surgery done, then undergo panretinal photocoagulation 1 month postoperatively, if possible.

If acute CME develops, it can be treated with topical steroids for up to 4 to 6 weeks.[37] I prefer difluprednate because of its excellent tissue penetration.[24] If the CME persists after treatment, more aggressive treatment with a periocular injection of a corticosteroid and a topical NSAID may be necessary.[38] If the CME still persists, at that point you have to think about intraocular steroid injection in conjunction with an NSAID.

If there is recalcitrant CME 4 to 6 months after the initial surgery, intravitreal corticosteroid implants are usually recommended.[39] Finally, vitrectomy is the last option.[40] We recommend longer treatment in these difficult cases because 20% of eyes with CME will rebound after discontinuation of topical therapy.[38]

So, back to our case. At 10 weeks postoperative, the patient began treatment with a topical steroid and a topical NSAID for 6 weeks; she was then given a periocular steroid injection and her edema still did not resolve. The patient came to me with this persistent edema **(Figure 2)**.

Fluorescein angiography in this patient indicated a case of Irvine-Gass, not DME **(Figure 3)**. There is no focal edema to be treated with a laser. There is a petaloid pattern in the macula. This is not an anti-VEGF therapy eye; it is inflammation. On the basis of that knowledge, we treated her with difluprednate and an NSAID 4 times a day. Looking at her OCT progression from the time of her initial visit with me **(Figure 4A)**, by 4 weeks the edema responded to treatment **(Figure 4B)**, and by 8 weeks the edema had resolved **(Figure 4C)**. I continued treatment for another 4 weeks before discontinuation.

This is but 1 example of combination therapy with a potent steroid and an NSAID that was able to treat CME successfully. Pretreating the eye with an NSAID likely would have prevented the CME.

CASE FOCUS

Inflammation and Corneal Transplant Surgery

Edward J. Holland, MD

An aggressive approach to preventing inflammation in patients who have undergone corneal transplantation is essential to promoting graft preservation. Years ago, corneal specialists believed we needed to start with low-dose steroids and become more aggressive if/when treatment failed, in the hopes we could control the inflammation with the lowest-dose steroid. Today, however, the collective thought is to start as aggressively as possible and taper quickly so that we can resolve the inflammation as fast as possible.

Patients with Fuchs dystrophy and visually significant cataract **(Figure 5)** are becoming more commonplace. Most corneal surgeons—myself included—plan a triple procedure, comprising phacoemulsification, posterior chamber lens implantation, and Descemet stripping endothelial keratoplasty (DSEK), for these patients. In the United States in 2012, DSEK overtook penetrating keratoplasty (PK) as the most commonly performed corneal transplant procedure.[41]

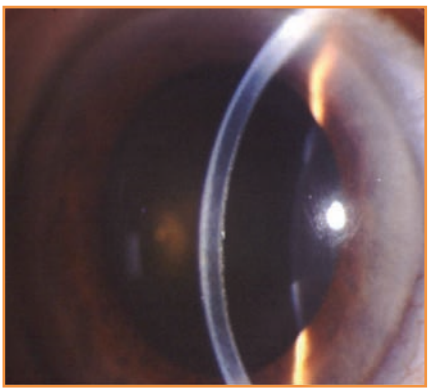

Figure 5. Slit lamp examination findings.

Photo Courtesy of Edward J. Holland, MD

Corneal Transplant Rejection

The leading cause of graft failure in all types of transplants is rejection. With PK, rejection reactions are approximately 25%, resulting in a 5% to 10% graft failure rate in routine patients and a 25% to 50% graft failure rate in high-risk patients.[42] DSEK has a reported 8% to 10% rejection reaction rate, resulting in a 1% to 3% failure rate.[43,44]

Our center has reported a 4% rejection reaction rate after DSEK, a low rate that is supported by our protocol of maintaining these patients on steroids indefinitely.[45] We found peak time for rejection after DSEK to occur between 19 and 24 months, a little later than we find it with PK. Unless steroids are contraindicated (ie, if IOP pressure spikes cannot be adequately controlled), we advocate their use over the long term to prevent rejection reaction rates.

Deep anterior lamellar keratoplasty (DALK) is commonly performed in patients with stromal disease who have healthy endothelium, but rejection rates still run between 2% and 10%.[46] This is mostly because of a significant antigen load in DALK (the epithelium and Langerhans cells, and the anterior stromal keratocytes, are all antigenic).

Any time a patient has an endothelial rejection reaction, he or she has lost cells, and the graft life has been shortened. Once a graft has failed because of rejection, the immune system has been forever changed and the patient is at a higher risk for rejection following any future procedures.

Panel Discussion: Combined Procedures and Perioperative Strategies

Dr Holland: What are your preoperative and perioperative routines for phacoemulsification-DSEK patients?

Dr Donnenfeld: I treat these patients in the same manner as I do my regular cataract surgery patients. I treat aggressively with an NSAID, starting approximately 3 days preoperatively. I also start

antibiotics 3 days preoperatively, and I like to pretreat with a little steroid. My steroid of choice for phacoemulsification-DSEK patients is difluprednate because of its potency, and I not only want to treat inflammation following cataract surgery, but I also want to prevent allograft rejection. It is inflammation that causes these corneas to not adhere.

If the patient is pseudophakic, I do not ever discontinue the steroids, but I will taper the difluprednate after approximately a month or 2 to a milder steroid such as loteprednol.

Dr Lane: I prescribe difluprednate every 2 hours initially for the first couple of weeks and begin to taper only after this time period. This case patient is at risk for macular edema. I would use the NSAID starting approximately 3 days beforehand and then continue for approximately 6 weeks. I taper down to a milder steroid at approximately 3 months, and keep the patient on a once- or twice-daily dosing indefinitely.

Dr Holland: In PK patients with epithelial problems, we were not typically using NSAIDs because NSAIDs can slow epithelial healing and produce issues in corneal transplant patients. In DSEK, the incision is a cataract incision, and these patients are at risk for CME as are all patients undergoing cataract surgery. In fact, combining DSEK and phacoemulsification results in more inflammation than that experienced in a typical cataract patient, and corneal surgeons are now adding NSAIDs to treatment regimens. Even with the advent of newer technologies such as femtosecond laser surgery, inflammation control remains imperative. For patients with previous corneal disease, there may be advantages to the use of laser phacoemulsification, as reported in a case study by Nagy and colleagues.[47]

Dr Donnenfeld: Epitheliopathy remains a problem, which is why a mild once-a-day NSAID is better than agents taken 4 times a day. You definitely do not want to be using a generic NSAID in patients with epitheliopathy.

Case Presentation: Monocular Candidate for Repeat DSEK

Dr Holland: A 78-year-old male, monocular patient, who lost his right eye because of glaucoma, presented to our clinic. He had a tube shunt with a failed DSEK secondary to rejection. The planned procedure was to repeat the DSEK. How would you treat this patient?

Dr Donnenfeld: I would want to avoid additional surgery in this patient, so I would treat with a strong corticosteroid. Difluprednate has been shown to have greater potency than prednisolone acetate and I would select the more potent option to facilitate corneal clearance.[24]

Surgeons also might consider the use of intracameral steroids. We now have triamcinolone in an approved on-label indication for use in ophthalmic surgery, and that agent can sometimes aid in corneal recovery.

Dr Holland: Another consideration is the establishment of the chronology of graft failure. The presence of corneal edema alone does not tell you anything about when the graft failed. If you can determine that the graft failed recently, be aggressive with anti-rejection management, including difluprednate hourly in hopes of reversing the graft rejection.

Dr Lane: We have to be aggressive against inflammation in this patient because he has only the 1 eye; he is very high risk because of the glaucoma tube shunt and his advanced glaucoma. I would consider oral anti-inflammatory as well as topical anti-inflammatory measures.

Dr Holland: Regarding intraoperative management, does anyone routinely perform a sub-Tenon's corticosteroid injection at the end of DSEK cases?

Dr Donnenfeld: I routinely inject a short-acting corticosteroid such as dexamethasone into the subconjunctival space at the conclusion of a DSEK procedure. In this case, it would be reasonable to give a longer-acting corticosteroid such as triamcinolone, particularly if the patient was not strictly compliant or at high risk for rejection.

Dr Lane: I will give a sub-Tenon's betamethasone injection after DSEK. It lasts for only approximately 7 to 10 days, so there is not as much to worry about with respect to a chronic steroid response.

Dr Holland: I do not typically use subconjunctival steroids, because of issues with patient discomfort and the efficacy of topical options like difluprednate. For this patient, we chose to use difluprednate every hour for the first few weeks, then tapered it down to every 2 hours. The key in treating these eyes is to prevent any inflammation in the anterior chamber. We use oral steroids and topical corticosteroids aggressively until the anterior chamber cells are gone and we are vigilant about not allowing any new cells to develop. Finally, surgeons may consider oral immunosuppression, such as mycophenolate. A 78-year-old patient may be at higher risk for some complications from mycophenolate, such as infections, gastrointestinal hemorrhage, or pulmonary edema, than a younger patient.[48] In addition, mycophenolate does not work immediately and may take weeks or months to achieve maximal effect. Either it must be started in advance, or a short course of oral steroids is needed to control the immediate postoperative inflammation. Some immunosuppressive medications such as tacrolimus also carry the potential for complications, but mycophenolate is generally very well tolerated.

Case Presentation: Bilateral Penetrating Keratoplasty

Dr Holland: A 30-year-old woman who had bilateral PK for pellucid marginal degeneration presented to our clinic. She had undergone the procedure before we had DALK to save a patient's endothelium. She was doing well postoperatively for quite some time and then developed bilateral chronic endothelial and stromal rejection. There was a little haze in the inferior part of that pupil, indicating stromal edema **(Figure 6)**. There is neovascularization into the cornea. At the time of this case, difluprednate was not available, so we used prednisolone acetate every 2 hours. She had persistent rejection, low-grade anterior chamber cells, and neovascularization.

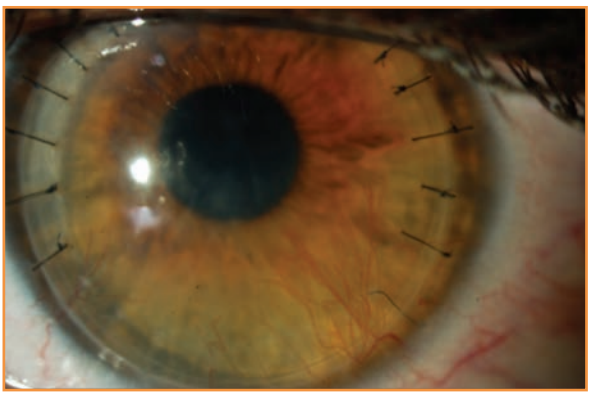

Figure 6. Stromal edema after PK.
Photo Courtesy of Edward J. Holland, MD

In this young patient, bilateral graft rejection might have led to keratoprosthesis as the only other option to treat her underlying pellucid marginal degeneration, so we needed to be aggressive. She was on prednisolone acetate every hour and on mycophenolate[49] and intracameral dexamethasone.[50,51] We gradually transitioned her steroid regimen to difluprednate when that corticosteroid became available.[52]

She had a slow regression of her stromal neovascularization. Her anterior chamber reaction cleared over the next 2 months. We tapered her oral mycophenolate to 4-times-daily dosing.[53,54] She has been maintained on chronic difluprednate twice a day to 3 times a day and has been off all the other anti-inflammatory agents. What would the panel have done?

Dr Donnenfeld: This patient presented with bilateral disease. It is neovascularization. It would be appropriate to add some oral immunosuppression for a bilateral case, but I would start with using difluprednate in an aggressive manner.

Dr Holland: If this patient has or develops an early cataract, does it change how aggressive one should be with regard to the dosing of topical steroids? Do you avoid daily maintenance with steroid medication in phakic patients?

Dr Lane: I do not, because maintenance of a clear cornea is more important to attain; and we have excellent treatments for cataract if it should become problematic.

Dr Donnenfeld: I agree—the complication of a cataract developing is insignificant compared with a vascularized/failed transplant. For the great majority of phakic patients who have undergone corneal transplantation, we discontinue topical corticosteroids shortly after the sutures have been removed and may continue them on a low-dose topical immunosuppressive such as topical cyclosporine, which does not cause cataracts or glaucoma. However, in phakic patients with allograft rejection and corneal neovascularization, we continue topical corticosteroids aggressively as long as needed.

Dr Holland: I think we are all in agreement—a failed PK due to rejection results in a poor prognosis for a repeat PK. Cataract surgery has an excellent prognosis if the need for cataract management arises.

Dr Lane: In terms of the IOP, do you need to see these patients more frequently than you would patients with noncomplicated grafts?

Dr Holland: The stronger the steroid, the higher the IOP potential in steroid-responsive patients. We have had some patients spike up into the 50s, but for the majority of patients, IOP spikes are not going to be an issue. Inflammation and loss of corneal endothelium is a bigger issue than dealing with secondary glaucoma. Our primary goal with these patients is to prevent inflammation before it emerges; inflammation can lead to endothelial rejection. There is a lasting effect on the tissue.

Patient education is key: patients have to understand the signs and symptoms of endothelial rejection and then notify the physician immediately instead of waiting 4 or 5 days.[55] We are very aggressive in our attempts to prevent inflammation and to prevent antigen recognition.[56]

CASE FOCUS

Cataract Surgery Risk Reduction and Optimal Management of Vitreous Loss

Eric D. Donnenfeld, MD

A 65-year-old male presented to our office for cataract surgery and preoperative evaluation, with a normal retinal assessment. Even in typical patients such as this, for whom the risk for postoperative inflammation is relatively low, it is still important to contemplate strategies to reduce that risk. Ophthalmic NSAIDs are a key component of treatment at our clinic for just that reason, and there is a good amount of evidence-based information to support our regimen.

We evaluated the use of an NSAID with various preoperative dosing schedules in routine cataract surgery: 3 days preoperatively, 1 day preoperatively, 1 hour preoperatively, and no use of a preoperative NSAID.[3] We found almost no difference between control patients and those dosed 1 hour before surgery, but predosing 1 to 3 days before surgery was beneficial.[3]

Without NSAID use in the preoperative period, pupils will constrict to approximately 1.5 mm, which means that with 1 standard deviation, there is a 3-mm constriction in approximately 5% of patients. If an NSAID is given 1 day preoperatively, the constriction will reduce to 0.42 mm; and when NSAIDs are started 3 days preoperatively, there is effectively no constriction.[3]

The larger pupil also means less ultrasound time, making it easier to perform the surgery; NSAID use also results in lower mean effective phacoemulsification time.[3] Even with novel techniques such as femtosecond laser therapy, which may also reduce effective phacoemulsification time,[57] prostaglandin levels rise immediately after laser use,[58] so consideration should always be given to NSAID therapy. NSAID use in the preoperative period *reduces* postoperative inflammation **(Figure 7)**,[3] but that should not be our only goal. We also want to *prevent* inflammation from occurring, and pretreating achieves both goals.

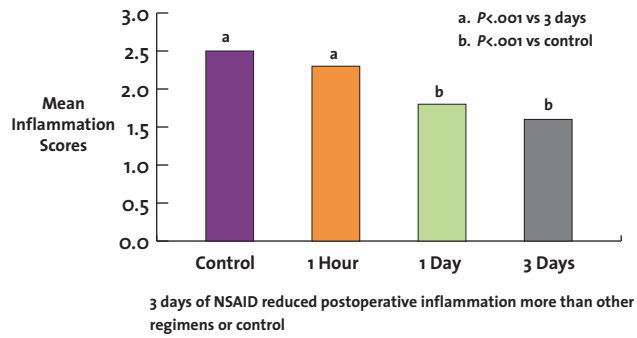

Figure 7. Preoperative NSAID dosing and inflammatory control.[3]

In our preoperative NSAID assessment study, we found no incidence of clinically significant CME if the NSAID was started at 1 or 3 days preoperatively, compared with a 12% incidence of CME when we did not use an NSAID (but did use a corticosteroid).[3]

Corticosteroids have a different mechanism of action than do NSAIDs, and as a result, predosing for 3 days is not necessary. We noted that neurosurgeons predose with corticosteroids to stabilize cell membranes and neural tissue. We have begun implementing that strategy at our facility, where we pulse-dose our patients starting 2 hours before surgery, and recommend surgeons have the corticosteroid available as soon as the cell membrane is cut so the arachidonic acid pathway is not started.[59]

In a contralateral eye study, we evaluated difluprednate vs prednisolone acetate, and pulse-dosed our patients.[59] As the corneal endothelium and retina are derived from the same neural ectoderm source as the central nervous system, it made sense to us to mimic the pulse-dose regimen neurosurgeons employ in brain and spinal surgery. Patients in our study were instructed to start instilling drops every 15 minutes for the 2 hours before scheduled surgery. Once they are in the preoperative area, they receive 3 drops immediately before surgery, and then they get 4 drops postoperatively, for a total of approximately 10 drops during the perioperative period. (This is an off-label dosing regimen, and what we now use in clinical practice as well.) There was a 30-µm difference in corneal thickness between the eyes dosed with difluprednate compared with those dosed with prednisolone at day 1, with the corneas in the prednisolone group being thicker; by day 15 and day 30, differences were not statistically significant.[59]

More than 70% of the eyes in the difluprednate group were 20/25 or 20/20 at postoperative day 1.[24] That is a "wow" effect patients are going to remember. Conversely, only approximately 30% of the eyes in the prednisolone group were at that level on postoperative day 1. I believe that these results are explained by the ability of difluprednate to facilitate corneal clearing.

Vitreous Loss

In cases of vitreous loss during cataract surgery, triamcinolone is capable of identifying vitreous strands and treating the resultant intraocular inflammation.[60,61] In my hands, using triamcinolone results in the quietest eyes on postoperative day 1, even after complex cataract surgery. Be aware there may be transient pressure spikes, but those usually resolve over a period of a week or so after surgery.

Part of my routine cataract surgery is to perform a bimanual vitrectomy. We use triamcinolone 0.1 mL to stain the vitreous and to reduce postoperative inflammation. Once all the vitreous strands are removed, we proceed with the IOL implantation.

Panel Discussion: Management of Vitreous Loss

Dr Donnenfeld: If you lose vitreous and a patient's eye is inflamed, what do you recommend?

Dr Warren: The eye would now be at high risk for CME, and I would use intracameral triamcinolone as an initial step in the management of inflammation. Next, I would treat aggressively with a topical steroid along with an NSAID.

If the patient shows any signs of increased inflammation in that setting, I would first evaluate if there is any traction on the vitreous, and if not, then consider an intravitreal injection of additional corticosteroid.

Dr Donnenfeld: In the case of this patient, I used an NSAID a little bit longer postoperatively, for 8 weeks instead of the typical 4 weeks.

Dr Warren: When there is vitreous loss, observation and inspection are the most important things to do initially. You want to assess the problems. Is there any nuclear material or cortical material left? Where is the vitreous? It is important to assess the tissue. Removing the vitreous can be accomplished from either an anterior or posterior approach, depending on your comfort. I prefer a posterior approach to remove the vitreous from the space where it originated.

The literature suggests final outcomes are best when the IOL is placed at the time of initial surgery rather than at a later time after the vitrectomy.[62] The reasons are 2-fold: First, you are separating the vitreous from the anterior segment so that vitreous does not exert any anterior-to-posterior traction on the macula; second, and more importantly, there is now a physical barrier between the vitreous and the anterior segment, so the incidence of CME and the incidence of glaucoma are much lower when the lens implant is placed at the time of surgery. Finally, these eyes with vitreous loss need to be treated with very aggressive anti-inflammatory treatment and for a longer duration.[63]

There are 3 main indications for removing lens fragments in the posterior segment:

- Media opacity obscures the visual axis, and the patient cannot see
- Significant and persistent intraocular inflammation
- Glaucoma

It should be noted that adequate cleanup of the anterior segment after the lens implant lowers the incidence of secondary glaucoma and CME.[64] The average time reported for planned removal of lens fragments is approximately 15 days after initial surgery.[65] The literature reports no difference in outcomes between same-day removal or delayed removal, within a 30-day window of the initial surgery.[65]

Patients can have really good outcomes provided the lens is implanted at the time of surgery, and the patient is treated aggressively to avoid CME.[66]

SUMMARY POINTS FROM THE PANEL

Given the increasing demand for cataract and refractive procedures, it is essential for practicing ophthalmic surgeons to be able to identify risk factors for complications in a timely manner and to be familiar with strategies that can help to prevent these complications as well as manage them when they do arise. Inflammation control is a key to successful outcomes for a variety of different procedures. An aggressive stance toward the prevention of inflammation can be extremely helpful in reducing the likelihood of CME development for patients undergoing cataract procedures (particularly those at high risk), and in increasing the likelihood of graft preservation for those patients undergoing combined procedures such as phacoemulsification/corneal transplant. Outcomes with premium IOLs can be optimized when inflammation is adequately controlled, particularly with regard to the key element of patient satisfaction. Even when complications such as vitreous loss emerge, prioritization of inflammation control can be extremely beneficial.

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1. Of the following, which is not a factor that increases the risk of inflammation after cataract surgery?
    a. Rheumatoid arthritis
    b. Iritis
    c. Diabetes
    d. Lighter irides

2. Published estimates indicate that by the year 2020, the number of Americans with cataracts will be:
    a. 10 million
    b. 20 million
    c. 30 million
    d. More than 30 million

3. Intracameral triamcinolone used in the setting of cataract surgery complicated by vitreous loss may be categorized as all of the following, except:
    a. A diagnostic agent that identifies vitreous strands
    b. A therapeutic agent that treats intraocular inflammation
    c. FDA approved
    d. A tool to help reduce further complications prior to IOL placement

4. Patients scheduled to receive multifocal intraocular lenses may experience _____ when prescribed an NSAID preoperatively.
    a. Increased glare
    b. Decreased glare and halo
    c. Reduced contrast sensitivity
    d. Decreased corneal sensitivity

5. Which of the following is true?
    a. Difluprednate is considered one of the more potent ophthalmic ketone steroids
    b. Loteprednol is associated with a higher incidence of elevated IOP than all ketone steroids
    c. Prednisolone acetate provides greater postoperative inflammation control than loteprednol in routine cataract surgery
    d. Topical steroid therapy must be started several days prior to cataract surgery

6. Without NSAID use in the preoperative period, patients undergoing cataract surgery experience a mean pupillary constriction of approximately:
    a. 0.5 mm
    b. 1.5 mm
    c. 3.0 mm
    d. NSAID use does not influence pupillary constriction

7. Which NSAID presurgical treatment duration has been associated with the lowest postoperative inflammation scores?
    a. 20 minutes
    b. 1 hour
    c. 1 day
    d. 3 days

8. All the following statements regarding the use of femtosecond cataract surgery are true, except:
    a. It may be useful for patients with corneal disease who are undergoing phacoemulsification
    b. Its use is associated with immediate elevation in prostaglandin levels
    c. There is no need for anti-inflammatory therapy in cases in which laser surgery is employed
    d. It may lower effective phacoemulsification time

9. For patients whose cataract surgery procedures are complicated by vitreous loss, which of the following intraoperative strategies may help to improve outcomes?
    a. Use an ophthalmic viscosurgical device for better viewing
    b. Remove the vitreous only through a posterior approach
    c. Consider an intravitreal injection with an NSAID
    d. Continue with the placement of the IOL

10. A study by Singh and colleagues found that 1 form of NSAID therapy could be used safely in an extended fashion to help reduce the risk of postoperative inflammation in high-risk patients undergoing cataract surgery. The duration of therapy for these patients was:
    a. 30 days
    b. 60 days
    c. 90 days
    d. 120 days

Activity Evaluation/Credit Request

Original Release: March 15, 2014 • **Last Review:** February 27, 2014 • **Expiration:** March 31, 2015

Cataract and Refractive Cases Jambalaya: Experts' Recipes for Preventing and Managing Complications

Highlights From a CME Symposium

To receive *AMA PRA Category 1 Credit*™, you must complete this **Evaluation** form and the **Post Test**. Record your answers to the **Post Test** in the **Answer Box** located below. Mail or Fax this completed page to **New York Eye and Ear Infirmary of Mount Sinai**–ICME, 310 East 14th Street, New York, NY 10003 (Fax: 212-353-5703). Your comments help us to determine the extent to which this educational activity has met its stated objectives, assess future educational needs, and create timely and pertinent future activities. Please provide all the requested information below. This ensures that your certificate is filled out correctly and is mailed to the proper address. It also enables us to contact you about future CME activities. Please print clearly or type. Illegible submissions cannot be processed.

PARTICIPANT INFORMATION *(Please Print)* ❑ Home ❑ Office

Last Name _____ First Name _____

Specialty _____ Degree ❑ MD ❑ DO ❑ OD ❑ PharmD ❑ RPh ❑ NP ❑ RN ❑ PA ❑ Other _____

Institution _____

Street Address _____

City _____ State _____ ZIP Code _____ Country _____

E-mail _____ Phone _____ Fax _____

Please note: We do not sell or share e-mail addresses. *They are used strictly for conducting post-activity follow-up surveys to assess the impact of this educational activity on your practice.*

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❑ Yes ❑ No I and/or my family member have a financial relationship with **New York Eye and Ear Infirmary of Mount Sinai** and/or refer Medicare/Medicaid patients to it.

❑ I certify that I have participated in the entire activity and claim 1.5 *AMA PRA Category 1 Credits*™.

Signature Required _____ **Date Completed** _____

OUTCOMES MEASUREMENT

❑ Yes ❑ No **Did you perceive any commercial bias in any part of this activity? IMPORTANT! If you answered "Yes," we urge you to be specific about where the bias occurred so we can address the perceived bias with the contributor and/or in the subject matter in future activities.**

_____

Circle the number that best reflects your opinion on the degree to which the following learning objectives were met:
5 = Strongly Agree 4 = Agree 3 = Neutral 2 = Disagree 1 = Strongly Disagree

Upon completion of this activity, I am better able to:

• Discuss the potential paradigm shift in the timing of cataract surgery based on Physician Quality Reporting System outcomes, patient demand, complications, and satisfaction for surgeons and their patients considering cataract surgery	5	4	3	2	1
• Identify preoperative risk factors in patients undergoing cataract surgery and apply appropriate therapies (preoperative, intraoperative, and postoperative) to minimize complications	5	4	3	2	1
• Discuss the role of inflammation control in patients choosing procedures such as femtosecond cataract surgery and those involving advanced technology IOLs	5	4	3	2	1
• Evaluate the anti-inflammatory agents used in cataract surgery on efficacy, safety, and patient comfort	5	4	3	2	1
• Apply appropriate perioperative therapies for inflammation prevention in patients receiving advanced technology IOLs, combination procedures (such as cataract/corneal transplant), and complicated cataract procedures	5	4	3	2	1

1. Please list one or more things, if any, you learned from participating in this educational activity that you did not already know. _____

_____

2. As a result of the knowledge gained in this educational activity, how likely are you to implement changes in your practice?
4=definitely will implement changes 3=likely will implement changes 2=likely will not implement any changes 1=definitely will not make any changes

4 3 2 1

Please describe the change(s) you plan to make: _____

_____

3. Related to what you learned in this activity, what barriers to implementing these changes or achieving better patient outcomes do you face?

_____

_____

4. Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced for you through participation in this activity.
❑ Patient Care ❑ Practice-Based Learning and Improvement ❑ Professionalism
❑ Medical Knowledge ❑ Interpersonal and Communication Skills ❑ Systems-Based Practice

5. What other topics would you like to see covered in future CME programs? _____

_____

ADDITIONAL COMMENTS _____

_____

POST TEST ANSWER BOX

1	2	3	4	5	6	7	8	9	10