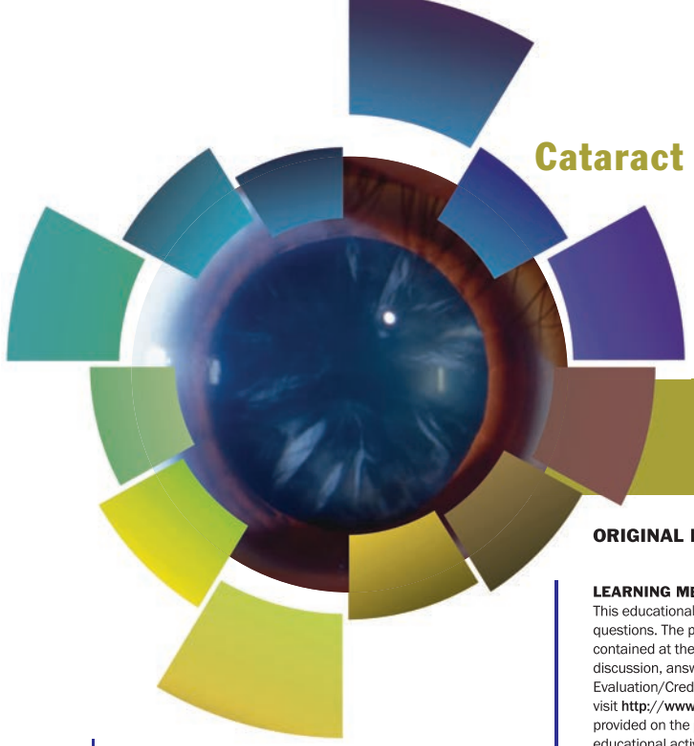

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*A Patient With Mixed Aqueous Deficiency/Evaporative Dry Eye Disease*

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## Program Chair

### John Sheppard, MD, MMSc

Professor of Ophthalmology
Eastern Virginia Medical School
President
Virginia Eye Consultants
Norfolk, Virginia

## Faculty

### Anthony J. Aldave, MD

Associate Professor of Ophthalmology
The Jules Stein Eye Institute
University of California, Los Angeles
Los Angeles, California

### Deepinder K. Dhaliwal, MD

Associate Professor of Ophthalmology
Director, Cornea, Cataract, and External Disease Service
Director, Refractive and Laser Surgery Center
Director, UPMC Eye Center Monroeville
Director and Founder, Center of Integrative Eye Care
University of Pittsburgh School of Medicine
Pittsburgh, Pennsylvania

### Bonnie An Henderson, MD

Clinical Professor of Ophthalmology
Tufts University School of Medicine
Ophthalmic Consultants of Boston
Boston, Massachusetts

### Jay S. Pepose, MD, PhD

Professor of Clinical Ophthalmology
Barnes-Jewish Hospital
Washington University School of Medicine
Medical Director
Pepose Vision Institute
St. Louis, Missouri

### William B. Trattler, MD

Volunteer Assistant Professor of Ophthalmology
Bascom Palmer Eye Institute
University of Miami
Director of Cornea
Center for Excellence in Eye Care
Miami, Florida

## CME Reviewer for New York Eye and Ear Infirmary of Mount Sinai

### Joseph F. Panarelli, MD

Assistant Professor of Ophthalmology
Associate Residency Program Director
New York Eye and Ear Infirmary of Mount Sinai
New York, New York


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**ACTIVITY DESCRIPTION**
Cataract surgery is the most commonly performed surgery among adults in the United States, and the number of patients undergoing this procedure is continuing to increase. For patients who are identified as candidates for cataract surgery, optimization of the ocular surface is critical for obtaining optimal patient outcomes. There are a host of new tools that can help cataract surgeons with their preoperative evaluations. Among these are several tests that are useful adjuncts for diagnosing dry eye/meibomian gland dysfunction. The purpose of this activity is to update ophthalmologists on recent advances in the care of patients with cataracts.

**TARGET AUDIENCE**
This activity is intended for ophthalmologists.

**LEARNING OBJECTIVES**
Upon completion of this activity, participants will be better able to:
- Manage preoperative ocular surface conditions with potential to affect surgical outcomes in patients with cataracts
- Describe the benefits of new diagnostic technologies for dry eye disease that might improve cataract surgery outcomes

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# A Patient With Mixed Aqueous Deficiency/ Evaporative Dry Eye Disease

*John Sheppard, MD, MMSc; Anthony J. Aldave, MD; Deepinder K. Dhaliwal, MD; Bonnie An Henderson, MD; Jay S. Pepose, MD, PhD; William B. Trattler, MD*

## Case from the files of Jay S. Pepose, MD, PhD

***A 62-year-old white female presents with complaints of decreased vision, visual fluctuation, glare, and foreign body sensation. Her medical history includes rheumatoid arthritis, xerostomia, epistaxis, recurrent bronchitis, and a history of pancreatitis.***

***Slit-lamp examination reveals inspissated secretions in the meibomian glands and waxy meibum on expression (Figure 1). There is moderate fluorescein staining of the central cornea (Figure 2), lissamine green staining of the inferior and central ocular surface, and a 1+ nuclear sclerotic cataract.***

***Tear osmolarity is 334 mOsms/L OD and 318 mOsms/L OS. Keratometry (K) readings on topography are 44.75/46.25 D @ 45° OD and 44.50/46.00 D @ 135° OS. A blood sample is obtained to screen for Sjögren syndrome and is positive for antinuclear antibody (ANA), rheumatoid factor (RF), salivary protein 1 (SP-1), carbonic anhydrase 6 (CA6), and parotid secretory protein (PSP; it is negative for Sjögren-specific antibody A (SSA) and Sjögren-specific antibody B (SSB).***

***The patient is started on treatment for meibomian gland dysfunction (MGD)/ aqueous deficiency dry eye disease, including oral doxycycline, oral omega-3 supplementation, lid hygiene, topical cyclosporine, nonpreserved artificial tears, and loteprednol etabonate gel. Topography is repeated 5 weeks later and K readings are now 44.50/45.25 D @ 32° OD and 44.75/45.50 @ 120° OS.***

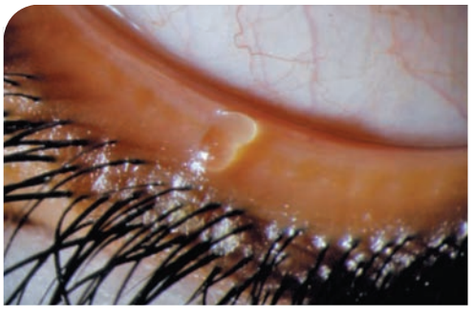

**Figure 1.** Expression of the meibomian glands produces a bolus of waxy meibum.

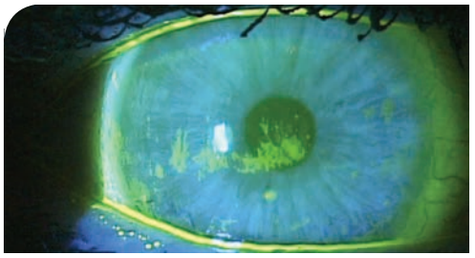

**Figure 2.** Moderate, consolidated central corneal staining with fluorescein is noted in this patient.

*Images Courtesy of Jay S. Pepose, MD, PhD*

## OVERVIEW

Dry eye disease is extremely common in the cataract surgery population and is important to detect and manage preoperatively because it has the potential to affect the accuracy of the keratometry readings used for intraocular lens power calculations and the visual outcome after surgery. In the Prospective Health Assessment of Cataract Patients' Ocular Surface (PHACO) study, which evaluated 136 patients presenting for cataract surgery at 9 centers across the United States, tear break-up time (TBUT) of ≤5 seconds was present in approximately two-thirds of patients, approximately three-fourths of eyes were positive for fluorescein corneal staining, and half showed central corneal staining, while approximately 1 in 5 patients had an abnormal result of ≤5 mm on Schirmer testing with anesthesia.[1] Less than one-fourth of patients in the study, however, had ever been diagnosed with dry eye.

The patient in this case presented with symptoms that are associated with dry eye disease—decreased vision, visual fluctuation, foreign body sensation. Other common symptoms include stinging, burning, itching, dryness, and eye fatigue.[1] Not all patients with dry eye disease, however, spontaneously report such symptoms or even relate certain symptoms to dry eye, resulting in a poor correlation between the severity of signs and symptoms. For example, some patients with severe dry eye may be hypesthetic and so have few subjective complaints, whereas patients who are earlier in the disease process may have more subjective issues because of enhanced sensitivity of the ocular surface. Thus, patients with significant complaints may appear to have only mild disease on objective testing while those with more advanced disease may actually be asymptomatic. Clinicians clearly need to be proactive in conducting a proper diagnostic examination.

## DRY EYE DIAGNOSIS

Several new technologies have emerged as point-of-care tests to improve the accuracy of the diagnosis of dry eye disease.[2] Opinions vary, however, regarding their role in clinical practice.

Both aqueous deficiency and evaporative dry eye disease lead to a more concentrated tear film (hyperosmolarity) that places stress on the corneal epithelium and conjunctiva. On the basis of a study by Lemp and colleagues and according to the device manufacturer, tear film osmolarity testing performed using a 50-nL sample is considered diagnostic for dry eye disease if the result is >308 mOsms/L in either eye, or if there is an intereye difference of >8 mOsms/L.[3,4] Tear film hyperosmolarity is a defining feature of dry eye disease and considered a core mechanism leading to ocular surface inflammation (International Dry Eye WorkShop [DEWS] definition and classification), yet such testing remains underutilized as a diagnostic tool.

## Sjögren Syndrome

*Jay S. Pepose, MD, PhD*

**Sjögren syndrome is a multisystem autoimmune disorder that can lead to significant morbidity and even mortality. It ranks as one of the most common autoimmune diseases,[1] and yet the diagnosis is often overlooked. Left untreated, patients with Sjögren syndrome are at risk for developing a number of serious sequelae, including vision loss, joint destruction, pulmonary fibrosis, interstitial nephritis, vasculitis, and lymphoma, among other complications. Considering that dry eye is often one of the earliest signs of Sjögren syndrome,[2] ophthalmologists should maintain a high index of suspicion for the condition because they have the opportunity to establish a timely diagnosis.**

**Key symptoms include recalcitrant joint pain, swelling and stiffness, dyspnea, dry cough, moderate to severe keratitis sicca, xerostomia, swollen salivary glands, excessive gingivitis and dental caries, skin rashes and dry skin, vaginal dryness, and profound fatigue. The manifestations are best addressed by multidisciplinary ophthalmologic, rheumatologic, and dental specialty care.**

**A high index of suspicion of Sjögren syndrome should be maintained for any patient with significant ocular surface disease, particularly women aged older than 40 years with dry mouth and other findings. Testing ordered proactively to confirm the diagnosis will enable appropriate treatment and tailoring of further studies.**


1. Helmick CG, Felson DT, Lawrence RC, et al; National Arthritis Data Workgroup. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. *Arthritis Rheum*. 2008;58(1):15-25.
2. Akpek EK, Mathews P. Hahn S, et al. Ocular and systemic morbidity in a longitudinal cohort of Sjögren's syndrome. *Ophthalmology*. 2015; 122(1):56-61.


Nevertheless, because tear film osmolarity has been shown to correlate better with dry eye severity than do other commonly used measures, including the Schirmer test, vital dye staining, TBUT, and the Ocular Surface Disease Index,[5] and because the testing is very quick, easy to administer, patient friendly, cost-effective, and well-tolerated, tear film osmolarity is a useful tool for determining dry eye severity as well as for monitoring the effectiveness of therapy.

Immunoassay of matrix metalloproteinase-9 (MMP-9) in a tear sample is another in-office test for diagnosing dry eye. MMP-9 is a marker of inflammation that is elevated in the tears of patients with dry eye[6]; the assay is considered positive when the concentration of MMP-9 is ≥40 ng/mL.[7] However, a negative result does not necessarily rule out dry eye disease, and the test result may be falsely negative if the sampling technique was inadequate. Furthermore, a positive result is not necessarily specific for dry eye disease because MMP-9 may also be elevated in individuals with recurrent corneal erosions or post-LASIK complications such as epithelial ingrowth, corneal ulceration, conjunctivochalasis, inflammation, and other tissue damage.[8]

There is evidence that the level of tear MMP-9 activity correlates with severity of various signs and symptoms of dry eye.[9] but the in-office test is only weakly quantitative because it does not provide an exact measurement of MMP-9 concentration. Rather, the test is interpreted as positive if a red line appears on the applicator used to collect the tear sample; and, the intensity of the red color increases with increasing MMP-9 concentration. For that reason, MMP-9 measurement is not ideally suited for following response to therapy. In addition, sample acquisition can be uncomfortable for patients with dry eye disease or blepharospasm.

Another instrument developed as an adjunct for diagnosing dry eye disease quantitates the thickness of the tear lipid layer using interferometry. In addition, it reports blink rate and allows identification of incomplete blinks. In its latest iteration, the device generates images of the meibomian glands using high-resolution infrared meibography (qualitative assessment of meibomian gland architecture and atrophy). There is, however, a lack of evidence demonstrating that tear film evaporation varies depending on the thickness of the lipid layer, and there is no normative database to use for interpreting blink rate data. The ability of this system to identify an incomplete blink seems to have clinical utility, particularly as an instructional tool for patients in that it enables the clinician to demonstrate the problem when it exists and helps encourage adherence to recommendations to "think blink".

A diagnostic kit for Sjögren syndrome is now available for in-office use. Blood is drawn either by venipuncture or by finger prick and applied onto a collection card. But some clinicians have found it challenging to acquire a sufficient blood sample using a finger prick and, rather than drawing blood by venipuncture, are giving patients a requisition for testing to be done at an outside laboratory. The test may be useful for earlier diagnosis of Sjögren syndrome because it measures the traditional autoantibodies that are diagnostic for the syndrome (SSA, SSB, ANA, and RF) plus 3 novel autoantibodies (SP-1, CA6, and PSP) that occur earlier in the course of the disease.[10,11] Earlier diagnosis of Sjögren syndrome is important for allowing affected patients to receive timely referral for rheumatologic care and initiation of treatment that can limit disease progression and permanent tissue damage *[see Sidebar: Sjögren Syndrome]*.

## TREATMENT OF DRY EYE DISEASE

For patients who are identified as candidates for cataract surgery because of visually significant lens opacification, optimization of the ocular surface is critical for obtaining reliable preoperative keratometry reading, for optimizing postoperative healing, and for maximizing postoperative vision. Dry eye disease should, therefore, be diagnosed and treated prior to surgery in order to allow determination of how much the reduced vision is due to the ocular surface irregularity vs the cataract itself.

Meibomian gland dysfunction is the most common cause of dry eye disease,[12] but the majority of patients probably have a combination of MGD and aqueous deficiency disease. Therefore, treatment should address both etiologies.

Artificial tears are a cornerstone in the management of all dry eye disease, and lid hygiene to relieve meibomian gland obstruction using heat and mechanical massage is a mainstay for treating MGD.[13]

Patients need to be educated, however, in the proper technique for lid hygiene because efficacy depends on applying sufficient heat for a sufficient duration. A washcloth wrung out after being soaked in hot water will not retain heat for a long enough period of time to be effective and also risks microbial contamination. A useful low-tech and inexpensive strategy employs a clean sock filled with uncooked rice that is heated in the microwave for 30 seconds. Also, a variety of eye masks and goggles developed specifically for eyelid warming is commercially available. Either of these techniques—using homemade or purchased products—should be applied for a minimum of 10 to 15 minutes, once a day.

There also are devices for in-office lid treatments that deliver heat alone or thermal pulsation therapy. Preliminary evidence suggests that intense pulsed light therapy in conjunction with meibomian gland expression may be useful for treating dry eye disease associated with MGD.[14]

Oral doxycycline can be beneficial for management of MGD because it has anti-inflammatory properties and inhibits lipase activity and MMPs.[13] There are no guidelines on dosing, although subantimicrobial doses are likely sufficient and might be better tolerated than the higher doses used to treat infection. The *Eye on Cataract* faculty consider a daily dose of doxycycline in the range of 20 to 100 mg/d reasonable for treating patients with MGD, perhaps taking into account body weight when choosing a specific dose for an individual patient. Topical azithromycin also can be used off-label for treatment of MGD.[13]

Oral omega fatty acids also have anti-inflammatory activity and may improve the quality of meibum secretions.[13] There is evidence from randomized, double-blind/double-masked controlled trials showing improvements in the signs and symptoms of dry eye/MGD in patients treated with certain nutritional supplements containing omega-3 and/or omega-6 fatty acids.[15-18]

The numerous omega fatty acid supplements available commercially can create confusion for consumers. Patients should be advised to look for mercury-free products. A daily dose of up to 4000 mg may be recommended, depending on patient tolerance and disease severity.

According to the severity of disease and the specific diagnosis, topical anti-inflammatory treatment with a corticosteroid and cyclosporine A also may be indicated.[19-21]

## DECIDING IF A PATIENT IS READY FOR SURGERY

Once told they need cataract surgery, some patients are eager for the procedure to be scheduled as soon as possible. Always counsel cataract patients with dry eye disease about the importance of first optimizing the ocular surface, explaining that the duration of treatment needed in order to obtain reliable keratometry readings is variable because it depends on the etiology of the problem, its severity, the aggressiveness of the intervention, and patient compliance with treatment. Thus, ocular surface rehabilitation may require anywhere from 1 to 6 months, encompassing 1 to 4 extra office visits before final biometry can be obtained.

Tear film instability and punctate keratopathy are the 2 most common ocular surface findings that cause fluctuating and unpredictable topography and keratometry data. Tear film instability is most often related to dry eye whereas there are many possible causes for punctate keratopathy. Anecdotally, when aggressive treatment is initiated with a topical corticosteroid and cyclosporine, punctate keratopathy may improve faster than tear film instability, and tear film osmolarity may also decrease.

Regardless of the initial findings, documenting stability with 2 consecutive keratometry readings is helpful for determining that a patient is ready for surgery.

## SUMMARY

Dry eye disease is a common occurrence in the cataract surgery population and is underdiagnosed. Meibomian gland dysfunction is the most common cause of dry eye, but its etiology can be multifactorial, and it is especially critical to make the diagnosis of Sjögren syndrome when it exists. Cataract surgeons must be proactive in identifying dry eye in cataract surgery patients and in optimizing the ocular surface prior to undertaking cataract extraction. New tools to help with diagnosis and new therapeutic interventions for disease management are emerging. Further, it is encumbent on ophthalmologists to make certain that patients with dry eye understand that they have a chronic disease that will necessitate continued treatment, even after their cataract surgery.

## REFERENCES

1. Trattler WB, Reilly CD, Goldberg DF, et al. Cataract and dry eye: Prospective Health Assessment of Cataract Patients Ocular Surface Study. Paper presented at: American Society of Cataract and Refractive Surgery/American Society of Ophthalmic Administrators Symposium & Congress; March 25-29, 2011; San Diego, CA.
2. Zeev MS, Miller DD, Latkany R. Diagnosis of dry eye disease and emerging technologies. *Clin Ophthalmol*. 2014;8:581-590.
3. Lemp MA, Bron AJ, Baudouin C, et al. Tear osmolarity in the diagnosis and management of dry eye disease. *Am J Ophthalmol*. 2011;151(5):792-798.
4. TearLab Corporation. TearLab™ Osmolarity System · Clinical Utility Guide. San Diego, CA.
5. Sullivan BD, Whitmer D, Nichols KK, et al. An objective approach to dry eye disease severity. *Invest Ophthalmol Vis Sci*. 2010;51(12):6125-6130.
6. Sambursky R, Davitt WF 3rd, Latkany R, et al. Sensitivity and specificity of a point-of-care matrix metalloproteinase 9 immunoassay for diagnosing inflammation related to dry eye. *JAMA Ophthalmol*. 2013;131(1):24-28.
7. Rapid Pathogen Screening, Inc. InflammaDry® Quick Reference Guide. Sarasota, FL. 2014.
8. Kaufman HE. The practical detection of mmp-9 diagnoses ocular surface disease and may help prevent its complications. *Cornea*. 2013;32(2):211-216.
9. Chotikavanich S, de Paiva CS, Li de Q, et al. Production and activity of matrix metalloproteinase-9 on the ocular surface increase in dysfunctional tear syndrome. *Invest Ophthalmol Vis Sci*. 2009;50(7):3203-3209.
10. Shen L, Suresh L, Lindemann M, et al. Novel autoantibodies in Sjögren's syndrome. *Clin Immunol*. 2012;145(3):251-255.
11. Beckman KA. Detection of early markers for Sjögren syndrome in dry eye patients. *Cornea*. 2014;33(12):1262-1264.
12. Nichols KK, Foulks GN, Bron AJ, et al. The International Workshop on Meibomian Gland Dysfunction: Executive Summary. *Invest Ophthalmol Vis Sci*. 2011;52(4):1922-1929.
13. Geerling G, Tauber J, Baudouin C, et al. The International Workshop on Meibomian Gland Dysfunction: Report of the subcommittee on management and treatment of meibomian gland dysfunction. *Invest Ophthalmol Vis Sci*. 2011;52(4):2050-2064.
14. Toyos R, McGill W, Briscoe D. Intense pulsed light treatment for dry eye disease due to meibomian gland dysfunction; a 3-year retrospective study. *Photomed Laser Surg*. 2015;33(1):41-46.
15. Sheppard JD Jr, Singh R, McClellan AJ, et al. Long-term supplementation with n-6 and n-3 PUFAs improves moderate-to-severe keratoconjunctivitis sicca: A randomized double-blind clinical trial. *Cornea*. 2013;32(10):1297-1304.
16. Donnenfeld ED, Holland EJ, Bucci Jr FA, et al. Effect of oral re-esterified omega-3 nutritional supplementation on dry-eye disease: double-masked randomized placebo-controlled study. Presented at: American Society of Cataract and Refractive Surgery/American Society of Ophthalmic Administrators Symposium & Congress; April 17-21, 2015; San Diego, CA.
17. Wojtowicz JC, Butovich I, Uchiyama E, Aronowicz J, Agee S, McCulley JP. Pilot, prospective, randomized, double-masked, placebo-controlled clinical trial of an omega-3 supplement for dry eye. *Cornea*. 2011;30(3):308-314.
18. Kangari H, Eftekhari MH, Sardari S, et al. Short-term consumption of oral omega-3 and dry eye syndrome. *Ophthalmology*. 2013;120(11):2191-2196.
19. Management and therapy of dry eye disease: report of the Management and Therapy Subcommittee of the International Dry Eye WorkShop (2007). *Ocul Surf*. 2007;5(2):163-178.
20. Sheppard JD, Scoper SV, Samudre S. Topical loteprednol pretreatment reduces cyclosporine stinging in chronic dry eye disease. *J Ocul Pharmacol Ther*. 2011;27(1):23-27.
21. Sheppard JD, Donnenfeld ED, Holland EJ, et al. Effect of loteprednol etabonate 0.5% on initiation of dry eye treatment with topical cyclosporine 0.05%. *Eye Contact Lens*. 2014;40(5):289-296.