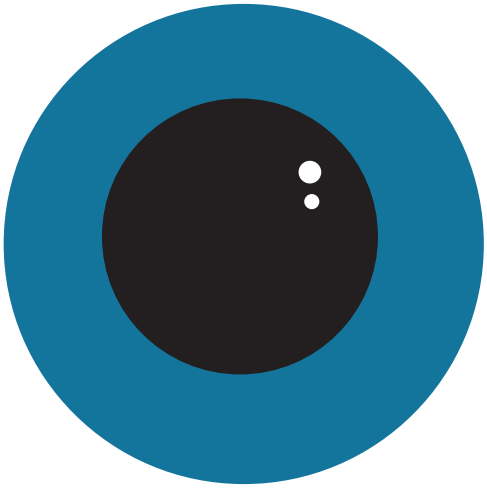
EURO TIMES
ESCRS
Supplement
May 2019

ESCRS/
EuCornea
Education Forum



Elevating Surgical Outcomes and Satisfaction with Advanced OSD Diagnostics and Therapeutics

Ocular Surface Diagnosis and Treatment Essential for Optimal Surgical Outcomes and Patient Satisfaction

Clinicians need to look beyond obvious signs and symptoms.

Mercè Morral, MD, PhD

Nine out of 10 of the patients I see in our highly specialised ophthalmology practice have ocular surface disease. Although that number may be high because I specialise in ocular surface disease, the Tear Film and Ocular Surface Society Dry Eye Workshop has reported that dry eye disease may be present in 5-to-50% of the population, being more frequent in the elderly population.[1]

According to the 2018 ESCRS Clinical Trends Survey, on average only 20% of cataract surgery patients have ocular surface disease symptoms when they are examined during a preoperative consult.[2] Furthermore, on average, respondents estimate that only 17% of their cataract patients present as asymptomatic of any ocular surface disease prior to surgery but develop symptoms after the procedure. Moreover, ocular surface disease may be missed on examination, particularly if there are no symptoms.

Ocular surface disease results from many causes, including environmental conditions, long work hours, the increasing use of computers and digital devices and other factors.

It is important that clinicians improve their strategies to diagnose and treat ocular surface disease, which impacts our patients' quality of life, vision quality and visual outcomes after cataract and refractive surgery.

Ocular Surface Disease Impact

Ocular surface disease adversely affects patients' vision. The tear film — the first refractive surface of the eye — must be stable each time a person blinks. If the tear film evaporates very quickly, it will become unstable, causing fluctuations in vision and ocular discomfort.

Patients with ocular surface disease may feel like their eyes are tired, uncomfortable, itchy or scratchy, or they may experience a foreign body sensation. In addition, ocular surface disease may cause pain.

All of these symptoms can impact patients' ability to read, work, drive and perform other tasks.[3] The optical effects of ocular surface disease are especially apparent at night while a person is driving, causing halos and glare. Furthermore, dry eye disease has been associated with depression.[4]

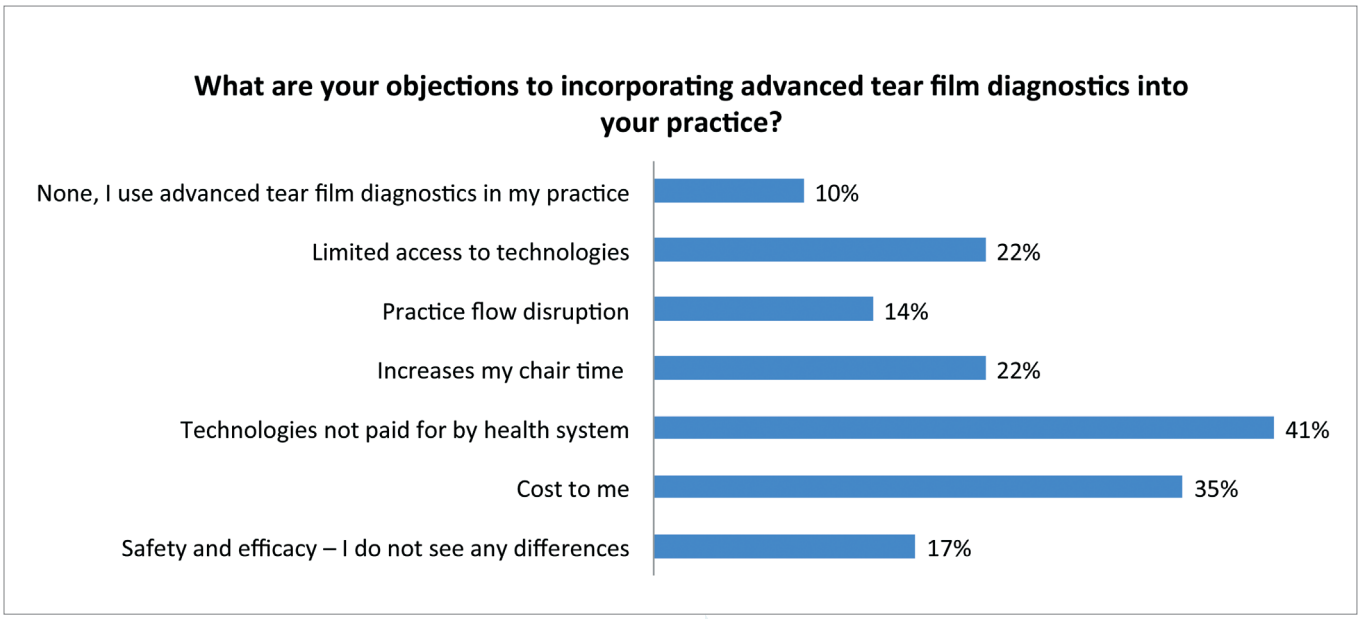


Figure 1. 2018 ESCRS Clinical Trends Survey Results: Key objections to including advanced tear film diagnostics in a practice.

Patients with ocular surface disease may feel like their eyes are tired, uncomfortable, itchy or scratchy, or they may experience a foreign body sensation

In addition, ocular surface disease affects preoperative measurements for refractive and cataract surgery patients and, ultimately, the outcome of surgery.[5] If our biometry and corneal topography measurements are not accurate because of ocular surface disease, they can affect intraocular lens calculations and refractive outcomes.

Furthermore, cataract and refractive surgery can worsen dry eye signs and symptoms, which also impact refractive outcomes and patient satisfaction. Therefore, it is important to identify dry eye beforehand so we can optimise the ocular surface before surgery and plan ahead for postoperative treatment.

Diagnosing Ocular Surface Disease

Ocular surface disease often is underdiagnosed on examination if patients do not have symptoms. Cochener et al. studied 342 eyes in 180 patients having cataract surgery.[6] Patients completed the Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire and researchers assessed tear break-up time, lipid layer thickness, partial blink rate, the structure of the meibomian glands and meibomian gland secretions. Among those in whom meibomian gland disease was identified, half had nto symptoms, which highlights the importance of a thorough eye exam before the surgery.

In a study by Gupta et al., 54% of patients completing questionnaires reported symptoms of ocular surface disease.[7] Eighty-five percent of patients with no symptoms had one or more abnormal results on tear osmolarity or MMP-9, and nearly half had abnormal results for both tests.

These studies show that ocular surface disease is much more prevalent than we believed, especially in the elderly population, who are having cataract surgery.

Diagnosis of ocular surface disease depends on a comprehensive examination. When examining patients at the slit lamp, many clinicians do not perform tear osmolarity or complementary tests. We may perform fluorescein staining but not take note unless there is a significant amount of staining.

However, many patients do not have very apparent signs of ocular surface disease. There may be subclinical inflammation that is not obvious at the slit lamp but might be detected using other tests such as tear osmolarity or MMP-9. Meibography also may be useful to image the meibomian glands. However, all of these tests are not routinely included in the preoperative cataract workup. At some point, these additional tests to detect signs of ocular surface disease may be part of the routine workup before cataract surgery, but we have not yet reached this stage (Figure 1).

The 2018 ESCRS Clinical Trends Survey Results demonstrated that less than half of respondents systematically check the ocular surface during a preoperative cataract surgery examination.[2] Thirty-seven percent use dry eye questionnaires on a case-by-case basis, 31% have no access to questionnaires, 18% use them at the initial point of care in most patients and 14% do not see value in questionnaires.

The survey showed that 46% perform fluorescein staining/tear break-up time at the initial point of care and 52% use it on a case-by case-basis; 72% perform Schirmer's and 65% perform meibomian gland expression on a case-by-case basis.

Although dry eye has become a popular topic during the past several years, there is much work to be done in terms of raising awareness of its importance and we need to educate our colleagues so they understand why it is so critical.

Managing Ocular Surface Disease

We await additional therapies to treat ocular surface disease. We have access to a wide range of tears substitutes, anti-inflammatories (topical steroids, cyclosporine, or lifitegrast) and other treatments for ocular surface regeneration (plasma derivatives), but we need additional options.

Treatment of meibomian gland disease has improved, with the emergence of thermal pulsation, intense pulsed light and other therapies. In my experience, thermal pulsation is very effective for meibomian gland disease.[8]

It is important for clinicians to recognise the prevalence of ocular surface disease and its impact on patients' quality of life and postoperative outcomes

Conclusion

It is important for clinicians to recognise the prevalence of ocular surface disease and its impact on patients' quality of life and postoperative outcomes. New therapies for inflammation and meibomian gland dysfunction are emerging. In addition, early phase II studies are investigating new mechanisms of action to decrease pain and symptoms associated with ocular surface disease; however, much work remains to be done in understanding the disease and determining the best ways to treat it.

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Using Diagnostic Tools to Better Understand the Ocular Surface

Multiple assessments are necessary for accurate diagnosis.

George D. Kymionis MD, PhD

Because ocular surface disease and dry eye disease are caused by multiple factors, it is challenging to develop a treatment algorithm. However, we have a multitude of traditional tests and advanced technologies to guide our diagnosis and help us monitor dry eye disease.

With the introduction of newer tests in the last decade, the world of dry eye disease has undergone an exciting evolution

Traditional Tests

Traditional tests include dry eye questionnaires, Schirmer's test to assess tear secretion, tear break-up time to evaluate tear film stability and dye staining to examine ocular surface damage.

A number of questionnaires are used to screen for dry eye, assess treatment efficacy and grade the disease. Although we ask patients about their symptoms, such as ocular discomfort, dryness and excessive tearing, the questionnaire enables a subjective evaluation with reliable results. However, we need to keep in mind that ocular sensitivity is reduced in advanced ocular surface disease. Questionnaires should be used in combination with objective findings to guide diagnosis.

Schirmer's test, which indirectly measures tear production, is one of the oldest tests in ophthalmology. Schirmer I measures reflex tearing and Schirmer II measures basal aqueous tear production. Both tests have variable repeatability, but accuracy appears to increase as the disease becomes more severe. As a result, neither is useful for early diagnosis.

Tear break-up time allows us to measure tear film stability and local evaporation from the tear film surface; however, it has a low specificity for dry eye. We cannot use it to distinguish between evaporative and aqueous-deficient dry eye. A measurement of 10 seconds or more is considered normal. If a patient has immediate dark spots with positive tear break-up time results in the same area, we should consider anterior basement membrane dystrophy as the cause.

We use three types of dye to evaluate dry eye: fluorescein, rose Bengal and lissamine green. Because they are dose dependent, we can easily have false-positive and false-negative results.

Fluorescein staining shows disruption in intracellular junctions in corneal and conjunctival tissue. Classical staining of the cornea includes superficial punctate keratitis of the central and inferior part of the cornea (Figure 2). This stain is not very specific because other conditions can cause superficial punctate keratitis, and only 10% of patients with dry eye have superficial punctate keratitis.

We use lissamine green and rose Bengal to evaluate the cornea and conjunctival surface, which stain areas not covered by mucin. However, rose Bengal is irritating to the cornea and may cause epithelial toxicity.

Most traditional tests are invasive, and measurements can be influenced by mechanical, chemical or other stimulation. They are mainly subjective, unquantifiable and poorly standardised, making it difficult to compare results. There is a poor correlation between subjective symptoms and objective signs, and there is no universal consensus on the guidelines for diagnosis or a gold standard.

As a result, we need quantifiable tests with increased sensitivity, repeatability and specificity to diagnose and monitor dry eye. We also need tests that reduce our chair time and are reimbursable.

Advancing Technology

With the introduction of newer tests in the past decade, the world of dry eye disease has undergone an exciting evolution. Only 15 years ago, we assumed that most patients with dry eye disease had decreased aqueous production. However, in more than 86%, the problem is meibomian gland dysfunction and evaporation.[1]

Tear osmolarity testing measures the concentration of solutes in the tear film (Figure 3). High levels indicate a reduced aqueous component. The test is much more sensitive to evaluate patients with dry eye compared with traditional tests.[2] It is quantifiable and indicates the presence or absence, as well as the severity, of dry eye disease. It is easy to obtain tear samples, and results are available immediately. Values greater than 308mOsm/L or inter-eye or inter-testing variability exceeding 8mOsm/L

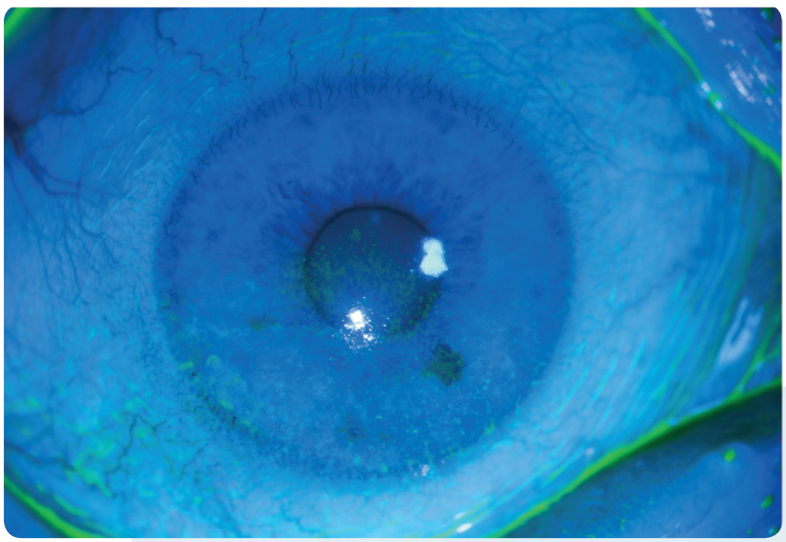

Figure 2. Slit lamp photo showing fluorescein staining in a patient with superficial punctate keratitis.

indicates that the patient has dry eye. It is specific and useful in monitoring response treatment, but it does not distinguish between aqueous-deficient and evaporative dry eye.

New tear interferometry devices use infrared light for meibography so the clinician can visualise the meibomian glands, capture blink dynamics and measure and grade the lipid layer thickness very precisely. A thin lipid layer, less than 60nm, is correlated strongly with symptoms of dry eye. Patients with a low lipid layer thickness are more likely to have meibomian gland disease.[3]

Abnormal images may show shortened glands and gland loss. Meibography can be used to grade meibomian gland disease.

Ocular surface thermography measures and records the temperature of the cornea and conjunctiva. When patients with dry eye keep their eyes open for 10 seconds, the temperature declines rapidly compared with controls, who have a stable corneal temperature.[4] The decrease in ocular surface temperature was significantly greater in dry eyes vs normal eyes.

Ocular sensitivity is reduced in patients with advanced ocular surface disease while patients receiving dry eye treatment may have worsening symptoms as sensation returns to normal levels

Another device measures tear protein patterns in the tear film. Patients with early dry eye do not have as many protective proteins and have increased levels of proinflammatory markers compared with patients who do not have dry eye. One marker is matrix metalloproteinase, proteolytic enzymes produced by epithelial cells in cases of ocular surface disease or inflammation. It has an 85% sensitivity and 94% specificity for dry eye.[5] If tear osmolarity is normal but MMP-9 is increased, the patient may have ocular surface disease that is not dry eye. It does not distinguish the type of dry eye.

Additional devices determine functional visual acuity, tear meniscus height, and tear film stability.

Conclusion

The diagnosis of dry eye remains challenging. Standard tests that we use in our offices have low positive predictive value, with a low specificity and sensitivity. Ocular sensitivity is reduced in patients with advanced ocular surface disease while patients receiving dry eye treatment may have worsening symptoms as sensation returns to normal levels.

Newer tests increase our ability to diagnose dry eye. However, the cost of this technology may hinder adoption.

Therefore, we need simple, inexpensive, highly sensitive and specific tests that will allow us to diagnose, grade, and monitor dry eye disease in our patients. Currently, we need to combine results from all of our tests for the most accurate diagnosis.

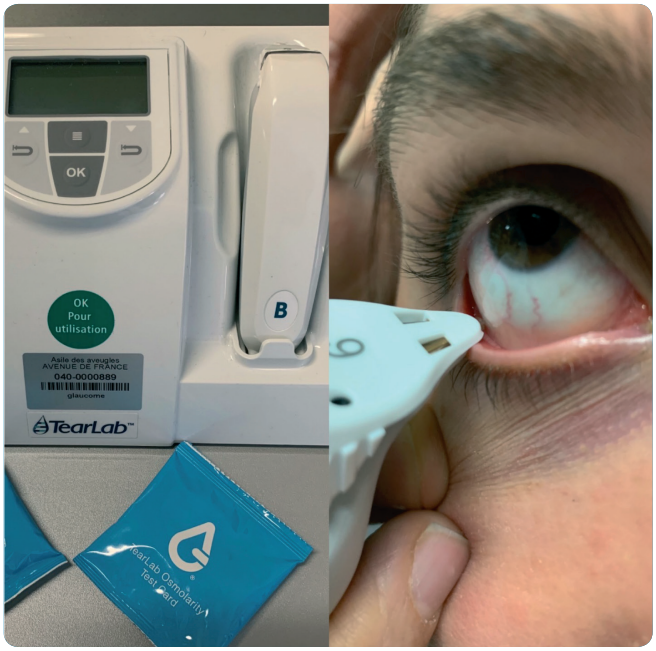

Figure 3. Tear osmolarity test measures the concentration of solutes in the tear film.

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Meibomian Gland Disease: Navigating Diagnostic and Treatment Options

Emerging diagnostics and therapeutics provide important management tools.

Marc Labetoulle, MD, PhD

Meibomian gland dysfunction (MGD) is a widespread condition, with a reported prevalence of 30-to-60% in patients older than 40, depending on the geographical location of the population, genetic background of subjects, study criteria and other factors.[1] MGD may be present in at least 50-to-80% of patients with dry eye.[2,3]

MGD is a major cause of evaporative dry eye, which can impact patients' vision, quality of life, refractive surgery outcomes and more. A comprehensive examination and an early and accurate diagnosis are essential to develop an effective treatment strategy to stop progression.

Defining Meibomian Gland Dysfunction

The 2011 International Workshop on Meibomian Gland Dysfunction defined MGD as "a chronic, diffuse abnormality of the meibomian glands, commonly characterised by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion. This may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation and ocular surface disease."[4] However, in clinical practice, we need to take this one step further to diagnose MGD.

Meibomian Gland Diagnostics

Determining meibomian gland function is a critical part of the examination. Tear break-up time, which demonstrates tear film stability, provides important information about a putative dry eye syndrome. If the patient's tear break-up score is low, combined with normal (or not severely altered) tear secretion as assessed by the tear meniscus height and/or the Schirmer I test, the patient probably has evaporative dry eye, even in the absence of keratitis on examination. The major reason for evaporative dry eye is a lipid deficiency related to MGD.

To assess for potential MGD, the clinician inspects the border of the eyelids at the slit lamp and the condition of the glands, looking for telangiectasias around the orifices or plugging of the orifices and determining the clarity and fluidity of the meibum, using manual expression (Figures 4 and 5).

Meibography is also useful to objectively assess the gland structure and quantify the level of gland dropout. Some meibography devices are also able to automatically assess the lipid layer thickness, which indicates the quality of the meibum and, thus, the function of the meibomian glands.

Several MGD scales have been proposed in the literature. More recently, Arita et al. proposed a classification system based on the aspect of the lid margins (vascularity, irregularity, and thickness) and glands (plugging of orifices and meibography aspects).[5]

Treating MGD

Findings from the clinical examination guide us in developing effective treatment strategies for MGD.

MGD is a major cause of evaporative dry eye, which can impact patients' vision, quality of life, refractive surgery outcomes and more

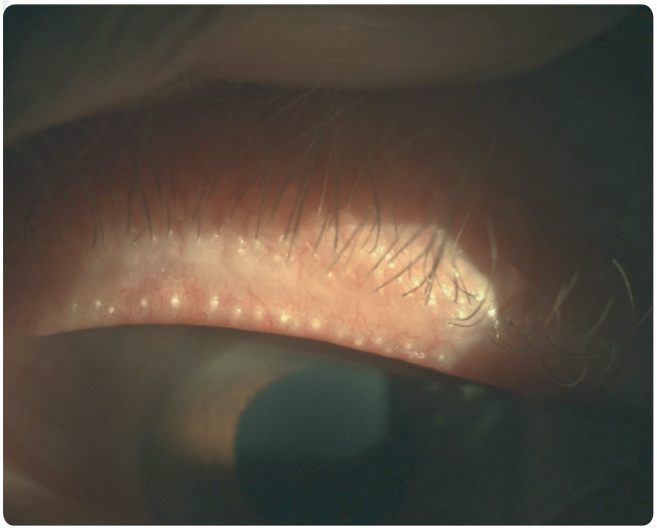

Figure 4. Plugging of the orifices of the meibomian glands in a patient who had been treated with anti-androgen drugs.

Manual lid hygiene and warm compresses and lid massage at home are the first line of treatment for all patients with MGD. They are inexpensive, and patients only need to invest time in the regimen. It is also legitimate to recommend topical lipid-based lubricants, which help compensate for lipid deficiency of the tear film.[6]

If patients show no improvement after using lid hygiene and lipid-based drops, several months later we generally add another treatment, which can target inflammation within the meibomian glands or meibum drainage.

Oral tetracyclines and oral/topical macrolides are frequently used to treat patients with inflammation because they can improve signs and symptoms. Additional research is needed on the use of immunomodulators (e.g. cyclosporine A or lifitegrast) in treating MGD.[7,8] The use of omega fatty acids (supplements and dietary intake) in treating MGD also has been debated because of contradictory results.[9] In addition, there is increasing interest in targeting hormone deficiencies in patients with MGD.[10]

Periorbital thermal pulsation, intense pulsed light and electric stimulation have been shown to improve meibomian gland function and reduce dry eye symptoms.[11-13]

Meibum drainage can be improved with mechanical strategies. In addition to mechanical and automated massage, intraductal meibomian gland probing

has been reported to be effective in patients with obstructive MGD; however, patients may find it painful. If the anatomy is good but there is significant keratinisation of the lid margins, microexfoliation can help remove debris and microbial biofilm and reduce keratinisation of the meibomian gland orifices, which may help increase secretions.

Conclusion

MGD is a common condition among patients with dry eye. With advances in research, we have expanding options to effectively diagnose and treat this condition.

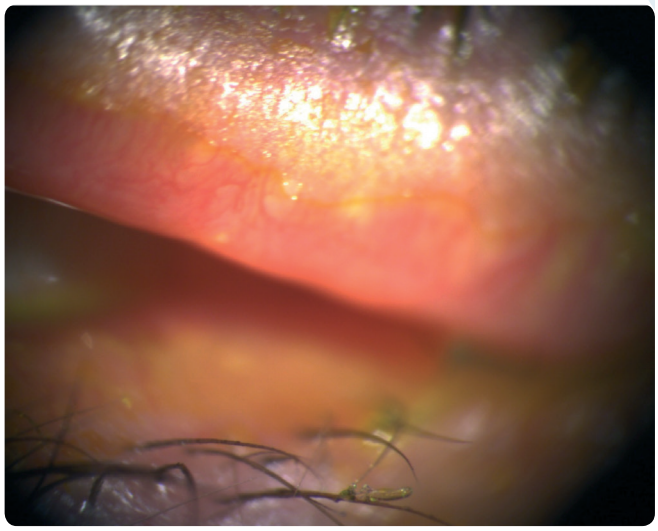

Figure 5. Patient has multiple telangiectasias and thickening of the eyelid border.

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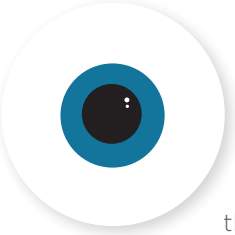
TREATING DRY EYE DISEASE



The Tear Film Society's Dry Eye Workshop II provides step-wise guidance for treating dry eye disease according to its severity.[1]

In patients with mild dry eye disease, we educate patients about their condition and recommend artificial tears and eyelid hygiene. This will be adequate in most cases.

For patients with moderate disease, we delay preoperative measurements and surgery until the ocular surface is optimised. We use the same treatments as for mild disease, but it is also necessary to treat meibomian gland disease (see main article), which is often present in these cases; it also may be legitimate to add non-preserved topical steroids (a short burst to optimise the ocular surface before surgery) in some cases.

If patients have severe dry eye, before considering surgery we should progress to immunomodulatory drugs such as cyclosporine or lifitegrast and use punctal plugs in recalcitrant cases. Patients requiring autologous serum or bandage or scleral contact lenses are probably not candidates for cataract surgery, at least at short- and mid-term.

Marc Labetoulle, MD, PhD

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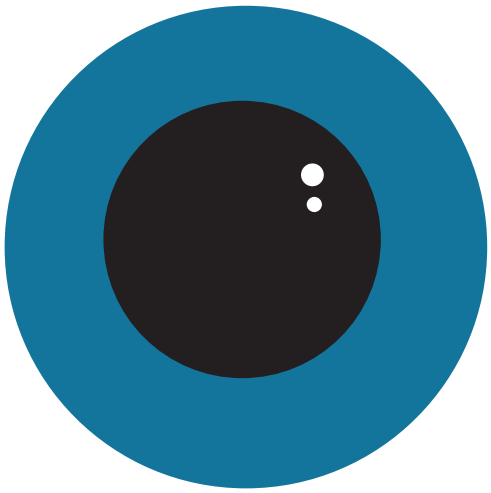

Supported by an unrestricted educational grant from

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