Today’s Methods for Managing Dry Eye Disease

A panel of renowned eye doctors share their day-to-day approaches to detecting, treating and managing patients with this common condition.

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What happens when six key opinion leaders in eye care participate in a roundtable on the latest strategies for managing patients with dry eye disease? They produce a good primer on the topic, with pearls on working up new dry eye patients, factors that impact symptoms and formulation parameters to consider when evaluating artificial tears. In the following pages, these clinicians impart their knowledge and experience in the hopes of enhancing your interactions with dry eye patients, as well as those with meibomian gland dysfunction.

Joseph T. Barr, OD, MS: Let’s start off by discussing the key objectives you consider when managing symptomatic dry eye patients; specifically, how you manage symptoms as well as how you manage the underlying mechanism of action or cause of those symptoms.

Paul M. Karpecki, OD: I’m glad you specified symptomatic patients. They are a little easier to deal with because they’re more likely to be compliant. And, of course, as clinicians, we tend to focus on alleviating our patients’ symptoms. That being said, we are aware that less than 60% of patients with clinical signs of dry eye disease are asymptomatic.

First and foremost with our symptomatic patients, we have to take care of how they feel. If that doesn’t improve, it’s a little more challenging to maintain compliance, but it’s essential. Second, we have to make an effort to slow the progression of this disease. And finally, we have to realize that sure, there’s an inflammatory response here and in-creased osmolarity, but meibomian gland dysfunction (MGD) is really a key contributor. Although, we still have to determine whether we have aqueous deficient or evaporative dry eye.

Randall Thomas, OD, MPH: One thing I will also look at is the volume of the lacrimal lake during the course of the slit lamp examination as well as the precorneal tear film break-up time. As Dr. Karpecki has already mentioned, MGD has been clearly established as the epicenter of the beginning of the demise of the precorneal tear film physiology. Therefore, whatever we can do to address MGD would be a foundational approach to intervening in the case of symptomatic dry eye.

Ron Melton, OD: Patients who have dry eye complain of burning and stinging because there’s instability of the tear film, which is mainly a result of poor lipid layer function. So when I’m looking to manage the patient who is complaining of these symptoms, I want something that is going to enhance and stabilize the lipid layer but also provide considerable long-term benefit to the patient. For example, a drop used two to four times a day instead of four to eight times a day is a win-win situation for both the patient and the doctor.

Dr. Barr: Dr. Hamrah, do you have any comments about inflammation, signs or symptoms in these patients?

Pedram Hamrah, MD: With new dry eye patients, it’s important to give them symptomatic relief and to realize that different comorbidities can contribute to their symptomatology. I try to address each of these components as quickly as I can; otherwise, you get partial symptomatic relief long term. Allergic disease, conjunctivochalasis and a neuropathic component can also develop and be...
inflamatory by slit lamp examination. A patient can have active meibomian gland changes may be evident on slit lamp time, mild injection, foreign body sensation, grittiness symptoms or contact lens intolerance, decreased wearing questions. Does the patient have any late-day symp-
toms you want to look for.

Also, dryness, photophobia and epiphora are other symptoms you want to look for. These symptoms are sometimes more severe at the beginning of the disease and then down regulation of the nerves can make patients less symptomatic. So we have to begin with the history and if there are any symptoms, such as burning and stinging or fluctuating vision, which are typically indicative of MGD or evaporative dry eye. Also, dryness, photophobia and epiphora are other symp
toms you want to look for.

Dr. Barr: Well, that’s a great segway into our next topic: how to work up and manage the dry eye patient. So, let’s talk a little bit about history taking and the use of questionnaires and your go-to diagnostic tests.

DEALING WITH THE NEW DRY EYE PATIENT

Dr. Karpecki: We first have to ascertain symptoms, but we can’t rely on symptoms alone to determine that we need to initiate a treatment. If we only treat symptomatic patients, we’re going to have a signifi
cant number who continue to progress. The symptoms are sometimes more severe at the beginning of the disease and then down regulation of the nerves can make patients less symptomatic. So we have to begin with the history and if there are any symptoms, such as burning and stinging or fluctuating vision, which are typically indicative of MGD or evaporative dry eye. Also, dryness, photophobia and epiphora are other sym-
toms you want to look for.

Contact lens intolerance is often related to early dry eye disease, so we have to ask specific or targeted questions. Does the patient have any late-day symp
toms or contact lens intolerance, decreased wearing time, mild injection, foreign body sensation, grittiness or dryness? But blurred vision—especially transient or fluctuating vision—is a critical aspect that we have to keep in mind because it affects so many patients who won’t typically mention it as they may feel it is a normal aspect of contact lens wear. It can cause fluctuations in biometry for cataract surgery patients and may result in over or undercorrection after refractive surgery.

I do a basic history and use the Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire (Tear-Science Inc.) quite a bit. I typically use a more extensive questionnaire that patients fill out while waiting in the lanes so they don’t feel like they’re waiting too long for me. Sometimes they get through it and sometimes they don’t; it does help to have all of their information relat-
ed to ocular surface disease (OSD) on one form.

Some amazing changes are taking place in terms of how we diagnose. Working up dry eye patients five years ago mainly consisted of lissamine and fluorescein staining, tear meniscus and tear break-up time, as well as a history. Now, we do quite a few things differently. I still use fluorescein dye, but not lissamine because I have other tests I can perform. I can’t be doing every test like a research center, so I have to focus on fewer, more accurate tests.

Osmolarity, blink analysis/eye apposition and mei-

bomography are measured ahead of time. I then put everything together to decide my next step in terms of management. I rely on multiple pieces of data to make the most accurate diagnosis of dry eye or help differentiate it from other conditions that have similar symptoms.

Dr. Thomas: I am very much a minimalist, and I rely more on symptoms than I do on signs. I listen very atten
tively to the patient, as I think it’s the centerpiece of the diagnostic workup. When my patients come to me saying their eyes burn and sting, and after a month of intervention, they are improved and happy, I am also happy. I don’t care about numbers or staining. To me, the essence of patient care is taking symptomatic patients and making them asymptomatic.

Dr. Melton: In diagnosing the patient with dry eye, you want to first take a careful history and pay attention to chief complaints. Even if your patients are in the office for a routine eye examination, always ask them if they experience any burning and/or stinging. A patient may not mention these symptoms on their own, but if you bring them up, many will realize that they do experience them. Part of the careful history is finding out what medication(s) the patient takes, as many (e.g., antihistamines, beta-blockers, overactive bladder control drugs) contribute to significant ocular dryness. Environmental factors should also be considered.

Next comes the physical examination. Donald Korb, OD, a world authority in dry eye and meibomian gland disease, emphasizes that we should try to judge the patient’s blink rate. There are quite a few lazy blinkers out there, and this contributes to significant drying of the eyes. Incomplete lid closure is also very contributo
ty to dry eye symptoms and can be detected by having a patient relax their eyes closed as if they’re falling asleep and observing for obvious lagophthalmus. Drs. Korb and Blackie have also shown us that even closed lids during sleep may not provide an adequate seal and
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Therefore leads to symptoms of ocular discomfort on awakening. A simple lid-light evaluation can be done to reveal this finding.

Even before you’ve gotten under a slit lamp to observe a patient, you can see a lot of different factors that can contribute to a patient’s dry eye. Once behind the slit lamp, you want to look at the quality and quantity of the tear film and really concentrate on the inferior lacrimal lake height to determine if it is low or deficient. I instill a small amount of fluorescein dye and observe the tear break-up time (TBUT). Any TBUT under 10 seconds indicates potential dry eye. I also look for staining patterns on the cornea or conjunctiva with the fluorescein. A significant amount of conjunctival or corneal staining tells me that I need to be more aggressive with my therapeutic approach in dealing with the patient.

Critically evaluating the oil gland function and assessing the quality of the meibomian glands is important and can be done using your thumb or preferably the meibomian gland expressor invented by Dr. Korb. Looking at the lashes for buildup is also key. Seborrheic or staphylococcal debris would indicate a significant blepharitis component to the dry eye, and all of these things help to determine the best therapeutic approach.

Dr. Barr: Dr. Hamrah, do you have something to add about the diagnostic workup?

Dr. Hamrah: Sure. I’m at a tertiary referral center and my dry eye patients have failed multiple therapies. So, I usually have to use a more extensive assessment to understand why these patients have not been responding to therapy.

As the others said, the most important thing initially is symptomatology. For documentation purposes, we use a SPEED questionnaire or the Ocular Surface Disease Index (OSDI) questionnaire because it is important to understand the pattern of the patient’s symptoms. Are their symptoms worse when they wake up in the morning, and then get better, which is typical of someone with nocturnal exposure, or vice versa, where they feel better in the morning, but as the day progresses and their eyes get tired, stinging and burning set in, which is typical of evaporative patients?

I ask about itching, allergic disease and specifically pain. I look for conjunctivochalasis and other aggravating factors. It’s also helpful to ask whether anything relieves the symptoms or makes them worse. I put a drop of lissamine green on one strip and a drop of fluorescein on another and use them at the same time. I look at the fluorescein in cobalt blue and then change it to white light to look at the conjunctival lissamine green staining. I still use lissamine green because I need to understand whether a patient has conjunctivochalasis that may be mild. In severe cases, you can see the overhanging conjunctiva, but in milder cases, you can see the areas of friction or the lid wipe epitheliopathy better with staining.

I use the modified flashlight test that Korb and Blackie recently published to look at the sealing of the lids, which helps with a diagnosis of nocturnal exposure diagnosis. I also instill a drop of proparacaine in the eye to determine whether there is a neuropathic component. Typically, a patient with neuropathy will not feel complete symptom relief, and some actually get worse afterwards. A patient who experiences complete relief most likely has dry eye or ocular surface disease.

We also perform Schirmer’s testing to assess tear wetting and routinely employ laser in vivo confocal microscopy at baseline, at least, for the lids and the cornea to assess the corneal nerves and determine whether there is a loss of nerves/neuropathy, as well as to look at the inflammatory response and its location.

Lastly, I assess whether the meibomian glands are obstructed (by applying pressure or using meibomography). If they are and it is partial, I might refer the patient for LiplFlow treatment (TearScience), or, in most cases, perform intraductal meibomian gland probing to unblock the obstruction. I then devise a regimen for the patient based on all of the above.

Dr. Hom: A lot of my dry eye patients also have ocular allergies, so not only do we ask them dry eye questions, but we also ask them about ocular allergies—more specifically, we ask about itch, watering, swelling and redness. I’m finding that a large number of patients have both conditions going on at the same time. I do the other tests I mentioned earlier, and also I like to look at the palpebral conjunctiva for diagnostic signs of allergy.

As far as tear break-up time goes, the new standard involves a shortened time. The clinical studies in which I’m currently involved use seven seconds, so I think we’re going to see more dry eye according to tear break-up time.

Meibography is pretty useful, but I can’t make a quick evaluation based on the grading systems that they give. I am looking forward to an automated grading system, like that seen with the Keratograph (Oculus), which I have been using.

Dr. Karpecki: I too believe blink analysis is critical. I use the Mastrota Meibomian Paddle (Cynacon/Ocufast) for my expression because it gives me a little more flexibility to adjust my pressure to see how much is being expressed.

Finally, it’s also important to look at the skin around the patient’s face for rosacea and their hands for rheumatoid arthritis. And look for demodex, staphylococcal and seborrheic blepharitis on the eyelash area.

Dr. Hom: I’ve started asking patients about dry mouth, I now have them rank their general fatigue on a scale of zero to 10 and I’m asking about joint pain. With the new tests that are available, I’m seeing a lot more Sjögren’s syndrome than I ever suspected.

Dr. Barr: Let’s talk about formulation parameters for ocular lubricants and tear supplements. Which are most compelling to you: pH, viscosity, lipid content, ingredients, preservatives, buffer, osmolarity, effect on clinical parameters, breakup time, vital staining, lipid layer thickness, drop comfort, symptom relief?
CONSIDERATIONS WHEN CHOOSING AN ARTIFICIAL TEAR

Dr. Thomas: It has now been well established that the preponderance of symptomatic tear film dysfunction is a result of an insufficient quality and quantity of the lipid being released from the meibomian glands. So, if patients are not getting enough lipid contribution from their meibomian glands, then supplementation with a lipid-based artificial tear is of paramount importance. I would even go so far as to submit that a majority of patients who have some component of aqueous deficiency also have lipid deficiency. The artificial tear cannot be too viscous or it would not be acceptable to most patients most of the time, and the drop has to be comfortable. Any transient blurring needs to be as minimal as possible to enhance patient symptom and visual recovery. So for me the lipid component is the absolute basis of artificial tear supplementation.

“...if patients are not getting enough lipid contribution from their meibomian glands, then supplementation with a lipid-based artificial tear is of paramount importance.”
- Randall Thomas, OD, MPH

Dr. Melton: I agree that our artificial tear products fall into two categories: aqueous- and lipid-based, despite the chemical components and the different classifications and categories, etc. Over the last few years, the medical literature has shown us that most dry eye complaints are because of an inadequate lipid layer. Clinically, I’m starting to incorporate lipid-based tears as first-line therapy in managing dry eye patients. I think it is much more therapeutic for the patient than just aqueous-based tears.

Preservative-free aqueous-based tears and preservative-free lipid-based tears come in to play with patients who have significant corneal breakdown or sensitivities to preservatives. Preservative-free solutions are also beneficial for patients on multiple medications that contain preservatives.

Dr. Barr: Thank you, Dr. Melton. Dr. Hamrah, what’s your thinking on formulation priorities?

Dr. Hamrah: For me, if a patient has an evaporative component, I like to use either lipid-based artificial tears— but not more than q.i.d. because of the preservatives. I don’t have much use for regular preserved artificial tears in this scenario. I will mix and match if the patient’s surface is significantly affected to initially provide more moisture, and I will use an ointment at bedtime. The condition of the patient’s ocular surface may influence my treatment choices, but I generally try to minimize the use of products that contain preservatives.

Dr. Hom: I agree with everybody else. I think that evaporative is the majority—or that there’s an evaporative component within the mixed category—and the first choice would be an emulsion tear. The MGD workshop recommends emulsion-based tears, or even artificial tears, at Stage Two, but in my protocol, I use them in Stage One, where there are minimal to no symptoms and minimal signs.

I have used Keeler’s Tearscope Plus to compare the lipid layer thickness of emulsion drops and in my preliminary assessment, I have found that Soothe® XP eye drops (Bausch + Lomb) have a high residence time, which is what I am looking for in an artificial tear.

Another attribute of these drops is osmolarity, and I was running an experiment in my practice to measure the osmolarity effects of emulsion artificial tears. However, I couldn’t find an effect or get a reading, and I think that’s because TearLab’s osmolarity test is based on electrical conductivity and these emulsion drops don’t have any ions. So, the use of osmolarity with electrical conductivity is not an indicator of whether an artificial tear is working.

Dr. Karpecki: Most emulsions will have osmolarity readings around 300 mOsm/L, which is considered normal, although many can be very low and help to offset high osmolarity cases. Regarding other formulation factors, I don’t look at pH too much because most artificial tears have taken that into account.

I look at osmolarity, lipid component and the frequency of instillation necessary. If a patient is using a drop more than three times a day, then I opt for preservative-free tears. And even when the frequency is t.i.d. or less, I don’t use artificial tears preserved with benzalkonium chloride; so I’m really down to either other preservative options such as Soothe XP and non-preserved options such as Soothe® Preservative Free Eye Drops (Bausch + Lomb), Retaine MGD ophthalmic emulsion (OcuSoft), etc.

Dr. Hom: If a patient has meibomian seborrhea, which is overproduction, the last thing you want to do is give them an emulsion drop. You have to look at whether the lipid layer is adequate.

Dr. Barr: Good. Let’s move on to insights on lipid-containing artificial tears. Is haze or blur a problem? What about duration of effect and frequency of use?

A CLOSER LOOK AT LIPID-CONTAINING ARTIFICIAL TEARS

Dr. Thomas: Every one of my patients underutilizes their artificial tears. I almost always start patients on a lipid-based tear, and when I see them back in two to four weeks to assess how they’re doing, I might at that point try a different approach, based on their symptomatic response. But I think the key is for the patient to use them as often as they would like to keep themselves comfortable.

Dr. Melton: I think the critical times for patients to use lipid-based artificial tears are right before they go to bed and when they wake up in the morning, because this is typically when eyes will be the driest. Patients often complain of blurry and fluctuating vision for the first 30 minutes or so after they get up, which is a result of their inadequate tear film. I have found that those who comply with this drop schedule notice quite a
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difference in their symptoms over the first month. And for patients who stare at a computer six to eight hours a day, using the drops mid-morning and mid-afternoon in addition to at bedtime and upon awakening is beneficial in helping them maintain a quality lipid layer. Normally, I recommend patients use the lipid-based artificial tears two to four times daily.

Dr. Hamrah: I haven’t had any complaints from my patients about blurriness or haziness lasting more than a few seconds with the lipid-based artificial tears. As I mentioned earlier, I typically don’t have them use it more than q.i.d. If I have to use more lubricants, which I usually don’t, then I will mix in a preservative-free product or a gel drop, which can help extend the duration a bit.

Typically, I have patients use lipid-based artificial tears at times when they typically have a decreased blink rate, such as when working on a computer, reading, watching television or before driving, rather than just randomly during the day.

Dr. Hom: If I express a patient’s glands and they have MGD going on and I take a look at the tear film and it looks like there’s not enough lipid there, then I would go to a lipid-based tear. But because MGD is so prevalent, if you just reach for an emulsion tear to begin with, I think you’re going to hit the mark pretty well regardless.

“For the last several years, lipid-based artificial tears have become my go-to artificial tear and I have clinically seen a significant therapeutic benefit.”

- Ron Melton, OD

Dr. Thomas: As far as blurring, it does occur, although transiently, and it’s important to make patients aware of this. I explain to all of my patients that when they first instill Soothe® XP eye drops, they will experience blurring, but that it will last about 15 to 20 seconds. And then once the drop disperses itself into the tear film and dissolves, clarity quickly returns.

Dr. Melton: If you let patients know upfront that there may be potential transient blurring for a few seconds as the lipids distribute across the surface of the eye, then they expect it that and it’s not an issue.

Dr. Karpecki: I agree that it’s a good idea to warn patients about blurring, but it’s very transient and I’ve not seen it be a major impediment for my patients. Of course, most of my patients have advanced ocular surface disease and are already blurred.

Similar to the other doctors, I don’t tend to like to use these drops more than q.i.d. and Soothe XP seems to be effective at t.i.d. or less for most patients. I’d rather keep it at t.i.d. and in cases of significant corneal staining, add in a gel drop. Otherwise, I would switch to Soothe® Preservative Free eye drops if greater dosing is required. I make sure the patient is using commercially available warm compresses—not washcloths or homemade options—and practicing good lid hygiene so that all the other comorbidities are well under control.

Dr. Hom: Is transient blur that only lasts a few seconds really a bad thing? I believe that the reason for the blur is that the emulsion is more stable. So the fact that there is a little bit of blur with Soothe XP gives me a reassurance that it will be stable over time.

Dr. Barr: Interesting comment. Well, are we really thinking about recommending a lipid-containing drop for the vast majority of patients, as opposed to the 11% or so who are actually using them now? Also, which products are you most comfortable with and how do you approach the patient with your first product selection?

Dr. Thomas: Overall, I think it’s best to begin with a lipid-based tear. Drs. Korb and Blackie have described using a golf club spud (Hilco Wilson Ophthalmics) to debride the line of Marx and keratinized lid margin, and simply rubbing back and forth tends to open up some blocked oil glands and enhances the flow of the meibum into the tear lake. This simple little maneuver can be helpful in more intrinsically bolstering the tear lake.

We have to also understand that it is well established that there is a significant inflammatory component to most all cases of dry eye, so I typically will initiate a topical corticosteroid drop q.i.d. for a couple of weeks, then b.i.d. for a couple of weeks. I find this can vastly enhance the efficacy of the artificial tear regardless of its composition.

Dr. Melton: Artificial tears aren’t anti-inflammatory agents. Needless to say, treating the ocular surface to get the inflammation under control at the same time you’re using lipid-based artificial tears is important.

For the last several years, lipid-based artificial tears have become my go-to artificial tear and I have clinically seen a significant benefit. I see a lot of patients with Sjögren’s syndrome and have even used lipid-based artificial tears on them for years. In my clinical experience, the lipid-based tears work better than aqueous-based tears.

As most of us are aware, only 11% of artificial tear users are using lipid-based artificial tears, while 89% rely on aqueous-based artificial tears, and those numbers need to be flipped.

Dr. Barr: Great; thank you. Dr. Hamrah, do you want to comment on aqueous deficiency versus evaporative dry eye and lipid-containing artificial tears?
Dr. Hamrah: Most (60% to 80%) of the patients I see fall into the mixed category. They have some component of evaporative deficiency and some component of aqueous deficiency, which basically makes most of them candidates for lipid-based artificial tears. I typically start patients on lipid-based artificial tears t.i.d. to q.i.d., but many of them respond rather quickly with improved tear break-up time when omega-3 fatty acids (e.g., flaxseed oil) are part of the regimen. And if there’s significant ocular surface disease, I’ll use a preservative-free artificial tear as well.

Sjögren’s syndrome and inflammatory patients should be treated with anti-inflammatory medication. However, given that most patients have an evaporative component, even these patients are candidates for lipid-based artificial tears, at least initially before their underlying pathology is addressed.

**“Lipid-based tears give us the best chance of affecting patients in almost any category of dry eye, and I think Soothe XP will be one of the key selections.”**

- Paul Karpecki, OD

Dr. Barr: Before we wrap up, why don’t we review everyone’s clinical criteria for recommending Soothe® XP eye drops specifically, and what you’re recommending for your meibomian dysfunction patients. What percentage of your dry eye patients in the future do you think you’ll be recommending a lipid-containing drop and Soothe XP specifically?

**SPOTLIGHT ON SOOTHE XP**

Dr. Karpecki: A lipid-based artificial tear is not the best for every patient, but it helps a large percentage of patients. It applies not just to patients who have meibomian gland dysfunction, but even to Sjögren’s patients, because those meibomian glands eventually stop functioning. Sometimes, I must first lower the osmolarity to then consider a lipid-based tear supplement in follow-up.

Lipid-based tears give us the best chance of affecting patients in almost any category of dry eye, and I think Soothe XP will be one of the key selections. It has a patented formula and seems to have a great patient response, which is ultimately what I think drives patient compliance and builds confidence with these products and the doctor. If a patient doesn’t get a good initial response, he may question his doctor, the other treatments; and he may wonder if he’s going through another cycle of someone not being able to manage this frustrating condition he’s had for so long.

Dr. Hamrah: Previous discussions of Sjögren’s syndrome heavily refer to aqueous deficiency, but recent literature identifies an MGD component associated with the disease, and I believe that the first-line treatment, even Sjögren’s syndrome patients, should be lipid-based, or emulsion, tears. We did upper tear meniscus studies and found that when you have a smaller tear meniscus, your inflammatory symptoms go up, so it’s actually a concentration thing. When you use an emulsion tear, the effect will be to increase the concentration and also wash out the inflammatory factors. And when you add the steroid in, which is an off-label use, then you have the anti-inflammatory effect.

We’re pretty much in agreement that emulsion tears should be the first choice or the first-line treatment. But I look at that 11% number—obviously there’s a gap going on, which is probably linked to awareness and also knowledge, so I think now is the time for our treatment protocols to catch up with what we know and what research tells us.

“...many patients who used to be on Soothe XP still ask for it regularly. Any patient who has an evaporative component—which is most (60% to 80%) of the patients I see—is a candidate for Soothe XP or other lipid-based artificial tears.”

- Pedram Hamrah, MD

Dr. Hamrah: I was a big fan of Soothe XP when it first came out and I used it until it was taken off the market. When it was unavailable, there was a void for these patients, which other artificial tears filled that temporarily, but a lot of patients didn’t like the alternatives. In fact, many patients who used to be on Soothe XP still ask for it regularly. Any patient who has an evaporative component—which is most (60% to 80%) of the patients I see—is a candidate for Soothe XP or other lipid-based artificial tears and I do use them regularly in these patients.

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