Dry eye is running out of places to hide. With the new diagnostic tests and devices available today, doctors can detect a key inflammatory marker of ocular surface disease (OSD); quantify tear osmolarity, which is a proven OSD diagnostic metric; help themselves differentiate between dry eye and ocular allergy, and objectively assess tear film quality. In addition, following the development of topical cyclosporine (Restasis, Allergan) as a breakthrough therapy for aqueous-deficient dry eye, a new appreciation of meibomian gland dysfunction (MGD) as a primary cause of evaporative dry eye has emerged and led to additional MGD treatment options.

“There has been a very nice evolution with every treatment option and innovation that we’ve experienced, and along the way, there have been some truly revolutionary new developments,” says Darrell E. White, MD, Skyvision Centers, Westlake, Oh. “Each of these has enhanced the ability of anyone who looks at the front of the eye to be a dry eye expert. We also have a growing realization that dry eye is a serious problem for patients. It’s satisfying to take care of patients with dry eye and actually great for a practice, too, because it generates new patients of all types.”

Tools for Targeting Treatment
Given the many new diagnostic tools at his disposal, James E. Croley III, MD, Cataract & Refractive Institute of Florida, no longer uses the Schirmer’s test, but still relies on corneal staining as an indicator of the health of the corneal epithelial cells and to monitor the effectiveness of treatment. Also, as he explains, “I use the TearLab Osmolarity System (TearLab), the LipiView device (Tear Science), and the Oculus Keratograph 5M (Oculus), which taken together, tell me whether a patient’s OSD is predominantly the tear-deficient type or the evaporative type and how severe it is, so I can base my treatment on that. LipiView measures the thickness of the tear film lipid layer. The Keratograph 5M measures several aspects of the tear film, such as break-up time and meniscus height, and it images the meibomian glands in 3D. The latter lets me really see what the glands look like, which can be valuable information. For example, in severe cases of MGD, the patient may have virtually no glands left, which means thermal pulsation with the LipiFlow (Tear Science) device, in general a successful treatment for MGD, would not be the best treatment option.” While he doesn’t use in-office testing for allergy, such as the Doctor’s Allergy Formula diagnostic system, Dr. Croley says such tests would be helpful. “Many patients have ocular allergy and dry eye at the same time, and we don’t want one to mask the other,” he says. “I suspect we’ll have more of these types of tests in the future, perhaps assessing lactoferrin and/or IgE.”

Dr. White uses the TearLab osmolarity test as well as the InflammaDry (RPS) tear test as part of his dry eye workup. InflammaDry identifies MMP-9, an inflammatory marker that is consistently elevated in the tears of patients with dry eye disease, often before any clinical signs appear. He’s in the process of evaluating in his practice how symptoms correlate with measurable MMP-9 levels and how best to use InflammaDry to guide treatment choices. For quite some time, he’s been using osmolarity to determine which artificial tears he recommends for patients. “I don’t think of osmolarity levels as normal and abnormal as much as high and low, and I can learn from both,” he explains. “For patients with
high osmolarity, 308 mOsmol/L or above, I recommend a ‘hydrator’ tear such as Thera Tears (Advanced Vision Research) or Refresh Optive (Allergan). For 300 mOsmol/L or lower, especially in conjunction with short tear break-up time, I find tears that provide more ocular surface stabilization, such as Soothe XP (Bausch + Lomb), Blink (Abbott Medical Optics) or Systane Balance (Alcon) to be the best options. I recommend what I consider ‘all-purpose’ tears in situations where the patient is symptomatic, osmolarity is between 300 and 308 mOsmol/L and tear evaporation is not pronounced. Drops that fit into this category include Refresh (Allergan) and Systane Ultra (Alcon).

Treatments for Aqueous-deficient Dry Eye

Artificial tears are a mainstay in Dr. Crole’s treatment protocols as well, and when the main culprit is lack of tear production, in addition to Restasis, he suggests patients use an all-purpose-type tear, not necessarily one that targets the lipid layer. He may also use punctal plugs, either temporary collagen or permanent Herrick-style, and he says plugs designed to remain in place for 3 to 6 months are also available and may be useful for treating dry eye in patients who plan to schedule cataract surgery or LASIK.

Dr. White adds that punctal plugs have improved over the years, thanks in part to “more effective, less invasive, less uncomfortable insertion techniques.”

To combat the inflammation that underlies dry eye, Dr. Crole also recommends HydroEye nutritional supplements (ScienceBased Health). “Along with other omega fatty acids and nutrients, HydroEye’s main ingredient is the fatty acid GLA, derived from black currant seed oil, which has been shown to increase production of prostaglandin E1, a potent anti-inflammatory chemical,” he says. A recent landmark multicenter, randomized, prospective, controlled study by John Sheppard and colleagues compared the effects of HydroEye to placebo in postmenopausal women. Only the supplements improved dry eye symptoms. In addition, the supplement group experienced no progression of ocular surface inflammation based upon conjunctival impression cytology T cell and HLA marker expression, while inflammation worsened in the placebo group. Corneal topographic smoothness was also maintained with supplement use, but surface irregularity progressed in the patients taking placebo.

Treatments for Evaporative Dry Eye

Nutritional supplements benefit patients with evaporative dry eye as well. “A recent revolution in the treatment of evaporative dry eye is the knowledge that we can provide extremely effective, long-term treatment for MGD by using high-quality Omega-3 fatty acids from marine sources, specifically fish oil,” Dr. White says. “In my opinion, Physician Recommended Nutraceuticals has done the best job of explaining and incorporating what we know about how the relative deficit of Omega-3s in the body in relation to levels of Omega-6s contributes to MGD.” Its supplement designed for dry eye patients (Dry Eye Omega Benefits) contains a high concentration of the anti-inflammatory Omega-3 eicosapentaenoic acid (EPA), highly purified and in its natural triglyceride form, which maximizes absorption and minimizes side-effects. Lower quality fish oil supplements tend to cause GI tract side effects.

Dr. White also says ‘the rediscovery’ of loteprednol, specifically Lotemax (Bausch + Lomb), has been very helpful for patients with any type of moderate to severe dry eye. Furthermore, its safety profile allows doctors who really don’t focus on dry eye to be comfortable prescribing a steroid long-term.”

Dr. White highlights the off-label use of topical azithromycin as a ‘quiet revolution’ in the treatment of MGD. “We can directly go after the inflammation in the glands, which seems to be controlled through the cytokine pathway. It turns out that azithromycin, formulated as AzaSite in particular (Akorn), has very powerful anti-inflammatory action in that pathway.”

Reducing inflammation in the gland improves the quality of the secretions and thus the functionality of artificial tears. Foulks examined
Cynthia Matossian, MD, Matossian Eye Associates in Hopewell and Hamilton, NJ, and Doylestown, Pa, has not brought LipiFlow into her practice, opting instead to incorporate intense pulsed light (IPL) therapy for patients with MGD who have not achieved adequate results with other treatments. “I’ve been using IPL for more than 3 years with great success,” she says. It was Rolando Toyos, MD, who first lower lids with a Q-tip. The entire process takes approximately 15 minutes. Over the course of four sessions, 4 to 5 weeks apart, I can clearly see the improvement, indicated by color and consistency, of the meibum.”

Concurrent with IPL treatment, Dr. Matossian has patients use a microwavable mask at home and take Omega-3 nutritional supplements, specifically Physi-
sees more patients with severe signs and symptoms of dry eye than the average practice and increasingly relies on ProKera Slim (Bio-Tissue) to heal damaged and uncomfortable corneas. ProKera Slim is a biologic corneal bandage composed of cryopreserved amniotic membrane set in a polycarbonate ring and elastomeric band system. “Cryopreserved amniotic membrane is such a valuable adjunct in corneal disease therapy, OSD included,” he says. “I use it for patients who have severe signs and symptoms of dry eye, patients who have signs that worry me or symptoms that worry them, and for those who are not responding to first-line therapies, indicating we have to move forward with something better.”

ProKera Slim is inserted into the patient’s eye in-office and held in place by the eyelids. “I insert the device in the exam room, usually utilizing a lid speculum, with the patient in a horizontal position to prevent the membrane from falling onto the floor,” Dr. Sheppard says. “It is a patient- and doctor-friendly treatment with very little downside and a superior benefit-to-risk ratio. It induces a very rapid epithelial response.”

Bio-Tissue recently released preliminary results from a survey collecting doctor and patient feedback on the effectiveness of ProKera Slim for dry eye. Among patients who had responded at the time these results were released, 75% had been suffering from dry eye for three years or more. After treatment with ProKera Slim, 93% of respondents felt better. In addition, based on doctor feedback, 95% said the treatment healed their eye, and 81% said it improved their vision. Among respondents who previously experienced pain with dry eye, 89% said ProKera Slim alleviated the pain. Also among the early results: 81% of respondents said they would request ProKera Slim if their symptoms returned. “Cryopreserved amniotic membrane treatment has expanded from the OR to the outpatient clinic, and from corneal melts, neurotrophic epitheliopathy and infectious keratitis to more commonplace OSD, a truly remarkable adaptation,” noted Dr. Sheppard.

A New Era in OSD

Taking a moment to summarize his assessment of the dry eye landscape, Dr. Croley says “We have so much to talk about with dry eye patients, so I’m personally spending more office time with them. But these patients, especially in advanced cases, are looking for relief from severe discomfort, and the bottom line is — we are making people better.”

References