

## **Dry eye treatments attack on hormonal, nutritional, systemic level**

**Nutritional supplements, drops, gels and even a cream enter the market to broaden the range of treatment options.**

*Jennifer Byrne*

Dry eye is considered the most common treatable eye condition, affecting as many as 33 million Americans to various degrees. The causes of dry eye are numerous, including hormones, nutrition, systemic disease and LASIK. As more is learned about this multifaceted condition, practitioners are able to approach its treatment on many different levels.

“The problem with dry eye is that practitioners tend to underdiagnose it,” said Charles G. Connor, PhD, OD, FAAO, director of research at the Southern College of Optometry. “It is more common than we think. And when we do diagnose it, we don’t always treat it aggressively enough.”

### **Transdermal testosterone cream**

The connection between hormones and dry eye is widely understood among clinicians, and as a result, hormone therapies are being developed. Dr. Connor has developed a testosterone cream for relief of dry eye, which currently has a patent pending. It can be obtained through a compounding pharmacist, but can be prescribed only by doctors with DEA numbers.

Dr. Connor cited a recent *Journal of the American Medical Association* study, which showed a higher incidence of dry eye among women on hormone replacement therapy.

“Of 25,000 postmenopausal women, those taking just estrogen had a 69% increased risk for developing dry eye, which is pretty dramatic,” he said. “It makes you wonder. The other thing we have noticed for years is that 90% of Sjögren’s syndrome patients are women.”

Dr. Connor went on to state that dry eye has a greater incidence in women overall. “If you look at a study done by Dr. David Sullivan, you will see that patients who have severe dry eye tend to have lower testosterone levels,” he said. “That correlates quite nicely with the postmenopausal female population.”

Dr. Connor added that a male rat, if castrated, will experience a decrease in tear output. A hysterectomy done on a female rabbit causes the lacrimal gland to degenerate, he said.

“If you take the same animal that will undergo a hysterectomy and give her testosterone, the breakdown in the lacrimal gland doesn’t occur,” he said. “So there are a lot of data to support this theory.”

Based on this research, Dr. Connor began to treat patients with testosterone. He has developed a transdermal cream, not unlike a nicotine patch, which is absorbed through the skin.

“A dry eye drop is cleared out of the eye in 90 seconds, and the effect is good for about 30 minutes,” he said. “With this cream, it is a pulsed delivery through the skin, and not all of the drug will get in at one time. It kind of trickles through. So we have almost continuous drug delivery, even though we are applying it between two and four times a day.”

Dr. Connor said, to date, he has had great success with the cream, and patients find it to be comfortable. “My patients have had success with this where nothing else worked,” he said. “In addition, testosterone can have the benefit of increasing bone and muscle mass, and some patients report that they just feel better.”

Dr. Connor strongly warns patients about the possible side effects of the medication. He said the cream would be contraindicated for those with prostate cancer, men with high PSA [prostate-specific antigen] counts, those with

cardiovascular disease, those with liver or kidney disease, pregnant women and children.

“It is really important that doctors know about these possible side effects,” he said. “I want to be sure that no one just goes ahead and prescribes it to someone who could be harmed by it.”

### **HydroEye: increased lactoferrin**

Manufactured by ScienceBased Health of Carson City, Nev., HydroEye is an oral nutritional supplement combining omega 6 fatty acids, mucin complex and nutrient cofactors. Frank Bucci Jr., MD, director of Bucci Laser Vision Institute and Ambulatory Surgery Center in Wilkes Barre, Pa., recently conducted a study involving HydroEye.

“I gave HydroEye to two groups of patients: LASIK patients and ‘normal’ patients,” he said. “Our outcome measure was the concentration of tear lactoferrin.”

Lactoferrin is a tear protein linked to ocular surface health, Dr. Bucci said. Severe dry eye patients are generally low in lactoferrin.

“We ran an assay in which we took a small sample of tears in order to get the lactoferrin concentration,” Dr. Bucci said.

Dr. Bucci started the “normal” non-LASIK subjects on two HydroEye capsules a day. Within 2 weeks, these patients’ tear lactoferrin had increased by 20% to 25%. At 4 weeks, the increase was up to 40%. By 8 weeks, the subjects’ tear lactoferrin had gone up by 60%.

“It was incredible, because these were not problem patients with initially low lactoferrin levels,” he said.

With the LASIK patients, Dr. Bucci started the subjects on HydroEye prior to the surgery date. At an average of 18.5 days after starting on HydroEye, the LASIK patients’ tear lactoferrin had increased by 40%.

“There have been numerous anecdotal reports,” Dr. Bucci said. “But this is the first objective, measurable finding that would indicate that it would help dry eye.”

### **Refresh Endura: treats all layers**

Allergan has recently added to its line-up a new over-the-counter dry eye product, Refresh Endura. This nonpreserved dry eye drop is designed to have three mechanisms of action, pertaining to each of the layers of tear film.

The oil in Refresh Endura enhances the lipid layer to minimize evaporation, the water enhances the aqueous layer, and the oil complex enhances the mucin layer.

These mechanisms of action combine so that Refresh Endura will ultimately benefit the tear film and, over time, reduce the symptoms of dry eye. In clinical studies, Refresh Endura has been well tolerated in patients, with no significant blurring or clouding of vision.

“This product truly bridges the gap between lubrication and sight preservation,” said Stephen Pascucci, MD, of the Northeastern Eye Institute in Scranton, Pa. “At the same time, it avoids the severe effects of ointments.”

### **TheraLife: relief for computer users**

One new dry eye product is specifically aimed at treating dry eye linked to computer vision syndrome. Founded in 2000, TheraLife Inc. (Los Altos, Calif.) has developed TheraLife Eye for the treatment of this condition.

The product is described as treatment for dry eye and eye strain conditions including irritation, redness, blurred vision, burning and excess tearing caused by overuse of computer display terminals, allergies, bicycling, skiing and contact lens use. The herbal extracts, vitamins, minerals and antioxidants in this formula increase circulation to ocular tissue, improve tear quality and maintain healthy function of the lens and retina.

The product has been shown to be effective in recent phase 2 clinical trials, according to Lily C. Yang, PhD, CEO and president of TheraLife.

“It provides vitamins and minerals specifically designed for the eye, encouraging the eye to secrete natural, salt-based tears,” said Dr. Yang. “We don’t just lubricate the eye by making tears thicker. We encourage eye tissues to become healthier.”

Initially, TheraLife capsules are taken twice a day, Dr. Yang said. “In the first week, patients take two capsules to encourage the uptake of the drug,” she said. “But once the week is over, we put them on maintenance — one to two

capsules per day.”

### **TheraTears Liquid Gel: preservative-free**

TheraTears (0.25% sodium carboxymethylcellulose, Advanced Vision Research) now comes in a new Liquid Gel formulation, which is intended for use at night or in dry eye patients who need a longer-lasting protective film during the day, according to Jeffrey Gilbard, MD, founder and CEO of Advanced Vision Research. “TheraTears Liquid Gel has just the right viscosity to maximize patient comfort while minimizing blurriness and crusting.

“We have already received a lot of positive feedback from doctors who for years have been asking us to put our patented electrolyte balance into a thicker, longer-lasting formula,” Dr. Gilbard continued. “These doctors clearly understand the critical role that electrolytes play on the ocular surface. The preservative-free aspect is especially important because patients will be using TheraTears Liquid Gel at bedtime. When you put a drop in your eye at night, it stays there all night long, and it has the potential to amplify any toxicity or irritation that a preserved eye drop can cause.”

Dr. Gilbard added that eye drops can also be irritating due to what he calls an “inappropriate electrolyte balance toxicity.”

“The ocular surface is dependent upon the specific electrolyte balance found in the normal tear film,” Dr. Gilbard said. “Unfortunately, other eye drops can wash that electrolyte balance away because their electrolyte make-up doesn’t match the normal tear film. TheraTears keeps that healthy balance of electrolytes intact for the entire night.”

### **TheraTears Nutrition for Dry Eyes**

TheraTears Nutrition for Dry Eyes is a nutritional supplement treatment for dry eye slated to be launched in January 2003, according to Dr. Gilbard.

After hearing talk of flaxseed oil, Dr. Gilbard began a thorough search for information on essential fatty acid metabolism and began testing his ideas in patients. “TheraTears Nutrition manipulates essential fatty acid metabolism to suppress meibomianitis, improve the oil layer of the tear film and stimulate tear secretion,” Dr. Gilbard told *Primary Care Optometry News*. “There are three mechanisms of action.

“First, omega-3s generate anti-inflammatory eicosanoids,” he said. “This is why we see resolution of the irritation that patients experience when they first wake up in the morning.”

The second mechanism of action is the fortification of the oil layer of the tear film. “It turns out that when the meibomian glands produce oils, they build these oils out of essential fatty acids,” he said. “And when they build these oils with omega 3 essential fatty acids, they make better, thinner oils. That’s one of the reasons these patients feel better throughout the day.”

Finally, the patent-pending essential fatty acid blend in TheraTears Nutrition creates an eicosanoid that stimulates tear secretion. “That’s what gives this product the extra effect I’m seeing in my patients,” said Dr. Gilbard.

“TheraTears Nutrition is the foundation of my dry eye treatment regimen. It provides a baseline of benefits and a platform for topically applied treatments,” he said. “I’ve seen that it takes about 4 weeks to take effect in patients.”

### **The role of nutrition**

Although the tear film is often thought of in terms of its lubricating function, it serves an important nutritional function as well, said Benjamin C. Lane, OD, FAAO, director of Nutritional Optometry Associates in Lake Hiawatha, N.J., and New York.

“When we think about what makes the tear film work well, we realize it requires very healthy epithelial cells in the various glands that supply the tear film,” Dr. Lane said. “These cells need to be replenished on a regular basis to be perfectly effective. And as most biochemists know, folic acid is essential for the body to synthesize new cells. Folic acid was one of the vitamins that we found to be most important in producing an ideal tear film.”

Dr. Lane cited a study he conducted with Dean Hart, OD, in 1987 regarding “jelly bump” lipid deposits on hydrogel contact lenses. (*Ophthalmology*, 1987; 94:1315-1321.)

“Previous research had shown that potassium is one of the nutrients essential to the tear film,” Dr. Lane said. “We found that one of the major problems was depressed tear potassium caused by excessive medications, such as anti-cholinergics, sympathomimetics and diuretics that don’t spare potassium, or lack of dietary fresh fruits or fruit-like vegetables, all rich in potassium.”

Other factors in the formation of the lipid deposits were excessive cholesterol intake, excessive alcohol intake and, most notably, excessive protein intake, Dr. Lane said. "We found that the most potent factor causing these deposits on the contact lenses was not too much fat in the diet or too much cholesterol, but too much protein," Dr. Lane said. "In particular, too much so-called well-cooked protein."

Dr. Lane explained that these medications, dietary excesses and/or especially alcohol potentiate the effect of lipid deposition on contact lenses by secreting triglycerides not normally found in the tear film into the tear film.

According to Dr. Lane, the tear film break-up test (TBUT), applied according to a consistent protocol, most usually can indicate or gauge folic acid nutrition.

For example, a low tear film break-up time (less than 10 seconds) indicates that there is too much table sugar in the diet, compared to folic acid, Dr. Lane said. "Too much sucrose intake in relation to folic acid intake or not enough food potassium can cause the tear film to be abnormal," Dr. Lane said.

Dr. Lane said although dietary supplements can be helpful, he added that they should be taken with caution and moderation.

"We also found and reported that common deficiencies of food vitamin C (ascorbic acid) or food vitamin B6 (pyridoxine) or uncommon-in-the-U.S. deficiency in vitamin A are all promoters of an abnormal tear film," he said.

### **Improper supplementation**

Dr. Lane discussed some of the risk factors related to taking supplements improperly.

"People who get too little arachidonic acid in relation to eicosapentaenoic acid increase the risk of bleeding," he said. "Those who get too much arachidonic acid and not enough eicosapentaenoic acid increase their risk of thrombosis. We don't want either extreme."

Dr. Lane said for short-term catch-up therapy, the suggested dosages printed with these supplemented oils generally are fine.

"But as the eye condition resolves, we need to moderate the dosage," he said. "We can be guided by the improving concentrations and balances in specific fatty-acid blood tests, such as the plasma phospholipid fatty-acid profile."

Dr. Lane said what may appear as irreconcilable conflict between omega-3 and omega-6 fatty acids in the treatment of dry eyes actually is caused by the competition between the fatty acids in our diet and in our bodies.

"Blood measurements of fatty acids are valuable and desirable in individual patients before and during diet and supplement intervention," he said.

### **For Your Information:**

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- Drs. Connor, Bucci, Pascucci and Lane have no direct financial interest in the products mentioned in this article, nor are they paid consultants for the companies mentioned.
  
- People's Custom Rx & Clinical Care Center, makers of Dr. Connor's testosterone cream, can be reached at 750 Brookhaven Circle E., Memphis, TN 38117; (901) 682-2273; fax: (901) 682-6337.
- HydroEye is available from ScienceBased Health, 3579 Highway 50 East, Carson City, NV 89701; (888) 433-4726; fax: (888) 433-6726; Web site: [www.sciencebasedhealth.com](http://www.sciencebasedhealth.com).
- Refresh Endura is available from Allergan, 2525 Dupont Drive, PO Box 19534, Irvine, CA

92623-9534; (714) 246-4500; fax: (714) 246-4214; Web site: [www.allergan.com](http://www.allergan.com).

- TheraLife Eye is available from TheraLife Inc., 101 N. First St., Suite 343, Los Altos, CA 94022; (877) 917-1989; (408) 328-8400; fax: (408) 720-9281; Web site: [www.theralife.com](http://www.theralife.com).
- TheraTears Liquid Gel and TheraTears Nutrition for Dry Eyes are available from Advanced Vision Research, 7 Alfred St., Suite 330, Woburn, MA 01801; (781) 932-8327; fax: (781) 935-5075; Web site: [www.theratears.com](http://www.theratears.com).