

## Rheum with a View

April, 4, 2009

### Thank you again for visiting the Sjögren's blog.

The **three basic legs** of therapy include:

- Topical therapy of dry mucosal surfaces
- Prevention and treatment of extraglandular manifestations
- Approaches to fibromyalgia in the patient with sicca symptoms.

Over the next several weeks, I hope to slowly move through different areas of treatment or diagnosis. My goal is to eventually provide a series of “handouts” with educational information that can be given (or emailed) to patients or referring physicians. Thus, we will aim to provide education for both the patient and physician, since the increasingly limited time for “patient interaction” makes such education difficult. Each physician can ultimately customize the recommendations, put it on their letterhead, and provide to the patient or referring physician.

This week I would like to share our basic approach at Scripps Memorial to **treatment of dry eyes** and solicit your opinion and discussion. As a rheumatologist, I do not attempt to replace the ophthalmologist—but they seem to have even less time than we do. I appreciate the help in preparing this starting point for discussion with Dr. Paul Michelson, our former head of Ophthalmology, who is now retired.

We all start by telling the patient to go to the local store and pick up a selection of different artificial tears. However, upon following my own suggestion and recently going down the relevant aisle at the grocery store, I was struck with bewildering choice of artificial tears that confront the patient (see PowerPoint figure 1).

In addition to finding the particular brand of tear suggested by the physician, the patient will discover that most brands comes in “mild,” “moderate”, and “severe” dry eye formulations. A literature search reveals relatively few crossover studies that compare different artificial tear preparations and most of these trials are all short-term trials<sup>1-4</sup>.

As a starting point for instruction, we simply tell the patient that it is a tradeoff between preserved tears (which are cheaper) and non-preserved tears (that can be used more frequently) as they lack preservative. Another tradeoff is the **“viscosity of the tear”** that makes it last longer but may lead to blurring of vision. The patient must be prepared to “mix” and “match” their environment with the frequency and type of tear.

Identification of environments such as windy, dry and low humidity environments including highly air conditioned office buildings and airplanes may lead to increase in use of artificial tears prior to conditions that challenge the tear film.

**Did *you know that your blink rate goes down almost 80% when using a computer screen and has been described as contributing to an epidemic of “dry eyes” among workers who sit all day in front of a computer screen?***<sup>5</sup>

Certainly, one or more of these situations increasingly constitute the job and work environment of our most of our patients.

Further, the patient must recognize the drying effect of certain medications that may have anti-cholinergic side effects. Many over the counter (OTC) drugs such as sleep aids (such as Tylenol PM® have a diphenhydramine) or cold remedies (such as Tylenol Cold, which contains phenylephrine), are both quite drying. Similarly, certain herbs or nutraceuticals (i.e. supplements) may contain anti-cholinergic agents. These OTC agents are not considered “medications” by the patient and therefore are not discussed with the physician. A wide variety of prescriptions medications such as amitryptline, blood pressure medications (such as clonidine) also have potent anti-cholinergic side effects and can exacerbate dry eyes. A search for substitution for less drying therapeutic alternatives may lead the rheumatologist to suggest changes in medications for blood pressure, depression, neuropathy, muscle relaxants or a multitude of other medications with less significant drying side effects.

Other aspects of topical treatment of dry eyes including the pro’s/con’s of punctual occlusion, recognition of blepharitis and other causes of a painful or red eye will be the topic of subsequent blogs. Each of these areas are covered in a physician/patient document in a much longer document (about 70 pages) that I have listed in downloadable form on my website (RobertFoxMD.com).

I recognize that I am a rheumatologist wandering in a veritable “desert” of dry eye territory that is the domain of ophthalmologists. But the patients do come to rheumatologists with these questions about artificial tears, the role of these medications and a frequent complaint that the ophthalmologist was out the door before they could ask their question.

As rheumatologists, we also have limited time to answer the questions of our intelligent patients who want to be informed of “what is the plan.” Given our limited time, I have taken the following approach:

- All of our patients (or their children) have email. And for those individuals that do not, the public libraries have computers and people to help them access a free email account.
- So, while I am in the exam room (which has its computer) and with the patient, I just email a copy of the instruction sheet to the patient.
- I ask them to read the paper, note their questions for their revisit and also ask them to have their spouse and their concerned relative (invariably a

physician who is very concerned and knowledgeable about all topics) also read the material prior to their next revisit.

- As I get your feedback on this blog, I expect that document to also reflect your changes and opinions.

Back to the topic for this week: the choice of artificial tears. I am guilty of telling the patient to just go to the store and grab a handful of different tears and use the one that feels the best. Surely, there must be a more rationale approach to this choice in selecting an eye drop or a serial method of comparing the drops.

Also, the cost of these drops is quite significant when we consider that they are used continuously. Years ago, when we started our local Sjogren's support group, I had hoped that the group might function as a "co-op." For those of you old enough to remember, co-ops were places where members made a decision on a product (whether oatmeal or vitamins or whatever) and bought en masse at a much better price from the manufacturer. The product was then shipped to the co-op "leader" for distribution. As everyone got too busy, the "co-ops" faded away—but perhaps in the age of the Internet, it is time to bring them back. One other point that is worth reminding our patients, the health savings account (HSA) now popular as a health cost tax management alternative, can be used to purchase these "out of pocket" items not covered by insurance.

Therapy of dry eye (or "lacrima keratoconjunctivitis sicca"-- KCS) in Sjogren's requires a multi-pronged approach aimed at:

- eliminating exacerbating factors,
- supporting tear producing glands,
- hydrating the ocular surface,
- restoring normal tear film osmolarity,
- stabilizing the tear film and
- inhibiting the production of inflammatory mediators and proteases.

The details of "pathogenesis" (the development of a disease) and basis of therapy are outlined in an excellent book by Pflugfelder and Stern "Dry Eye and Ocular Surface Disorders" published by Marcel Dekker (2004), New York (power point figures 2).

The bottom line is that successful treatment with artificial tears is a lot more than just "add water" (and stir). We frequently refer our patients to an informative website called <http://www.dryeyezone.com>.

This is just one of many websites that serves as a resource to purchase eye drops and other accoutrements for dry eyes. Of course, we want to hear about your discoveries of resources.

In future blogs, we will approach subjects such as the potential role of topical steroids (such as lotemax), androgenic hormones, mucolytic agents, topical growth factors, goggles and side shields, Restasis®, bandage contact lens,

humidifiers, “plasma or autologous serum tears” and punctal occlusion that have been published for dry eyes.

Artificial tears are aqueous solutions that contain polymers that determine their viscosity, shear properties, retention time and adhesion to the ocular surface. Frequent installation of artificial tears combined with reduced tear turnover (in some cases exacerbated by punctal occlusion) makes patients with aqueous tear deficiency particularly susceptible to ocular surface epithelial toxicity from **preservatives in artificial tears, particularly benzalkonium chloride.**

The advent of preservative-free lubricants allows these patients to use the products if tears are required more than four times a day.

### Types of Polymers used for Dry Eyes

Polymer	Properties
Cellulose esters (hypromellose, hydroxyethylcellulose, methylcellulose, carboxymethylcellulose)	Viscoelastic polysaccharies increase the viscosity of tears; large increase in viscosity when concentration is increased
Polyvinyl alcohol	Low viscosity, optimal wetting at 1.4%
Polvidone (polyvinyl pyrrolidone)	Wetting is improved when combined with polyvinyl alcohol
Carbomers (polyacrylic acid)	High molecular weight polymers of acrylic acid; high viscosity when eye is statin, the tear thickness dynamically changes during blinking to maximize the thickness and longer retention time than polyvinyl alcohol
Hyaluronic acid, autologous tears	Glycosaminoglycan biopolymers that exhibit long retention times. However, expense prohibits these as usual alternatives

\* Table taken from book by Pflugfelder and Stern (described above) pg. 312

As a starting point, I am providing several tables with different types of artificial tears. It is unclear whether we should stay in a single category (going from mild to moderate to severe) or whether to change to a different type of polymer or preservative. There does seem to be agreement that frequent use of benzalkonium chloride preserved tears (more than 4 times a day), esp. in the patient with punctal occlusion, can lead to preservative buildup and epithelial toxicity. It should also be recognized that even if we avoid this preservative in our dry eye patients, that they may also be receiving other drops (such as

treatment for glaucoma or infection) that may contain this preservative and thus we have to consider the entire cumulative effect of preservatives on the eye.

#### Preserved Artificial Tears for Mild to Moderate Dry Eyes

<b>Brand Name</b>	<b>Major Components</b>	<b>Preservative</b>
Gen Teal®	HPMC .3%*	Sodium Perborate
Gen Teal Mild®	HMPM .2%	Sodium Perborate
Tearisol®	HPMC .5%	Benzalkonium chloride EDTA
Lacritears®	HPMC, Dextran 70	Benzalkonium chloride EDTA
Tears Renewed®	HPMC, Dextran 70	Benzalkonium chloride EDTA
Clear Eyes®	HPMC, Glycerin	Sorbic Acid, EDTA
Visine for Contacts®	HPMC , Glycerin	Sorbic acid, EDTA
Visine Tears®	HPMC, Glycerin PEG 400	Benzalkonium chloride
Akwa Tears®	Polyvinyl alcohol 1% PEG	Benzalkonium chloride
Hypo Tears®	Polyvinyl alcohol 1%, PEG 400, Dextran	Benzalkonium chloride
Murine Tears®	Polyvinyl alcohol Providone 1.4%	Benzalkonium chloride
Moisture Eyes®	Glycerin .3%	Benzalkonium chloride
Refresh Tears®	CMC .5%	Purite
Murocel®	MC, 1%	Methyl-propylparaben
Aquasite®	Polycarbophil PEG-400 Dextran 70	EDTA, sorbic acid
Systane®	PEG, Propylene glycol	Polyquaternium-1
Tears Naturale Forte®	HPMC, Glycerin, Dextran 70	Polyquad
Computer Eye drops®	Glycerin 1%	Benzalkonium chloride, EDTA

\* CMD= methylcellulose

HPMC=hydroxypropylmethylcellulose

EDTA= ethlenediaminetetra acetic acid

### Non Preserved Tears for Mild to Moderate Dry Eyes

Brand Name	Major Component	No Preservative
Refresh Plus®	CMC, .5%	√
Theratears®	CMC, .25%	√
Bion Tears®	HPMC, Dextran 70	√
Tears Naturale Free®	HPMC, Dextran 70 Glycerin	√
Visine Preservative free	HPMC, Dextran 70 Glycerin	√
Hypo Tears PF®	Polyvinyl alcohol 1% PEG-400, Dextrose	EDTA
Lacrisert® (biodegradable insert)	Hydroxypropyl cellulose	√
Celluvisc®	CMC, 1%	√
Aquasite®	Polycarbophil PEG-400, Dextran 70	EDTA

### Ophthalmic Ointments and Gels

Trade Name	Composition
Akwa Tears Ointment®	White petrolatum, liquid lanolin and mineral oil
Hypotears ointment®	White petrolatum and light mineral oil
Lacri-Gel®	Petrolatum, mineral oil, lanolin
Refresh PM®	Mineral oil, white petrolatum and lanolin alcohol
Tears Naturale PM®	White petrolatum, mineral oil
Gen Teal Gel®	Polyacrylic acid, perborate preservative

### General Rules for the Dry Eye Patient

1. Identify dry eye environments: including airplanes, highly airconditioned building, windy and dusty locations, wood burning fireplaces at home
2. Sitting at a computer screen leads to a significantly decreased blink rate, so take periodic breaks to massage the eyelids and apply artificial tears
3. Start increased treatment to “build” the tear film 2-3 days before the “challenge” to the eyes, as it can take several days to build the tear film and about half an hour for it to get damaged
4. Three omega fatty acids as a supplement may help build the lipid layer, reduce the rate of evaporative loss, and stabilize the tear film
5. Avoid the use of preserved tears over four times per day
6. Consideration of eye glass side shields, punctal occlusion in selected patients
7. Cool mist humidifiers may play a role at night
8. Artificial tear use must be flexible, balancing the frequency of use and viscosity

to the conditions of the environment and concurrent medications
9. Recognize that blepharitis (infection of the lids) may mimic a dry eye flare
10. Patients with dry eyes may have other causes for a sudden increase in symptoms ranging from corneal abrasions to infections (both bacterial and viral)
11. Providing patients with written information and suggestions (including by email) will help education and compliance
12. Identification of medications (including over the counter cold and sleep remedies) and nutritional supplements/herbs with anti-cholinergic side effects may help minimize dryness.

In summary, there is a generally high level of dissatisfaction with the care for dry eyes. The difficulties in managing a chronic, variable and multi-factorial problem, often inadequate appreciation by clinicians of the true impact on the patient's lifestyles, and the time and resources required to educate and treat patients appropriate to their individual needs, represents a challenge for the treating physician. To put this problem in perspective, a fairly recent study found that patients equated their dry effects on their "quality of life" at the level of moderate angina<sup>6</sup> and the impact on their quality of work (especially those using computers) at the 40% impairment level<sup>7</sup>.

So we invite your comments, corrections and approach to this difficult problem.

#### References

1. Albietz JM, Lenton LM, McLennan SG, Earl ML. A comparison of the effect of refresh plus and bion tears on dry eye symptoms and ocular surface health in myopic LASIK patients. *The CLAO Journal*. 2002;28(2):96-100.
2. Aragona P, Papa V, Micali A, Santocono M, Milazzo G. Long term treatment with sodium hyaluronate-containing artificial tears reduces ocular surface damage in patients with dry eye. Vol 86: *British Journal of Ophthalmology*; 2002:181-184.
3. Donshik PC, Nelson JD, Abelson M, McCulley JP, Beasley C, Laibovitz RA. Effectiveness of BION tears, Cellufresh, Aquasite, and Refresh Plus for moderate to severe dry eye. *Advances in experimental medicine and biology*. 1998;438:753.
4. Noecker RJ. Comparison of Initial Treatment Response to Two Enhanced-Viscosity Artificial Tears. *Eye & Contact Lens: Science and Clinical Practice*. 2006;32(3):148.
5. Hagan S, Lory B. Prevalence of Dry Eye Among Computer Users. *Optometry and Vision Science*. 1998;75(10):712.
6. Schiffman RM, Walt JG, Jacobsen G, Doyle JJ, Lebovics G, Sumner W. Utility assessment among patients with dry eye disease. *Ophthalmology*. 2003;110(7):1412-1419.

7. Mertzanis P, Abetz L, Rajagopalan K, et al. The relative burden of dry eye in patients' lives: comparisons to a US normative sample. *Investigative ophthalmology & visual science*. 2005;46(1):46-50.