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Eight Reasons to Focus on OSD in Women

When health needs are unmet despite the prevalence of disease, it's time to work harder

Kendall E. Donaldson, MD, MS: OSD is a widespread problem that can negatively affect our patients' daily lives, so it's vital that we understand this disease and how it affects our patients, including all of the medical and environmental factors that impact them.

My fellow panelists — Drs. Epitropoulos, Matossian, and McDonald — are friends, colleagues, and experts in ocular surface disease (OSD), and we are very excited to delve into a discussion about women and OSD, a subject that is often overlooked despite having a tremendous impact on our daily practice of ophthalmology. To expand our profession's understanding of the relationship between women and OSD, we will discuss eight key factors that affect the medical treatment of OSD in women.

#1 Most OSD patients are women, and OSD is costing them.

Dr. Donaldson: Most of the patients in our dry eye clinics are women. In the U.S., women make up about 51% of all adults and 56% of all people older than age 65.[1] According to the Beaver Dam Eye Study, women ages 48 to 91 are nearly 50% more likely than men of the same age to experience dry eye syndrome.[2] Women also make up 55% of the Medicare patient population, and they live significantly longer than men.[3]

In my practice, these differences translate to about 53% of my patients being women. Do you find that the bulk of your patients are women as well?

Cynthia Matossian, MD, FACS: Not only are the bulk of these patients women, but OSD directly impacts their daily lives. It impacts their reading speed and their productivity at work. This is a real disease, not just a nuisance. I'm so happy that OSD is finally getting its time on stage, so to speak, because for years it was viewed only as a nuisance. Now, eyecare providers are paying attention and understanding that OSD poses a serious issue in the lives of their patients.

Marguerite McDonald, MD, FACS: We published a paper about the international economic burden of dry eye disease.[4] In the United States alone, the indirect costs are more than $55 billion. Direct costs to the American healthcare system are $3.84 billion, on par with costs in Asia and Europe.

The costs include absenteeism and low work productivity. People are at work, but they aren't functioning at full capacity because they're struggling with their vision and comfort. Many of these people are paying

hundreds of dollars per year to alleviate dry eye symptoms, and those with severe cases are spending thousands. That's a serious problem with serious economic consequences.

#2 Women's hormonal changes worsen OSD.

Dr. Donaldson: There have been some very interesting studies on hormonal changes with aging. I think we see a great deal of OSD related to these changes in women.

Dr. McDonald: One of the hormonal changes that influences OSD is testosterone. Men start off with far more testosterone than women, but women do have some from the adrenal gland. Both sexes lose testosterone as they age, but only women's testosterone levels often fall below the critical amount required for a healthy lacrimal gland. That reduces women's aqueous tears.

Dr. Matossian: Because of a decrease in testosterone due to age, I prescribe off-label, compounded testosterone eye drops for both my female and male patients. Since more female patients suffer from dry eye, more of my women patients receive this prescription. They use the testosterone 0.05% ophthalmic drops two to four times a day.

Dr. McDonald: And usually, by the time patients get testosterone eye drops, they've had plugs, so there is virtually no systemic absorption of the drops. As the nasolacrimal drainage system is occluded by the punctal plugs, there is no pathway for the testosterone drops to make contact with the nasopharyngeal mucosa.

Another hormonal influence is hormone replacement therapy (HRT). The Women's Health Study followed more than 25,000 women for a decade and concluded that HRT actually makes dry eye a little bit worse.[5] This isn't conclusive, and we need more research, but it looks like HRT is not the answer.

Dr. Donaldson: The use of HRT also has been debated because of the associated risks. When I discuss HRT with patients, I often refer them back to their gynecologists to have a discussion about cancer and other risks, so they can weigh those risks against the benefits of HRT. But compounded testosterone drops may be worth a try in refractory patients because they are topical and, thus, avoid the systemic side effects associated with HRT.

#3 Women are more susceptible to autoimmune diseases linked to OSD.

Dr. Donaldson: Certain autoimmune diseases increase the risk for OSD, and these diseases are more prevalent in women. How do these diseases affect our female patients?

Alice T. Epitropoulos, MD, FACS: Women are more susceptible to developing systemic autoimmune diseases that often are related to dry eye disease. These include Sjögren's syndrome, rheumatoid arthritis, and lupus, as well as dermatological conditions, such as psoriasis and rosacea. One in 10 dry eye patients has Sjögren's. What's more, Sjögren's is now thought to be much more prevalent than we thought, affecting more than 4 million Americans, 90% of whom are women.[6]

Until recently, Sjögren's was very difficult to diagnose because the traditional antibodies are non-specific. Auto-antibodies directed against Ro/SSA and La/SSB autoantigens are positive in only 40% to 50% of patients.[7,8] Now we have the Sjö test (Bausch + Lomb), which tests for the four traditional biomarkers and three novel biomarkers. It allows for improved sensitivity and specificity, which means earlier diagnosis and treatment.

Dr. Donaldson: Many times, when the SSA and SSB antibody tests were negative, patients were offered a biopsy, but no one wants a biopsy of the mucosa. The Sjö test can provide answers with a much less invasive blood test.

Dr. Epitropoulos: That's right. We can also outsource the test so it doesn't interfere with patient flow in the office.

Dr. McDonald: After we had been using the Sjö test for a year, we looked at our results. In one office, 66% of patients tested positive. I realized that I should be ordering the test more often, because, obviously, I was missing people, and the diagnosis really helped them.

Dr. Matossian: I've noticed that when we've ordered the Sjö test in our office, we are able to diagnose Sjögren's earlier in the disease process. Traditional biomarkers are positive as the disease progresses. Patients are testing positive for these novel biomarkers earlier, with some overlap right in the middle. Because Sjögren's is a progressive disease, this is exciting information.

Dr. Donaldson: I think patients appreciate the diagnosis. They tell us they feel validated. They know there is a concrete reason for their frustrating symptoms, which is satisfying. It is a relief to know why they're feeling the way they are.

Dr. Matossian: The feeling of validation is very strong. These women have gone from doctor to doctor, to surgeon to psychiatrist to GI specialist to gynecologist because they are desperate. They are suffering all over their bodies, and no one has been able to pinpoint a diagnosis. Now we have access to the Sjö test. We order a test in the laboratory, and our patients finally get definitive answers.

Dr. McDonald: Our technicians report negative results to the patients, but when the results are positive, I make the call. I tell them, "This is not cancer. It won't shorten your life. However, it does have a huge impact on quality of life, and it elevates your risk for non-Hodgkin's lymphoma, which is cancer." Five to 10% of Sjogren's patients will develop this cancer. It is quite curable if caught early, but less so if caught late, so the internist should screen you on a regular basis for non-Hodgkin's lymphoma. We mail a copy of the positive test results to patients and explain that they need to distribute the results to everyone on their healthcare team, including their internists — particularly for cancer-screening purposes — and their dentists, who need to watch for dry mouth, caries, and halitosis.

Dr. Epitropoulos: Another autoimmune disease affecting women is thyroid eye disease, or Graves' disease. Although it can affect both men and women, thyroid eye disease is six times more common in women.[9] It usually begins when people are in their 20s and 30s and worsens with age. Dry eye disease can be multifactorial in these patients. It may be autoimmune from Graves' disease or mechanical from exophthalmos, lid retraction, or incomplete blink, resulting in exposure keratopathy. Lacrimal gland dysfunction also can contribute to aqueous-deficient dry eye.

Rheumatoid arthritis is another systemic disease that affects women two to three times more than men.[10] And even though more than 70% of patients with rheumatoid arthritis suffer from dry eye disease, only 12% are being treated.[11,12]

Dry eye disease is clearly prevalent, underdiagnosed, and undertreated in patients with these conditions.

We need to actively evaluate and treat these patients with ocular surface disease. Communication and referral to specialists — including dermatologists, rheumatologists, and ophthalmologists — for these systemic conditions can help to facilitate earlier access to appropriate treatment.

Dr. Donaldson: Many of these diseases come in clusters. Patients might have not only rheumatoid arthritis or Graves', but possibly both, and other autoimmune or inflammatory conditions as well. It's very important that we have relationships with rheumatologists and general practitioners for these cases. We have to set referral patterns and not just work in a vacuum as ophthalmologists.

Dr. Matossian: Educating the patient's primary doctor is important as well. It's shocking how often internal medicine and family practice physicians don't understand the connection between rheumatoid arthritis, thyroid disease, and dry eye disease.

Dr. Donaldson: I'd add dermatologists to that mix for our patients with rosacea. I think patients feel more comfortable when they know we work in collaboration with their dermatologist or rheumatologist. Patients feel reassured and it creates a more effective and integrated care system.

#4 Women have more elective procedures on their eyes.

Dr. Donaldson: In addition to the physiologic changes and medical conditions that may lead to OSD in women, women also increase their risk for OSD by having more elective ophthalmic procedures than men. What are some examples in your practices?

Dr. McDonald: We have known for years that LASIK can exacerbate dry eye, and we've gotten smarter about diagnosing dry eye in advance and controlling it before surgery. Surgical advances have reduced dry eye as well. We make smaller, thinner, beautifully centered flaps. We know that the exact location of the hinge is important so we don't cut the trunk nerves at both 3 and 9 o'clock.

In the past, thicker, larger flaps with small hinges required cutting all the nerve trunks, so LASIK could cause dry eye that lasted — in rare cases — up to 2 years. Today, it's quite rare to find a case of LASIK-induced dry eye that lasts that long. With PRK, patients might have dry eye for a few weeks after surgery, at most.

The larger problem is patients who have dry eye before LASIK. They often seek out the procedure because they can no longer comfortably wear contact lenses, which is a red flag for the presence of dry eye.

Dr. Matossian: More women than men have cosmetic procedures, such as eyelid surgery. If too much skin is removed during blepharoplasty or if the eyelid skin heals in an unpredictable way, patients can develop a gap between the upper and lower lids — the lids don't come together tightly anymore — this may even occur years after successful surgery.

We see two issues related to this problem. First, when the upper and lower lids don't come together for a healthy blink, the meibomian glands don't release oil to create the lipid layer on the tear surface. That leads to meibomian gland dysfunction and OSD. Second, if too much skin is taken, the gap causes exposure keratopathy. The cornea is exposed, so more tears evaporate.

If a plastic surgeon doesn't understand the causes of dry eye disease and doesn't look into the patient's other risk factors, such as a previous LASIK procedure, then these problems are more likely to occur. An oculoplastic surgeon may be more attuned to coexisting conditions related to OSD, including previous LASIK, thyroid disease, and other factors. When possible, it is important to help patients select a cosmetic surgeon.

Dr. Donaldson: The interesting thing is that we're talking about the same group of patients. The same people who pursue LASIK also pursue lid procedures — sometimes multiple lid procedures. They are in tune with cosmesis. They try not to reveal that they've had these procedures. I've had both blepharoplasty patients and laser vision patients who don't want to admit their surgical history.

If patients had eyelid surgery 15 years ago, they think it doesn't count any longer. They think that successful plastic surgery 15 years ago doesn't affect their eyes today. But as the skin's elasticity

changes and the lower lids droop, OSD symptoms emerge. We tend to see an exposure pattern that makes patients become more symptomatic, even 15 years after surgery.

Do you find you need to explain these risks to blepharoplasty patients?

Dr. Epitropoulos: I recently treated a patient who was miserable with dry eye. We did everything from medications to in-office procedures, and finally got the dry eye under control. Then she told me she was planning to have blepharoplasty. I had to warn her that this procedure might exacerbate her dry eye disease. She had no idea that dry eye was a possible side effect. Most oculoplastic surgeons are aware of this crucial piece of information and are able to address this problem; however, it is often missing from a plastic surgeon's patient education.

#5 Cosmetics contribute to women's OSD — and the latest trends are troubling.

Dr. Donaldson: Cosmetics are a contributing factor to certain eye health problems, and, obviously, women use them much more than men. What makeup-related OSD problems do you see in your practice?

Dr. Matossian: Eye makeup is nothing new — both women and men have used it in various forms for centuries. Today, we are learning the costs of beautifying our eyes, and while mascara and other common products have their drawbacks, new trends are particularly concerning.

Right now, eyelash extensions have reached an all-time high in popularity. These are synthetic lashes individually glued onto natural lashes. The glues are formaldehyde-based and often contain latex. Most patients have no idea that this is the case. Moreover, most extensions are applied in nail and hair salons where people aren't adequately trained in eye hygiene. The result is an increased risk of blepharitis, chemical keratitis, and conjunctivitis from this procedure.

False eyelashes are very popular now as well. People glue the strip of false eyelashes onto the edge of the eyelid, where the weight of the false lashes or the applied fixatives can cause problems on the lid margin. In addition, a study by the Georgia Tech Engineering Department found that the longer, Kim Kardashian-style lashes actually cause air to funnel down to the ocular surface, along with pollution and particulate matter in the environment.[13]

Eyelash adornments, such as beads and crystals, have become a trend as well. They are attached with a very fine thread wrapped around the eyelashes. These different manipulations of the lashes cause something called traction alopecia. The weight of the ornaments attached to eyelashes damages the lashes and lids, causing lashes to fall out. The lashes are also pulled out during removal of the embellishments or the false lashes.

Dr. Donaldson: Do you see many patients with permanent eyeliner in your practice?

Dr. Matossian: Permanent eyeliner, which is actually a tattoo applied in very small strokes along the upper and sometimes lower lids, is very common in Korea and Japan. The concern is that permanent eyeliner can cause meibomian gland dropout.[14,15]

Dr. Donaldson: I wasn't familiar with some of these cosmetic practices, but when I asked my scrub techs if they had heard of them, they had. In fact, a few of them go every few weeks for eyelash extensions. Apparently, it has become very popular in recent years.

Another cosmetic procedure we've seen in the news is conjunctival whitening, which is a bit controversial.

Dr. Matossian: People want to look youthful, awake, and alert, so they want their eyes to look whiter and less pink or red. As a result, they're resorting to conjunctival whitening procedures. The whitening process is done with antimetabolites, such as mitomycin C.

In some cases, physicians have made a small incision into the conjunctiva, placed white tattoo ink in the sub-conjunctival space, and spread it to create a whiter appearance. These are very, very controversial procedures with a very high risk of complications.[16,17] The AAO does not condone conjunctival whitening.

Dr. Donaldson: Another cosmetic challenge to the ocular surface is the cosmetic contact lens. Real contact lenses can cause or exacerbate OSD, but exotic cosmetic lenses pose a particular threat because,

often, they're not fit properly by trained eyecare providers. Previously available at the mall or other random shops, access to these lenses — at least in the United States — is now better controlled.

Dr. McDonald: In some instances, the lenses are imported illegally from outside the U.S. and have toxic dyes. I have treated numerous cases of limbal stem cell failure from these contact lenses that have not received FDA approval.

#6 Women are still underdiagnosed and doctor-shopping for answers.

Dr. Donaldson: Do you find that women with OSD have taken a lengthy route to diagnosis?

Dr. Epitropoulos: In my practice, the average patient with moderate to advanced dry eye has seen eight or nine eyecare practitioners. In fact, it's the most common reason why patients leave their eyecare practitioner; most likely they didn't have a therapeutic relationship. When we finally diagnose them, make that connection, and really educate patients about the disease, it goes a long way.

Dr. McDonald: I did a Medline search for the association between dry eye and depression. More than 80 published papers in the peer-reviewed literature link those two diseases.

Dr. Donaldson: As physicians, we don't always have time to spend with patients, which is probably why they see eight or nine doctors and get so frustrated. They just keep doctor-shopping. But, to have a dry eye center of excellence, you have to have someone — a physician or staff member — who truly loves to build relationships with patients.

Fortunately, I have a technician who loves developing relationships with dry eye patients. She connects with them and enjoys spending the time, so we allow her longer time slots. She might perform a treatment or just talk and be supportive. Patients love it. They don't even care if they see me — they want to come back to see her!

Dr. Matossian: When patients have support and hope, and they hear that there are treatment options that can help, it means the world to them. Again, they've been going from doctor to doctor. Nobody has believed in them. To find someone who listens to them and understands is an enormous relief. They become your best advocates, and they refer more patients to you.

Dr. Epitropoulos: It's a long-term commitment, too. I tell my patients, "I won't give up if you don't give up." They have to know we'll stick with them until they find relief.

#7 With a therapeutic relationship, women can get relief from chronic OSD.

Dr. Donaldson: Dry eye and related OSD are chronic conditions and carry many of the other issues associated with chronic disease. Successful control requires a therapeutic relationship between patients and physicians.

Dr. McDonald: All of us on this panel have a dry eye center of excellence. The longer the dry eye center is open, the more desperate dry eye patients we attract, and we develop many therapeutic relationships with these patients. It's a long-term situation.

They come in with newspaper or magazine clippings, or they email us: "Did you read this? Do you think it would help me?" I have three people who come once a week and many who come once a month. They are mostly middle-aged women, but the patients are trending younger as the face of dry eye changes due to the increased use of digital devices.

These women are suffering. They need to know that we understand, we take OSD seriously, and we're on their team. This is very different from, say, managing someone with glaucoma. That patient has to be convinced to use her drops because she doesn't have any discomfort. OSD patients are chronically uncomfortable and kept from the activities they enjoy, so the relationship is very different.

Dr. Donaldson: Once, when I was preparing to give a lecture on dry eye, I went on some of the chat sites for dry eye patients. Several of them were on disability for dry eye. People were discussing suicide. This can be an incapacitating condition, and sometimes people feel helpless and hopeless, so they just give up. It places an even greater responsibility on us to make a long-term commitment to their care.

#8 With greater awareness in the medical community, women will find the help they need.

Dr. Donaldson: The purpose of this discussion is to spread awareness of the prevalence of OSD among women, as well as the unique health factors that influence their disease. As physicians and our clinical teams learn more, we hope that will translate into more physicians — and practices — diagnosing and treating these patients. The work is both challenging and rewarding.

We also need to raise awareness among patients. Many times, I've had patients start talking in my waiting room and realize, "Wow! This woman's eyes are burning, red, and irritated, and she can't work. She has the same problem I do!"

The diagnosis is completely unfamiliar to many people. It is up to us spread the word, because dry eye can be incapacitating and life-altering. It also helps patients to know that other people are experiencing what they're experiencing, so any dry eye center of excellence can benefit from a support group. It's another component of the supportive, long-term relationship and care that we need to provide to ensure that patients are getting the help they need for this chronic disease. ■

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