EXPERTS:

Esen Karamursel Akpek, MD (Moderator)
Wilmer Eye Institute

Giacomina Massaro-Giordano, MD
Scheie Eye Institute

Paul Karpecki, OD
Kentucky Eye Institute

Jacob Lang, OD
Associated Eye Care

Reaping the Benefits of Serum Tears In Practice

How leaders in ocular surface care are incorporating this important tool

Research has revealed the positive safety and efficacy profile of autologous serum eye drops (ASEDs) and their ability to improve the signs and symptoms of ocular surface manifestations.[1,2] Autologous serum eye drops have been shown to be particularly useful in patients who don't improve sufficiently with first-line therapy.[1,2]

A number of studies reveal that autologous serum drops perform better than conventional eyedrops in improving ocular surface health and patient comfort.[3-5] Significant improvements in tear stability, ocular surface vital staining scores, and pain symptom scores have been documented in patients treated with autologous serum compared to those treated with non-preserved artificial tears.[6] Patients with chronic and severe ocular surface disease report a 58% decrease in Ocular Surface Disease Index (OSDI) score as a result of using autologous serum eye drops.[7]

As more eye care providers include autologous serum tears in their armamentarium of therapeutic agents, they will want to identify the right patient candidates to try the therapy and consider how best to incorporate autologous serum tears into existing treatment protocols. This panel of eye care leaders has successfully added autologous serum eye drops into practice, and offers clinical and practical considerations on optimally using autologous serum tears in eye care practice today.

Patient Considerations

DR. AKPEK: What types of patients would benefit from autologous serum tears?

DR. MASSARO-GIORDANO: Most patients with varying degrees (mild to severe) of ocular surface disease can benefit. These are patients with conditions that range from dry eye due to autoimmune conditions such as Sjögren's syndrome, rheumatoid arthritis, and thyroid eye disease, etc., in addition to those with graft-versus-host disease (GVHD), neurotrophic keratitis (NK), recurrent erosions, neuropathic pain, chemical burns, and Stevens-Johnson syndrome.

DR. LANG: Autologous serum eye drops (ASEDs) have very broad anti-inflammatory and regenerative properties, which give them a widespread application profile in eye care. I tend to reach for ASEDs in patients who have an inability to supplement their own cornea and ocular surface with the proper nutrients and growth factors found in healthy, natural tears. This includes many autoimmune patients, aqueous deficient dry eye patients, anyone with neurologic abnormalities (neurotrophic and neuropathic) of their cornea that may affect the supply of nerve growth factors and neurotrophins, as well as patients with other inflammatory corneal conditions including corneal erosions, and even poor wound healing after injury or surgery.

DR. KARPECKI: The great thing about autologous serum is that it can be utilized for many patient conditions. The obvious is dry eye disease, especially keratoconjunctivitis sicca (KCS) and Sjögren's syndrome KCS. But other conditions also benefit significantly, such as NK, limbal stem cell deficiency, neuropathic corneal pain, GVHD, and superior limbic keratoconjunctivitis (SLK), to name a few.

DR. AKPEK: Autologous serum eye drops are particularly beneficial in healing punctate erosions or non-healing epithelial defects in the cornea and for maintenance treatment for patients who make no tears, among other uses.

DR. AKPEK: How do your patients benefit from autologous serum tears?

DR. MASSARO-GIORDANO: Often my patients report their eyes feel more comfortable after using autologous serum tears. The eyes look less irritated, and my patients are not using their artificial tears as often.

DR. KARPECKI: Most patients prefer serum tears over artificial tears for comfort. They like the fact that they are natural and derived from their own blood serum. And while patients experience the comfort of the drops upon instillation, the therapeutic benefits continue to help treat the disease.

DR. LANG: Patients benefit from a natural, biological therapeutic that is preservative-free and delivers the nutrients and biochemical support that their eye is unable to produce, or adequately produce. The

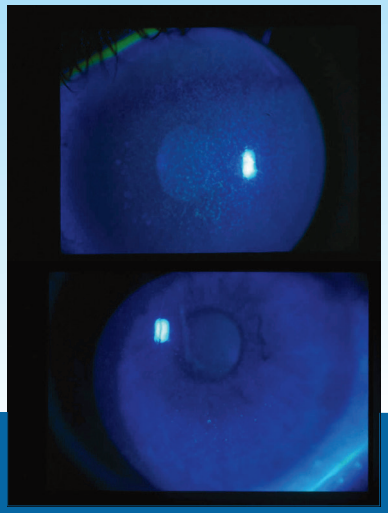
CASE: Sjögren's Disease-Related DED

By Esen Karamursel Akpek, MD

A 63-year old female patient with Sjogren's disease-related dry eye presented for cataract surgery evaluation. Slit-lamp examination demonstrated significant corneal punctate erosions highlighted with topical fluorescein.

The patient, who had been on topical cyclosporine drops and over-the-counter preserved artificial tears for several years prior to presentation, was advised to switch to preservative-free artificial tears, and increase the topical cyclosporine drops from 2 to 4x daily. In addition, inferior permanent tear duct plugs were inserted and autologous serum tears at 50% concentration 4x daily were added to the regimen.

Eight weeks into the new treatment using autologous serum tears, slit-lamp appearance of the corneal fluorescein staining demonstrated significant improvement.



Slit-lamp examination demonstrated significant corneal punctate erosions highlighted with topical fluorescein (top). Eight weeks into the new treatment using autologous serum tears, slit-lamp appearance of the corneal fluorescein staining demonstrated significant improvement (bottom).

dosing schedule is also somewhat beneficial as the frequent instillation promotes hydrating effects as well.

DR. AKPEK: Autologous serum tears help optimally heal the patient's ocular surface and restore the homeostasis of the corneal epithelialization process in this important segment of patients.

Prescribing Insights

DR. AKPEK: When prescribing autologous serum tears for dry eye, where do they fit into your treatment protocol?

DR. MASSARO-GIORDANO: They are the second step after the patient has tried artificial tears, immunomodulators, steroids, and more viscous tears and or ointments.

DR. KARPECKI: With some conditions, such as Sjögren's syndrome KCS, autologous serum tears are my initial or primary treatment. For other forms of dry eye, they become an option when corneal staining is not resolved with other drops. In these cases, I might begin with topical corticosteroids but if after one month I am seeing minimal resolution, I immediately start to add autologous serum tears.

DR. LANG: I find ASEDs lend themselves well when chronic and ongoing therapy is needed. This is not typically a pulsed or flare treatment, but an ongoing supplement and supportive therapy for the ocular surface. Many ocular conditions are chronic, and "cure" is not a common word in my clinics (unfortunately). In these cases, ongoing therapy with ASEDs makes a lot of sense. I also find myself discussing ASEDs more once the initial presentation is stabilizing but not resolving. It's a good option to keep the healing going.

DR. AKPEK: I follow the TFOS DEWS II guidelines in that we use a sliding scale to first address environmental factors, followed by preservative-free over-the-counter drugs, then prescription drugs, and treatments specifically for meibomian gland dysfunction. If the patient continues to exhibit corneal epithelial fluorescein staining despite the previous interventions, I find that autologous serum tears are often highly effective at this stage in alleviating symptoms and promoting healing of the ocular surface.

DR. AKPEK: How do you determine what concentration to order? How many times per day are your patients using autologous serum tears?

DR. MASSARO-GIORDANO: Studies vary. I do 50% 4x daily, although some other practitioners do 20% 6-8x daily, based on the significant effect that 50% concentration has had in several studies.[1]

DR. KARPECKI: It depends on the condition. For most dry eye patients, I typically begin with 20% or 25% concentration. However, if I'm dealing with NK or GVHD, I typically begin at 40% or 50%. I recommend 6 drops per day spaced out about every 2 hours while awake. Once the condition is showing improvement, patients may taper down to QID. However, many patients tell me that 6 times per day works best for them and continue with that dosing long-term. The 20% concentration, when the condition allows for it, enables the patient to obtain an ample amount of autologous serum drops.

DR. LANG: In general, much of the clinical research around ASEDs utilizes 20% serum,[8] although concentrations up to 100% have been used. Twenty percent tends to be the starting point as it mimics the concentrations of biologically active components in natural tears. I start with 30%, 6-8x per day, every 2 hours during waking hours, for most conditions.

DR. AKPEK: There's no evidence-based answer to these questions. It's based on experience. I believe that putting too many drops on the eye surface is detrimental, especially to meibum- or mucin-deficient dry eye patients. I would rather deliver the same amount of nutrients using a less frequent regimen, so I use 50% concentration and have patients use it only 4x a day. Usually, these patients also wear some kind of therapeutic contact lens. If that is the case, I ask them to place a couple of drops into the reservoir of the contact lens as well, so they use even less, maybe 2 or 3x a day.

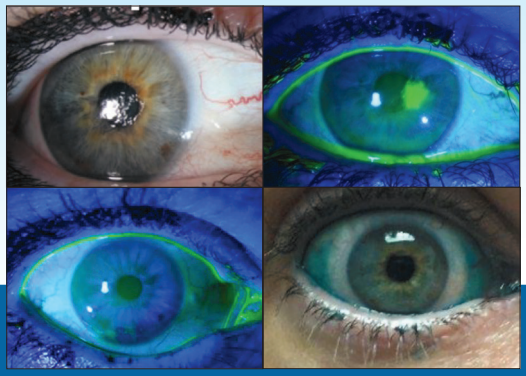
Management of the Patient Using Serum Tears

DR. AKPEK: How long do you keep your patients on autologous serum tears?

CASE: The Perfect Storm

By Giacomina Massaro-Giordano, MD

A 57-year-old female and former LASIK patient presented to the clinic with Sjögren's syndrome, herpes keratitis, NK, and allergic conjunctivitis. She was prescribed autologous serum tears, anti-inflammatory medications, and a mini-scleral lens. The patient returned for follow up after five weeks of treatment. Staining showed that the corneal surface was much smoother with significantly less punctate staining.



These photos show staining of the patient's ulcer before (top) and after (bottom) treatment with serum, anti-inflammation medications, and a scleral lens. Note the improvement of stain in the second set of photos.

DR. KARPECKI: For most patients, especially those with KCS, GVHD, neuropathic pain, etc., autologous serum tears are a lifetime medication, unless their lacrimal glands somehow can improve on their own. When treating conditions like NK, mild/moderate LSCD, or SLK, patients can discontinue use once the condition has improved or resolved.

DR. LANG: This is definitely a marathon, not a sprint. I suggest patients take ASEDs for 6 months before deciding to continue therapy. I hope for some improvements around 3 months but typically stay the course for 6 months. If we are seeing improvements, I usually continue therapy with ASEDs for the foreseeable future.

DR. MASSARO-GIORDANO: I keep them on for 3-6 months depending on severity and response. I may repeat the cycle 1-2x a year. Cost is an issue so I will usually give patients prescription drops in the winter months when dryness may be worse.

DR. AKPEK: What do you look for at follow up to determine whether autologous serum tears are an effective therapy?

DR. MASSARO-GIORDANO: I look for subjective improvements on questionnaires, in addition to objective signs, i.e., corneal stain with fluorescein and conjunctival stain with lissamine green, as well as overall conjunctival hyperemia.

DR. KARPECKI: I look at corneal and conjunctival staining, and also monitor osmolarity. An improvement in either indicates they are working. I don't expect symptoms to improve until I've improved the ocular surface and provided a homeostatic tear environment. At that point the nerves begin to normalize and symptom improvement follows. Most patients are encouraged by the improvement in signs knowing that symptom resolution may lag. Fortunately, autologous serum tears are very comfortable as a drop, which helps the patient while their dry eye disease continues to improve.

DR. LANG: I evaluate symptoms by using a symptom survey (typically SPEED) although other surveys, such as the Ocular Pain Assessment Survey (OPAS), may have more merit when treating neuropathic eye pain. Regarding clinical signs, corneal and conjunctival staining, tear break-up time, conjunctival erythema, and visual acuity are all measures I lean on.

Practical Guidance

DR. AKPEK: How do you present autologous serum tears to your patients?

DR. MASSARO-GIORDANO: I simply state that I feel that they will benefit from this treatment and, unlike artificial tears, serum tears contain growth factors and proteins that may indirectly help with inflammation and promote healing. I explain that the serum facilitates the repopulation of epithelial cells on the surface of the eye.

DR. KARPECKI: It is an easy recommendation in dry eye and other advanced ocular surface disease conditions because I explain how, for example, this autoimmune disease has damaged the patient's lacrimal glands. These glands once served to take the serum from their blood to make tears but they can no longer do that, so we will have their blood drawn and use the serum within it to make their own personalized tears. I then discuss how this will typically lessen or eliminate the need for artificial tears, which is a cost savings, and how autologous serum tears are typically more comfortable than artificial tears, are a natural biologic, and are far more effective. From there I discuss how tears and medications can cost over $100 per month and patients often nod in agreement. I then state that this option will offset much of that and although the cost is similar, autologous serum tears are far more effective and biocompatible having come from their own serum.

DR. LANG: I usually review how patients' eyes are unable to produce the necessary nutrients that their ocular surface needs to stay healthy

Vital Tears are prepared in a medical laboratory using validated safety procedures and delivered throughout the US. Vital Tears autologous serum eye drops can be obtained in as little as 48 hours from the patient's blood draw.

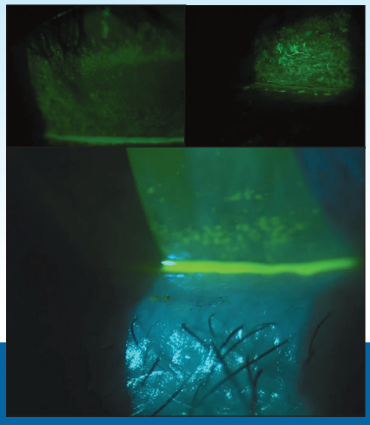
CASE: "Severe Dry Eye," Likely Sjögren's KCS

By Paul Karpecki, OD

A 78-year-old female was referred to the clinic for severe dry eye. She was an avid reader and had not been able to read for over a year. Her current medications included artificial tears every one to two hours and erythromycin ointment twice daily.

The patient was diagnosed with keratoconjunctivitis sicca (KCS) and superficial punctate keratitis (SPK). A lab test for Sjogren's Syndrome was ordered and later returned positive.

Steroid drops, preservative-free artificial tears, vitamin A ointment, and nutritional supplements provided minimal improvements. She was then prescribed serum tears at 20% concentration twice daily. Six weeks later, she reported a noticeable improvement in symptoms.



The patient presented with grade 3+ corneal staining and a relatively low tear meniscus height (top). At the final exam, significantly reduced staining and normal tear meniscus height were observed (bottom).

because of their disease state and explain that many of the healing components of tears are the same as blood. By utilizing this natural therapy, we can harness the power of the patient's own blood in a drop form to help the eye and rehabilitate the ocular surface.

Even though autologous serum tears have been around for many years and proven to be safe and effective, insurance companies do not pay for them. This doesn't surprise most patients because many are used to getting denial letters and prior authorization forms for everything from antibiotics to cold medicine. Compared with some of the other therapeutic options in this space, cost is usually not too much of a shock to the patient.

DR. AKPEK: If patients still have significant corneal, or central corneal, staining after having tried environmental modulations, over-the-counter eyedrops, and prescription medications, then I will bring it up to them. Most of my patients are referrals and have talked to people who are on serum tears; they usually come in asking for them. Or when I bring it up, they usually say, "Oh okay. I heard about them." So it's not very difficult for me to explain that they are going to take eye drops made out of their own blood. In general, dry eye patients are pretty educated, and they understand how autologous serum tears can help heal the surface vs. just artificial tears.

DR. AKPEK: How does your practice order/source autologous serum tears for your patients?

DR. MASSARO-GIORDANO: I have used various compounding companies in the past but now use Vital Tears, a national company with numerous labs and a mobile phlebotomy service to aid in collection.

DR. KARPECKI: Vital Tears is a national outfit that provides incredible customer service and uses trained phlebotomists, the highest level of care and safety, and a sterile environment to process the serum tears. They are experts at this. They can also do the blood draw from the patient's home or office, offering convenience for busy people. And they have renewal plans, which makes it easy to follow and maintain your supply of serum tears.

DR. LANG: I utilize Vital Tears for all my ASEDs orders. Their program and organization streamline my staff's workflow and make the process easy for both doctor and, more importantly, patient.

For additional cases, see https://info.vitaltears.org/case-studies

1. Semeraro F, Forbice E, Braga O, et al. Evaluation of the efficacy of 50% autologous serum eye drops in different ocular surface pathologies. Biomed Res Int. 2014;2014:826970.
2. Soni NG, Jeng BH. Blood-derived topical therapy for ocular surface diseases. Br J Ophthalmol. 2016 Jan;100(1):22-7.
3. Noble BA, Loh RS, MacLennan S, et al. Comparison of autologous serum eye drops with conventional therapy in a randomised controlled crossover trial for ocular surface disease. Br J Ophthalmol. 2004 May;88(5):647-52.
4. Celebi AR, Ulusoy C, Mirza GE. The efficacy of autologous serum eye drops for severe dry eye syndrome: a randomized double-blind crossover study. Graefes Arch Clin Exp Ophthalmol. 2014 Apr;252(4):619-26.
5. Urzua CA, Vasquez DH, Huidobro A, et al. Randomized double-blind clinical trial of autologous serum versus artificial tears in dry eye syndrome. Curr Eye Res. 2012 Aug;37(8):684-8.
6. Kojima T, Higuchi A, Goto E, et al. Autologous serum eye drops for the treatment of dry eye diseases. Cornea. 2008 Sep;27 Suppl 1:S25-30.
7. Lomas RJ, Chandrasekar A, Macdonald-Wallis C, et al. Patient-reported outcome measures for a large cohort of serum eye drops recipients in the UK. Eye (Lond). 2021 Dec;35(12):3425-32.
8. Pan Q, Angelina A, Marrone M, et al. Autologous serum eye drops for dry eye. Cochrane Database Syst Rev. 2017 Feb 28;2(2):CD009327.