

Autologous Serum as a Dry Eye Treatment Modality



Dry eye is a multifactorial condition with numerous treatment options, and it sometimes proves recalcitrant to standard therapies such as artificial tears, ointments, eyelid hygiene, moisture masks, glasses, goggles, and punctal plugs. But as doctors of optometry become increasingly and aggressively involved in treating ocular surface conditions, autologous serum eye drops are rising in popularity as a treatment paradigm.

Autologous serum isn't new. Through the last several decades, blood derived eye drops have been used to treat dry eye disease, persistent corneal epithelial defects, corneal ulcers, ocular surface burns, recurrent corneal erosions, and limbal stem-cell deficiency. By supplying an active mixture of growth factors and cytokines at the ocular surface, the proposed mechanism of action is the stimulation of cellular proliferation and migration, imitating a function of the deficient tear film. Theoretically, a malfunctioning lacrimal gland may be mimicked by using the serum components topically that are utilized in tear fluid generation. Within the overall category of blood derived eye drops, both autologous (from the patient themselves) and homologous (donor derived) products are available. The original and most frequently used product in eye care is autologous serum obtained from the patient's own blood.¹

Preparation protocols for autologous serum eye drops vary, but fundamentally: the patient donates blood; the blood coagulates and is centrifuged to extract the serum; and a quantity of serum is placed into a dropper bottle, usually with diluent—typically a sterile saline solution. The level of dilution varies, but most drops are 20% serum. Patients must not have any blood-borne infectious conditions and have their blood drawn regularly (i.e. every six weeks). Once compounded, the autologous serum

eye drop vials must be kept frozen or refrigerated to avoid contamination and/or the degradation of the components. Patients are instructed to store all of the bottles in the freezer except for the current bottle they are using, which should be stored in the refrigerator. The drops are usually dosed anywhere from two to eight times per day.

There is clinical research that supports the use of autologous serum to combat ocular surface disease. Autologous serum performs better than conventional artificial tears, improving Schirmer's scores, goblet and epithelial cell density, and tear film debris with statistical significance². Autologous serum has been shown to improve corneal staining and reduce dependence on artificial tears³. Improved subjective comfort and tear film stability have also been demonstrated in dry eye patients⁴.

Autologous serum is demonstrating usefulness in anterior segment surgeries by accelerating corneal epithelial healing after surface ablation corneal refractive and pterygium procedures^{5,6}. It also may have a role in improving both the signs and symptoms of ocular surface disorders associated with systemic autoimmune diseases such as Sjögren's syndrome, mucous membrane pemphigoid, graft-vs.-host disease, and rheumatoid arthritis⁷.

Large, high quality, randomized control trials are still needed to examine the

benefits of autologous serum therapy for dry eye. The utilization and analysis of standardized questionnaires to measure patient-reported outcomes, objective clinical tests, and objective biomarkers is critical. Numerous national and international guidelines on dry eye treatment have been published, but they differ in dosing, concentration, and indication of autologous serum eye drops, making a reaching a consensus challenging, and there is also no universal protocol for preparing and storing the eye drops. A 2017 Cochrane review of randomized controlled trials in which autologous serum was used to treat dry eye found inconsistencies in the literature and concluded that current evidence did not necessarily support a benefit. However, limited studies were available for review, and the study data only focused on two weeks of treatment. The authors acknowledged that more research is still needed⁸. Of note, the International Task Force Delphi Panel on Dry Eye identified autologous serum eye drops for earlier utilization in the dry eye disease process; it is now a recommended treatment for patients with level three disease as opposed to only for the most severe disease⁹.

The use of blood serum eye drops continues to evolve. Current research is helping us understand more about the positive effects of platelet rich plasma, umbilical cord serum, and allogenic albumin, among others. It's hard

to predict how blood serum products and their utilization will change and grow over the next several years; it's certainly a topic to be watching. When conventional therapy is not acceptable for moderate to advanced dry eye patients, autologous serum eye drops are becoming more accessible and offer another strategy that can make the difference for our patients.

1. Giannaccare G, Versura P, Buzzi M, Primavera L, Pellegrini M, Campos EC. Blood derived eye drops for the treatment of cornea and ocular surface diseases. *Transfus Apher Sci*. 2017 Aug;56(4):595-604. doi: 10.1016/j.transci.2017.07.023. Epub 2017 Aug 8. PMID: 28844373.
2. Jirsova K, Brejchova K, Krabcova I, et al. The application of autologous serum eye drops in severe dry eye patients; subjective and objective parameters before and after treatment. *Curr Eye Res* 2014;39(1):21-30.
3. Dalmon CA, Chandra NS, Jeng BH. Use of autologous serum eyedrops for the treatment of ocular surface disease: First US experience in a large population as an insurance-covered benefit. *Arch Ophthalmol*. 2012;130(12):1612-3.
4. Celebi AR, Ulusoy C, Mirza GE. The efficacy of autologous serum eye drops for severe dry eye syndrome: A randomized double-blink crossover study. *Graefes Arch Clin Exp Ophthalmol* 2014;252(4):619-26.
5. Akcam HT, Unlu M, Karaca EE, et al. Autologous serum eye-drops and enhanced epithelial healing time after photorefractive keratectomy. *Clin Exp Optom*. 2018;101(1):34-7.
6. 7. Sul S, Korkmaz S, Alacamli G, et al. Application of autologous serum eye drops after pterygium surgery: A prospective study. *Graefes Arch Clin Exp Ophthalmol*. July 18, 2018. [Epub ahead of print].
7. Ali TK, Gibbons A, Cartes C, et al. Use of autologous serum tears for the treatment of ocular surface disease from patients with systemic autoimmune diseases. *Am J Ophthalmol*. 2018;189:65-70.
8. Pan Q, Angelina A, Marrone M, et al. Autologous serum eye drops for dry eye. *Cochrane Database Syst Rev*. February 28, 2017.
9. Behrens A, Doyle JJ, Stern L, et al; Dysfunctional tear syndrome study group. Dysfunctional tear syndrome: A Delphi approach to treatment recommendations. *Cornea*. 2006;25:900-7.

Autologous Serum as a Dry Eye Treatment Modality

The Surgical Perspective



MIDWEST COMMENTARY

Kavitha Sivaraman, MD

Specializing Corneal & External Diseases and Cataract Surgery
CINCINNATI EYE INSTITUTE

How do you get a patient started on Autologous Serum in your region?

An order for “Autologous Serum” is entered into the medication module of our EMR system. The prescribing doctor then enters the percentage and directions. The patient is sent to our front desk to schedule a

blood draw with one of our nurse practitioners. The pharmacy then processes the sample based on the electronic order.

Alternatively, an order can be called in or faxed to our local hospital whose inpatient pharmacy also formulates autologous serum.

How much does Autologous Serum cost and does insurance cover it?

\$120 for a 6 week supply. Insurance is not billed for the service at CVP.

How do you educate patients on why they need Autologous Serum therapy?

Autologous serum requires time, effort, and expense on the part of patients. It is therefore important for them to understand your rationale for prescribing this treatment. In my practice, Autologous serum is generally reserved

for patients who have not responded to commercially available treatments for dry eye or those with complications from severe ocular surface disease. I discuss how AS is more similar in composition to natural tears and can thus provide benefit beyond what manufactured lubricant eye drops can. Treatment of severe OSD is often a moving target and usually requires a multi-faceted approach, so it is also important to point out that AS may not work for everyone. However, it is an important part of our arsenal for treating some forms of OSD.

In the Greater Cincinnati area, referral partner optometrists can utilize our CEI Blue Ash location to acquire autologous tears for their dry eye patients as needed. With a written prescription, a patient simply needs to make an appointment to have their custom serum processed. Upon arrival, our nurse practitioner will perform the blood draw. The drawn

blood will be processed, packaged, and put on ice in our compounding pharmacy for when the patient comes back to pick it up 2 to 3 hours later. The nurse practitioner can also schedule the patients future appointments and will contact you when the prescription expires. Please reach out to your CVP professional relations specialist if you have further questions.



MID-ATLANTIC COMMENTARY

Albert Y. Cheung, MD

Specializing Cornea, Cataract, Anterior Segment Surgery
VIRGINIA EYE CONSULTANTS

How do you determine what percentage Autologous Serum to use?

I typically start with 20% as this was the most commonly used percentage in the literature. There are more recent studies that have examined higher concentrations, 50% and 100%, for ocular surface disease. It is reasonable to titrate up to 50%, especially for more advanced

ocular surface conditions such as neurotrophic corneal ulcers or inflammatory/autoimmune conditions. It is important to remember that serum may contain certain components that can be detrimental to the ocular surface (e.g. TGF- β may suppress ocular surface wound healing at high concentrations), so there may be safety considerations with a high percentage such as 100%.

Where does Autologous Serum fit in to your treatment armament for Ocular Surface Disease in particular dry eye disease?

Although I've seen significant success with refractory cases, Autologous Serum represents an advanced treatment for my dry eye patients. This is largely due to cost (lack of insurance coverage), availability, and inconvenience (needing to drive 1-2 hours from my Virginia office to the lab/compounding pharmacy). Patients have often already tried other therapies, i.e. aggressive lubrication, punctal occlusion, corticosteroids, and/or commercially available

dry eye medications such as cyclosporine and lifitegrast.

How long do you keep patients on Autologous Serum either short-term or long-term?

I ask patients to trial Autologous Serum for at least 2-3 months to gauge if they respond well. Those that do will often stay on Autologous Serum long-term, especially given the often-chronic nature of their condition. This also tends to help with cost as they can obtain a 6-month supply from a single blood draw.