

On behalf of Vision Expo, we sincerely thank you for being with us this year.

Vision Expo Has Gone Green!

We have eliminated all paper session evaluation forms. Please be sure to complete your electronic session evaluations online when you login to request your CE Letter for each course you attended! Your feedback is important to us as our Education Planning Committee considers content and speakers for future meetings to provide you with the best education possible.



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Financial Disclosures

- Consultant with LKC 
- Consultant with Adnexa Ocular Amniotic Membranes 
- Consultant with Sight Science 
- Member Board of Directors 

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Autologous Serum in Optometric Practice

Presenter: Ansel T. Johnson, O.D.

Bringing Tear Serum to the forefront of Dry Eye Therapy

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Course Objectives

- Understanding the composition and mechanism of action autologous serum
- Understanding indications and possible utilizations for autologous serum
- Understanding how to prescribe autologous serum
- Knowledge of other biologic options to autologous serum

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About Ansel T. Johnson, OD

- Adjunct Professor:
 - Midwestern Chicago College of Optometry (Externship site)
 - Kentucky College of Optometry – UPIKE (Externship site)
 - New England College of Optometry (Externship site)
 - Southern College of Optometry (Externship site)
- Additional Clinical Externship Site
 - UAB College of Optometry
- Medical Director – United Eye Care Providers
- Founder, CEO – Healthy Living With A Vision Foundation
 - (A 501c3 Organization)

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Replenishing The Eye's Moisture

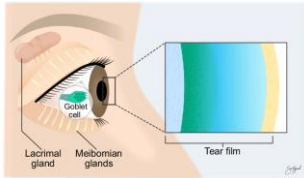


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Homeostasis of the Tears is Complex



- The tear film is a unique thin fluid layer that covers the outer mucosal surfaces of the eye.
- It is the interface of the ocular surface with the environment.
- It has an aqueous, mucin and lipid layers.
- Each layers or regions contain distinct biochemistries which underlie distinct functions



Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4225770/>

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Homeostasis of the Tears is Complex



Lipid

- The lipid layer of the tear film is thin yet contains many different lipid species including non polar cholesterol and wax esters which make up it bulk, and polar lipids such as (O-acyl)- ω -hydroxy fatty acids and phospholipids which interact with the aqueous layer.
- The majority of these lipids, with the possible exception of the phospholipids, are secreted from meibomian glands located at the lid margin.
- The biggest role of the lipid layer is in retarding evaporation of tears from the ocular surface.

Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4225770/>

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Homeostasis of the Tears is Complex



Aqueous

- The aqueous/mucin layer forms the bulk of the tears. Most of the aqueous fluid is secreted from the lacrimal glands, which also secretes a specific variety of **proteins, electrolytes, and water**. The conjunctival epithelium is a second source of electrolytes and water in the tears.
- The aqueous phase provides oxygen and nutrients to the underlying avascular corneal tissue and flushes away epithelial debris, toxins and foreign bodies.

Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4225770/>

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Homeostasis of the Tears is Complex



Mucin or Mucus layer

- Many of the mucins are secreted by specialized goblet cells in the conjunctival epithelium, and some transmembrane mucins are released into the tear film from corneal and conjunctival epithelial cells. When anchored into the epithelial cells, these transmembrane mucins project into the aqueous phase and help stabilize the tear film.

Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4225770/>

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Homeostasis of the Tears is Complex



What do you tell your patients
the causes of their dry eyes?

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Homeostasis of the Tears is Complex



Some health problems that cause abnormal tear production

- Viruses
- Hepatitis C
- HIV and AIDS
- Lymphoma
- Sarcoidosis
- Hemochromatosis
- Amyloidosis
- Graft versus host disease
- Damage to tear glands or tear ducts

Source: webmd

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Autologous Serum Defined

- The cells or tissue given or used for treatment is from the same individual.
- First noted use is in a 1975 study testing to test the ability of a perfusion pump to keep chemically burned eyes moist
- First investigated for ocular use in 1984 by Robert Fox, Raymond Chan et al
 - Autologous serum used in patients that did not get relief or subjective improvement with available artificial tear supplements
 - Patients continued use without complications

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Autologous Serum Acquisition

- How is the serum acquired?
 - venipuncture
- Patient's blood is drawn at a lab, doctor's office or patient's home. No fasting is required.
- The blood draw is centrifuged separating blood it into its various components.
- The serum to saline ratio may vary according to the prescribing doctor's assessment
- It is important to keep the eye drops away from light because some of its components (vitamin A) degrade quickly with light exposure



Source: <https://doi.org/10.1199/S0004-27490208000700010>

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Autologous Serum Possible Risks & Complications

- Blood is extracted from patient's vein with vacuum extraction tubes without anticoagulant.
- Subsequently, the tubes are left in vertical position at 22°C for about 2 hours to allow coagulation.
- After blood clot is formed, supernatant is centrifuged to separate the serum from the solid components.
- A bottle of serum eye drops with the desired concentration, adequately identified and preserved from light is given to the patient.
- It is important to keep the eye drops away from light because some of its components (vitamin A) degrade quickly with light exposure.

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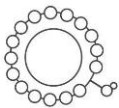
Autologous Serum Mechanism of Action

- "What is in your blood serum?"
 - Contains multiple growth factors, vitamins, proteins and other components that have been considered important for corneal and conjunctival integrity. Human serum has similar biochemical properties normally found in tears
 - **Epidermal growth factor(EGF)** – By promoting cell migration and proliferation EGF is a major stimuli for promotion of corneal wound healing.
 - **Transforming growth factor-β** – part of intricately balanced interactions between cells. Helps cooperative interactions that involve numerous cytokines engaged in corneal surface integrity.
 - **Fibronectin** - A structural extracellular protein that binds to collagen and cells. A major factor in corneal development.
 - **Cytokines** – regulate immune response
 - **Vitamin A** - deficiencies cause corneal scarring and opacifications Important in goblet cell health and integrity.

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Autologous Serum Mechanism of Action

- **Epidermal growth factor(EGF)** – By promoting cell migration and proliferation EGF is a major stimuli for promotion of corneal wound healing.
- Promoted for skin care and antiaging.



Growth Factor
(EGF)



Source: Cell Biol Int. 1995 May;19(5):413-30. doi: 10.1006/cbir.1995.1086

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Autologous Serum Mechanism of Action

- **Transforming growth factor-β** – part of intricately balanced interactions between cells. Helps cooperative interactions that involve numerous cytokines engaged in corneal surface integrity.
- Transforming growth factor beta (TGF-β) is a multipotent growth factor affecting cell differentiation, proliferation, apoptosis and matrix production.

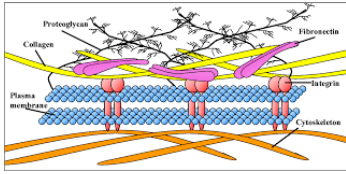


Source: <https://www.sciencedirect.com/topics/neuroscience/transforming-growth-factor-beta>

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Autologous Serum Mechanism of Action

- **Fibronectin** - A structural extracellular protein that binds to collagen and cells. A major factor in corneal development.
- **Fibronectin (FN)** is a ubiquitous extracellular matrix (ECM) glycoprotein that plays vital roles during tissue repair.



Source: <https://fibrogenesis.biomedcentral.com/articles/10.1186/1755-1536-4-21>

Autologous Serum Mechanism of Action

- **Cytokines** – regulate immune response
- Cytokines are small proteins that are crucial in controlling the growth and activity of other immune system cells and blood cells. When released, they signal the immune system to do its job. Cytokines affect the growth of all blood cells and other cells that help the body's immune and inflammation responses.



Source: <https://www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy/cytokines.html#:~:text=Cytokines%20are%20small%20proteins%20that,by%27%20immune%20and%20inflammation%20response>

Autologous Serum Mechanism of Action

- **Vitamin A** - deficiencies cause corneal scarring and opacifications Important in goblet cell health and integrity.
- Involved in mediating the relationship between gut bacteria and the immune system
- A key for good vision, a healthy immune system, and cell growth.

PROPERTIES OF VITAMIN A
By Botanical-online.com

- Vitamin A appears in the retina of the eye, and it's important for the vision health.
- To treat eye fatigue, glaucoma, night blindness, myopia, astigmatism, ...
- It strengthens the immune system.
- In animal fats: milk, cheese, eggs (yolk), ...
- The body can get vitamin A from **beta-carotene**: carrots, spinach, chard, mango, peach, ...

www.botanical-online.com

Source: immune.system.to.get.bacteria.How.vitamin.A.helps.the.pair.16octobertoday.com
Vitamin A (Retinol; Beetrots, Ice, Yellow and, Health, System.com)

Autologous Serum A Supper Food for the Eyes

Provides for Homeostasis Within the Eye

- Homeostasis is the tendency toward a relatively stable equilibrium between interdependent elements on the ocular surface
- Maintained by physiological processes of tear production.
- Whatever the initial causes of dry eye, the subsequent chronic dryness of the **ocular surface** results in inflammatory reactions and destruction of the lacrimal glands and **conjunctival epithelium**.
- Once dry eye disease has developed, inflammation is the key mechanism of dry eye disease causing ocular surface injury, as both the cause and consequence of cell damage. In practice
- Dry eye disease can be associated with **Sjögren's syndrome**, allergies, infection, blepharitis, and preservative-containing eye drops.

Source: <https://www.sciencedirect.com/topics/medicine-and-dentistry/ocular-surface>

Commercial Artificial Tear Products

- Drawbacks and limitations of commercial over the counter tear supplements:
 - Lack essential tear components such as growth factors, vitamins, and immunoglobulins.
 - Often contain preservatives, stabilizers, and other additives, which potentially induce toxic or allergic reactions

Comparison of Systane Complete Eye Drops and Refresh Plus Mega-3 Eye Drops. The image shows boxes and bottles of both products along with their respective labels and drug facts.

Autologous Blood Serum Eye Drop Solution Processing Using PALA™ Kits Dr. Gale H. Thome Ph.D., P.A. Gale H. Thome Jr., MBA Healthcare Management May 4, 2019

Autologous Serum Indications

- A viable alternative for the most severe cases of dry eye and ocular surface disease.
- 1.5 million people in the US are estimated to live with severe dry eye not resolved with OTC or prescription eye drops.
- Conditions that can result in severe dry eye-related ocular surface disorders:
 - Sjögren's syndrome
 - Superior limbic keratoconjunctivitis
 - Graft-versus-host disease
 - Stevens-Johnson syndrome
 - Ocular cicatricial pemphigoid
 - Recurrent or persistent corneal erosions
 - Neurotrophic keratopathy
 - Mooren's ulcer
 - Atrophic keratopathy
 - Filtering blebs after trabeculectomy
 - Post-keratorefractive surgery

Autologous Serum Indications

- Sjögren's syndrome
 - Rheumatoid arthritis patients that suffer with secondary Sjögren syndrome generally have the highest level of damage to the ocular surface with sever ocular complications and subsequent visual impairment.
- Diagnostic tests:
 - SS-A (Ro) and SS-B (La) antibodies:
 - Antinuclear Antibody (ANA)
 - Rheumatoid Factor
 - Complete Blood Count (CBC)
 - Complete Metabolic Panel
 - Erythrocyte Sedimentation Rate (ESR)
 - C-Reactive Protein (CRP)
 - Immunoglobulins:
 - Serum Protein Electrophoresis and Serum Immunofixation
 - Complement Proteins



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Autologous Serum Indications

- Steven Johnson Syndrome
 - much more likely to occur in people infected with the human immunodeficiency virus (HIV), with an estimated incidence of 1/1000.



Source: <https://www.ncbi.nlm.nih.gov/books/NBK459323/>
 Episode 182.0 - Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis - Core EM - Stevens-Johnson Syndrome - Causes, Symptoms, Diagnosis, Treatment, Prevention & Prognosis (podcast44)

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Autologous Serum Indications

- Superior limbic keratoconjunctivitis
 - A chronic and recurrent eye disease which affects the superior bulbar conjunctiva and tarsal conjunctiva, as well as the superior limbic aspect of the cornea.

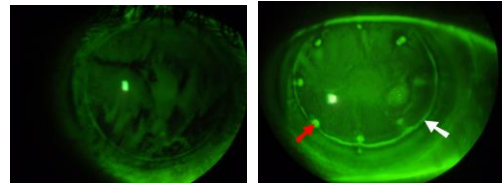


Source: <https://entokey.com/superior-limbic-keratoconjunctivitis-2/>

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Autologous Serum Indications

- Post-keratorefractive surgery (ie. Lasik)

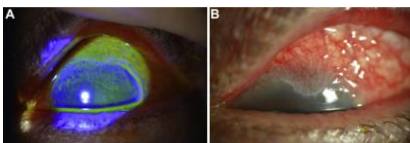


Source: https://www.lasikcomplications.com/case_reports.htm

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Autologous Serum Indications

- Graft-versus-host disease
 - Ocular involvement, either in an acute or chronic presentation, may range from mild to severe with accompanying vision loss present in 60-90% of patient

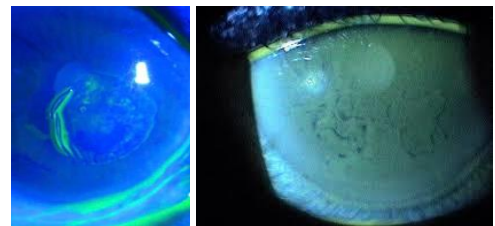


Source: Graft versus host disease: clinical evaluation, diagnosis and management EM Espana, S Shah, MR Santhiago, AD Singh Graefe's Archive for Clinical and Experimental Ophthalmology, 2013

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Autologous Serum Indications

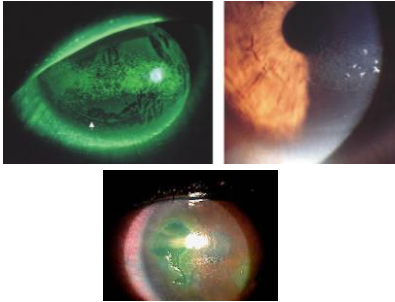
Recurrent or persistent corneal erosions



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Autologous Serum Indications

Neurotrophic keratopathy



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Autologous Serum Possible Risks & Complications

- **Concerns about bacterial or fungal contamination**
- Very rare complications
 - Immunoglobulin deposits
 - Presence of corneal infiltrates
 - Conjunctivitis
 - Decreased corneal sensitivity
 - Immune complex deposition with 100% serum

Source: long-term-use-of-eye-drops PDF (8839W.FM3CH.EDU)

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Autologous Serum Barriers to Treatment

Cost

- Lack of Insurance Coverage
- Complex processing methodology
- Proximity of dispensing lab for blood draw and preparation
- Other social determinates of health
- Necessity for freezer and refrigeration storage

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Most Popular Autologous Serum Brands



- A leading source of Analogous serum, Needs sterile hoods for fabrication of vital tears.

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Most Popular Autologous Serum Brands



- NovoTears can be produced with 20%, 33% or 50% serum
- Can also choose NovoTears Plus: combines NovoTears with cyclosporine.

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Most Popular Autologous Serum Brands



- 6-month supply
- Different and innovative packaging
- Sterile kits and inserts within a sterile production kit that is never exposed to the elements. No need for heavy duty equipment. Production time reduced to 90 min compared to several hours. Most times patients can receive their tears within 24 hours.

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Most Popular Autologous Serum Brands



- **Opticyte Tears Autologous Serum**
- **Certified** specialists perform the procedure conveniently at your home or doctor's office

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Prescribing Autologous Serum

- A prescribed serum concentration generally ranges from 20% to 50%
- Eye drop application per day is prescribed at 2 to 6 times per day which gages amount of blood needed to draw. Various factors can help determine concentration.
- On average 60ml supplied at a time. Each vial is 5 ml estimate 4 drops per vial per day.
- Four drops per day is average dosage.
- Average concentration is 20% to 50% serum to saline. Hyaluronic acid may be used instead of saline.

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Biologic Options to Autologous Serum

- **d-MAPPS(•derived-Multiple Allogeneic Proteins Paracrine Signaling (Branded name Regener-Eyes®)**
 - a first in class, natural, sterile biologic ophthalmic solution that is preservative free
 - contains a large number of immunoregulatory factors
 - acellular however it contains proteins and cytokines in addition to the water, glucose, lactates and electrolytes, and placental-derived biomaterials
 - microRNAs (miRNAs)
 - Ocular conditions for utilization
 - Meibomian gland dysfunction
 - Dry Eye
 - Sjogren's Syndrome
 - Dosages and Prescribing

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Biologic Options to Autologous Serum

- Hydrated Amniotic Membranes
 - Composition
 - Applications and Procedures
- Dehydrated Amniotic Membranes
 - Composition
 - Applications and Procedures

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Biologic Options to Autologous Serum

- **Cenegermin(Branded Oxervate)**
 - Composition
 - Applications and Procedures
 - Utilized for recurrent corneal erosion

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Prescribing Autologous Serum for Asepti Kits

The image shows a medical order form for Asepti PALA™ 12 Autologous Serum Tears. The form includes fields for Patient Name, Patient Date of Birth, Patient Cell Phone, and Physician Name. It also features checkboxes for 'New Concentration' and 'Refill Period (Circle)'. To the right of the form is a 'Patient Instructions' box with the following text:

Patient Instructions:

- This medication (2 drops) is a suspension that settles at bottom layer.
- Amount of serum tears is an approximation of month supply (4 dispensing).
- After using home, keep it for one week or more time.
- Keep vial clean and refrigerate during period of use.
- There each bottle is needed during time of use.
- Use as directed per physician.

Steps to ensure safe and effective use:

- Always wash hands before and after use.
- Bring to prescriber to transport serum tears.
- Call to 800-Cenegermin and visit cenegermin.com.
- No insurance accepted.

Call 708.963.1200 to Schedule Your Appointment

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Autologous Serum Lab Location Information

Vital Tears Information
<https://vitaltears.org/physicians>

Merakris.com
[Opticyte Serum Tears Home \(opticyteteams.com\)](https://opticyte-serum-tears-home)

NovoTears
<https://aiscaregroup.com/our-divisions/ophthalmics/novotears-hcp/>

ARC Point Labs location
<https://www.arcpointlabs.com/locations-by-state/>

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Informed Consent

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Questions



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