Treating the Eye with Autologous and Allogeneic Serum Administration
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Abstract: This one-hour course will detail the use of blood serum in the treatment of anterior ocular surface disease. The details and logistics of prescribing and acquiring autologous and allogenic blood serum will be detailed. Further, modern techniques for fortifying serum will be covered.

Course Objectives: Attendees of this course will learn the following:

- The evidence-base for using blood serum as a therapy for the eye
- The indications for using serum
- The methods for prescribing and acquiring serum
- The concepts of concentration selection and fortification of serum
- The clinical implications of allogeneic serum administration
- The clinical management of the serum patient

1) Introduction
   a) Statement of the Problem
      i) Blood / Eye Barrier
   b) Definitions
      i) Whole Blood
      ii) Plasma vs. Serum
   c) Components of Tears and Plasma (See Appendix, Table 1)
   d) Soluble Protein Clotting Factors
   e) Antigens
   f) Exogenous Substances
   g) Drugs
   h) Pathogens

2) The Evidence Base
   a) Autologous Serum Works for KCS and Sjögren’s Syndrome, Fox, et al, 1984
   b) Autologous Serum Works for Sjögren’s Syndrome, Tsubota, et al, 1999
   f) Autologous Serum Works in Neurotrophic Keratitis, Matsumoto, et al, 2004
   g) Autologous Serum Works on Dye Eye Syndrome, Creuzot-Gartcher, et al, 2004
   i) Umbilical Serum Works for Dry Eye, Yoon, et al, 2006
m) Plasma Rich in Growth Factors Works for Dry Eye, López-Plandolit, 2011

3) **Indications for Serum Use**
   a) Aqueous Dry Eye Disease
   b) Sjögren’s Syndrome
   c) Non- Sjögren’s Deficient Disease
   d) Superior Limbic Keratoconjunctivitis
   e) Neurotrophic Keratitis
   f) Adjuvant LASIK Therapy
   g) Other Ocular Surface Disease States

4) **Prescribing and Acquisition of Autologous Serum**
   a) Prescribing
      i) Written Instructions for Patient, Phlebotomist, and Compounding Pharmacist
      ii) Prescribing Order (See Appendix, Example Prescription Order)
   b) Process for Creating Serum
      i) 40 cc Whole Blood Draw by Venipuncture into Red Top Serum Tube
      ii) Clot 15 minutes in the Dark! (Preserve the Vitamin A)
      iii) Centrifuge at 1,500 rpm for 5 Minutes at 4° C
      iv) Draw Off Supernatant Using Sterile Technique into Red Top Tubes
      v) Quickly Get Into Patient’s Ice Chest
      vi) Patient Transports Immediately to the Compounding Pharmacist
      vii) Dilutes Using Sterile Technique to the Prescribed Concentration
      viii) Divide Evenly Into Six 5ml Dark Glass Bottles with Rubber Dropper Tops (Clear Bottles Kill the Vitamin A, Making the Serum Ineffective) or Forty-Two 1ml Bottles (See Appendix, Table 2)
      ix) If Using 5ml Bottles, Patient Refrigerates One and Freezes the Rest—Change Weekly or Upon Contamination
   c) Use According to the Prescribed Dosing Schedule
   d) High Dosing Schedules May Require More
   e) FDA Guidelines on Re-Injecting Biologicals
   f) Fortification
      i) Fibronectin
      ii) Calcium Carbonate Activated Platelets

5) **Allogeneic Serum Administration**
   a) Stevens-Johnson Syndrome
   b) Graft vs. Host Disease
   c) Severe Autoimmune Disorders
   d) Blood Donor Screening for Compatibility and Blood Borne Pathogens
   e) Chain of Custody
6) **Managing the Serum Patient**
   a) Informed Consent
   b) Managing Expectations
   c) Advanced Beneficiary Notification
   d) Follow-Up Schedules
   e) Patient Counseling
   f) Risk Management and Counseling
   g) Alternative Therapies

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Comparison of Tears and Plasma</th>
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<tbody>
<tr>
<td></td>
<td>TEARS</td>
</tr>
<tr>
<td>Ph</td>
<td>7.40</td>
</tr>
<tr>
<td>Osmolarity</td>
<td>298—300 mOsm/kg</td>
</tr>
<tr>
<td>H2O</td>
<td>98.2%</td>
</tr>
<tr>
<td>Na+</td>
<td>120—170 mmol/L</td>
</tr>
<tr>
<td>Ca2+</td>
<td>0.3—2.0 mmol/L</td>
</tr>
<tr>
<td>Mg2+</td>
<td>0.5—1.1 mmol/L</td>
</tr>
<tr>
<td>HCO3-</td>
<td>26 mmol/L</td>
</tr>
<tr>
<td>CO2</td>
<td>Varies</td>
</tr>
<tr>
<td>K</td>
<td>26—42 mmol/L</td>
</tr>
<tr>
<td>Glucose</td>
<td>2.5 mg/100ml</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.392 g/100ml</td>
</tr>
<tr>
<td>Globulins</td>
<td>0.2758 g/100ml</td>
</tr>
<tr>
<td>Epithelial Growth Factor (EGF)</td>
<td>0.20—0.30 ng/ml</td>
</tr>
<tr>
<td>Transferring Growth Factor Beta (TGF-β)</td>
<td>2—10 ng/ml</td>
</tr>
<tr>
<td>Fibronectin</td>
<td>21 μg/ml</td>
</tr>
<tr>
<td>Transferrin</td>
<td>0</td>
</tr>
<tr>
<td>Lactoferrin</td>
<td>1.51 gm/L</td>
</tr>
<tr>
<td>Lysozyme</td>
<td>1—2 mg/ml</td>
</tr>
<tr>
<td>Lypocalin</td>
<td>Varies</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>0.02</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>0.117 mg/ml</td>
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<thead>
<tr>
<th>Table 2</th>
<th>Expected Volumes For Different Concentrations of Serum</th>
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<tbody>
<tr>
<td></td>
<td>20% (1:4)</td>
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<tr>
<td>20 cc of Serum</td>
<td>100 ml</td>
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## Ocular Autologous Serum Prescription

<table>
<thead>
<tr>
<th>Date:</th>
<th></th>
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<tbody>
<tr>
<td>Patient Name:</td>
<td></td>
</tr>
<tr>
<td>Patient Address:</td>
<td></td>
</tr>
<tr>
<td>Patient Phone:</td>
<td></td>
</tr>
<tr>
<td>Patient DOB:</td>
<td></td>
</tr>
<tr>
<td>Blood Draw:</td>
<td>40 cc venipuncture draw of whole blood, allowed to clot for 15 minutes, and centrifuged at 1,500 rpm for 5 minutes. Transferred in a red top vial.</td>
</tr>
<tr>
<td><strong>Rx</strong></td>
<td>Autologous Serum Solution, Compounded According to the 2009 Tsubota Protocol</td>
</tr>
<tr>
<td></td>
<td>□ 20% □ 30% □ 40% □ 50%</td>
</tr>
<tr>
<td></td>
<td># Evenly divide into 6, 5 ml brown glass, dropper tipped bottles</td>
</tr>
<tr>
<td>SIG:</td>
<td>Instill one drop on:</td>
</tr>
<tr>
<td></td>
<td>□ the Right Eye □ the Left Eye □ Both Eyes</td>
</tr>
<tr>
<td></td>
<td>□ tid □ qid □ q4h □ q3h □ q2h □ q1h</td>
</tr>
<tr>
<td>Refills:</td>
<td>For □ One Month □ Two Months □ Three Months</td>
</tr>
<tr>
<td></td>
<td>□ None □ One □ Two □ Three □ Six-Months □ One Year</td>
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Dallas, TX 75231
214-349-8000
**Patient Instructions and Informed Consent**

The use of your blood serum as an eye drop for the treatment of problems on the eye surface is called “Autologous Serum Administration,” or “AS.” AS is one of several treatments that may be used to improve or cure the problems you are having with your eyes.

**The benefits of using AS** to treat your eyes may include rapid resolution or improvement of the problem you are experiencing, with a reduction in symptoms that you may be experiencing.

**The risks of using AS** include eye infections (even when used properly), treatment failure, expense, and / or a return of symptoms after AS is stopped in some cases (Dr. Newman will discuss this issue with you).

**The alternatives to AS** include, but are not limited to and depending on the condition being treated, commercial eye drops for eye dryness, ocular steroid medications, bandage contact lenses, and amniotic membrane application.

AS has not been approved by the US Food and Drug Administration (FDA), but is considered a standard of care, and has been researched thoroughly.

Using AS involves the drawing of blood with a needle from your body by a Certified Laboratory Improvement Amendments (CLIA) Certified Laboratory (www.cms.gov/clia). The blood serum is then separated by the person who draws the blood (phlebotomist). This process will take up to thirty minutes. The blood serum will then be given to you to transport IMMEDIATELY to the compounding pharmacist. **YOU WILL NEED TO CARRY A SMALL ICE CHEST FILLED WITH ICE WITH YOU TO THE PHLEBOTOMIST.** Upon arriving at the pharmacy, tell the receptionist that you have blood serum for compounding so that they address your needs immediately. **DO NOT EXPOSE THE BLOOD SERUM TO LIGHT.** Call for an appointment with the phlebotomist before you go.

**Instructions for Use**

- Keep only one bottle open at a time.
- The open bottle should be refrigerated at all times.
- All unopened bottles must stay in the FREEZER until opened.
- Unused serum must be discarded after 60 days
- If a bottle is contaminated by touching the dropper tip to anything, it must be discarded immediately and replaced by an unopened bottle.

**Patient Acknowledgement**

I understand these instructions and I acknowledgement of the risks of using serum:

_____________________________   _______________________
Patient Name                Patient Signature

Date: _____/_____/201__