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### MY 1ST CASE:

**PERTINENT EXAM FINDINGS INCLUDE:**

- BEST-CORRECTED VISUAL ACUITY: 20/25- O.D., 20/25- O.S.
- MILD CONJUNCTIVAL INJECTION O.U.
- DIFFUSE SUPERFICIAL PUNCTATE KERATOPATHY O.U.
- 3+ LISSAMINE GREEN STAINING O.U.
- WELL-POSITIONED FREEMAN STYLE SILICONE PUNCTAL PLUGS O.U.
- INTERMITTENT INCOMPLETE CLOSURE ON BLINK O.U.
- SCHIRMER TEAR TEST WITHOUT ANESTHESIA: <1MM IN EACH EYE
- BLINK RATE: FREQUENT (APPROXIMATELY EVERY THREE TO FOUR SECONDS)

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### SYMPTOMS OF DRY EYE

Dry Eye Severity Level	1	2	3	4
<b>General Symptoms</b>	Mild Symptoms	Moderate Symptoms	Severe Symptoms	Severe Symptoms
Symptoms: Itchy, Sandy, Gritty, Dry	Never to Seldom	Sometimes	Frequent	Always
Discomfort: Stinging, Burning, Pain	No	Yes	Yes	Yes
Vision: Blurring, Interrupted	No	No	Sometimes	Usually
Use of Artificial Tears	Less than 2X per day	Several times per day	Several times per day	Several times per day

McDonnell et al. ARVO. 2004.

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### SIGNS OF DRY EYE

Dry Eye Severity Level	1	2	3	4
<b>General Symptoms</b>	Mild Symptoms	Moderate Symptoms	Severe Symptoms	Severe Symptoms
Diagnosis	Mild	Moderate	Marked	Scarring
Conjunctival Staining		Mild punctate	Marked punctate central	Severe punctate erosions
Corneal Staining		Visual signs		
Tear Film			Filamentary keratitis	
Other				
Example Staining				
Tear Film Breakup Time	< 12	> 2 < 7	< 3	< 3
Schirmer Score	> 10	> 5 < 10	< 5	< 2

McDonnell et al. ARVO. 2004.

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## FUNCTIONS OF A HEALTHY TEAR FILM

- OPTICAL CLARITY, REFRACTIVE POWER
- OCULAR SURFACE COMFORT, LUBRICATION
- PROTECTION FROM ENVIRONMENTAL AND INFECTIOUS INSULTS
  - ANTIBACTERIAL PROTEINS, ANTIBODIES, COMPLEMENT
  - REFLEX TEARS FLUSH AWAY PARTICLES
- TROPHIC ENVIRONMENT FOR CORNEAL EPITHELIUM
  - NECESSARY ELECTROLYTES MAINTAIN PH
  - PROTEIN FACTORS FOR GROWTH AND WOUND HEALING
  - ANTIOXIDANTS

Rolando et al. *Dry Eye and Ocular Surface Disorders*, 2004.  
Stem et al. In: *Dry Eye and Ocular Surface Disorders*, 2004.

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**AU·TOL·O·GOUS**

**DEFINITION:**  
**DERIVED OR TRANSFERRED FROM THE SAME INDIVIDUALS  
BODY!**

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## AUTOLOGOUS SERUM EYE DROPS

- SERUM = FLUID COMPONENT OF FULL BLOOD WHICH REMAINS AFTER CLOTTING
- USE FIRST DESCRIBED IN 1984 BY FOX ET AL (FOR KERATOCONJUNCTIVITIS SICCA)
- UNPRESERVED, NON-ANTIGENIC
- BIOMECHANICAL AND BIOCHEMICAL PROPERTIES SIMILAR TO NATURAL TEARS

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## UNSTIMULATED TEARS VERSUS SERUM

- |                            |   |
|----------------------------|---|
| • PH = 7.4                 | • PH = 7.4  |
| • OSMOLALITY = 298         | • OSMOLALITY = 296  |
| • EGF (NG/ML) = 0.2 - 3.0  | • EGF (NG/ML) = 0.5   |
| • TGF-B (NG/ML) = 2 - 10   | • TGF-B (NG/ML) = 6 - 33  |
| • VITAMIN A (MG/ML) = 0.02 | • VITAMIN A (MG/ML) = 46  |
| • LYSOZYME (MG/ML) = 1.4   | • LYSOZYME (MG/ML) = 6  |
| • SIGA (UG/ML) = 1190      | • SIGA (UG/ML) = 2  |
| • FIBRONECTIN (UG/ML) = 21 | • FIBRONECTIN (UG/ML) = 205   |
|                            | • HEPATOCYTE GF, NGF, IGF-1, SUBSTANCE P, COMPLEMENT, FIBROBLAST GF, CGRP, OTHER IG, ETC. |

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## AS - IN VITRO ACTIONS

- CONTAINS EPITHELIO-TROPHIC / MODULATING FACTORS
- PROMOTES GROWTH AND MIGRATION OF OCULAR SURFACE EPITHELIAL CELLS IN VITRO
  - DOSE-DEPENDENT EFFECT ON SV40 TRANSFECTED HUMAN CORNEAL EPITHELIAL CELL LINE (TSUBOTA)
  - EXPRESSION OF MUCIN-1 FROM IMMORTALIZED CONJUNCTIVAL EPITHELIAL CELLS (TSUBOTA)

JAY C. BRADLEY MD & SANDRA BROWN, MD - AUTOLOGOUS SERUM EYE DROPS: FACT OR FICTION?

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## AS – IN VITRO ACTIONS

- MAINTAINS CORNEAL EPITHELIAL CELL MORPHOLOGY AND FUNCTION BETTER THAN PHARMACEUTICAL TEAR SUBSTITUTES (GEERLING ET AL)
- INCREASES TRANSCRIPTION OF RNA FOR NERVE GROWTH FACTOR AND TRANSFORMING GROWTH FACTOR-BETA IN CULTURED HUMAN KERATOCYTES (EBNER ET AL)

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## AUTOLOGOUS SERUM EYE DROPS

- KERATOCONJUNCTIVITIS SICCA DUE TO
  - SJOGREN SYNDROME
  - GRAFT-VS-HOST DISEASE
  - NEUROTROPHIC KERATITIS
  - SUPERIOR LIMBIC KERATOCONJUNCTIVITIS
  - RHEUMATOID ARTHRITIS

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## PREPARATION OF ASE

- **PROTOCOLS IN PUBLISHED REPORTS ARE INCOMPLETE AND VARY SIGNIFICANTLY**
- CONCENTRATION → 20 – 100 % (DILUTENT BSS OR NACL)
- FREQUENCY OF APPLICATION → TID TO HOURLY
- ANTIBIOTIC AS PRESERVATIVE (EG CHLORAMPHENICOL)
- CLOTTING TIME PRIOR TO CENTRIFUGATION → 0 – 2 DAYS
- STORAGE CONDITIONS → -20 TO +4 DEGREES CELSIUS

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## SLK

- PROSPECTIVE COHORT STUDY WITH 11 PATIENTS (GOTO ET AL)
- USED 20 % ASE AS ADDITIONAL THERAPY 10 TIMES DAILY
- WITHIN 4 WEEKS DISCOMFORT IMPROVED IN 9 OF 11 AND EPITHELIOPATHY IMPROVED IN ALL PATIENTS
- SIGNIFICANTLY INCREASED TBUT AND DECREASED CONJUNCTIVAL SQUAMOUS METAPLASIA
- DISCOMFORT RECURRENT WITH DISCONTINUATION OF ASE

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## RECURRENT EROSION SYNDROME

- PROSPECTIVE COHORT STUDY OF 11 PATIENTS WITH UNILATERAL POST-TRAUMATIC RES (DEL CASTILLO ET AL)
- USED NPAT AND ASE 20 % TID FOR 3 MONTHS IN TAPERED FASHION
- MEAN RECURRENCE RATE WAS REDUCED FROM 2.2 TO 0.028/MONTH OF F/U (MEAN F/U 9.4 MONTHS)
- GIVEN SELF-HEALING NATURE OF POST-TRAUMATIC RES, THE FACT THE DURATION SINCE TRAUMA WAS NOT SPECIFIED, AND THE FAILURE TO STATE IF OTHER PREVIOUSLY USED MODALITIES WERE SUSPENDED DURING ASE USE, THESE DATA HAVE TO BE REVIEWED WITH CARE

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## PERSISTENT EPITHELIAL DEFECTS

- 4 MAJOR REPORTS
- N = 112 EYES
- 20 – 100 % ASE AT 6 X/DAY TO HOURLY FREQUENCY
- OVERALL SUCCESS > 73 %
- MOST HEALED WITHIN 2 – 4 WEEKS OF ASE INITIATION
- 18 % RECURRENT UPON ASE DISCONTINUATION

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## ADJUNCTIVE TREATMENT IN OCULAR SURFACE RECONSTRUCTION

- 14 EYES OF 10 PATIENTS RECEIVING LIMBAL STEM CELL TRANSPLANT, AMNIOTIC MEMBRANE, AND/OR PK WERE TREATED WITH 20 % ASE (TSUBOTA ET AL)
  - OCP/SJS WITH SCHIRMER = 0
  - 12 OF 14 HAD STABLE EPITHELIUM AT 20 WEEKS
- 2 PATIENTS UNDERGOING PK FOR PED (POON ET AL)
  - ACHIEVED STABLE EPITHELIUM WITH ASE
  - EPITHELIOPATHY RECURRED UPON ASE DISCONTINUATION

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## CRITICISMS

- VARIATIONS IN THE STUDY POPULATIONS SUCH AS DEGREE OF AQUEOUS DEFICIENCY
- VARIATIONS IN PRODUCTION AND TREATMENT PROTOCOL FOR ASE
- ADDITIVE RATHER THAN SUBSTITUTIVE THERAPY
- THERAPEUTIC CTL OR PUNCTAL OCCLUSION
- INCREASING FLUID SUPPLY RATHER THAN THE EPITHELIO-TROPHIC NATURE OF ASE MAY HAVE YIELDED THE BENEFICIAL EFFECT
- COMPARISON OF PUBLISHED DATA IS FURTHER LIMITED BY VARIATIONS IN REPORTING "SUCCESS OF TREATMENT" AS
  - NUMBER OF PATIENTS IMPROVING
  - MEAN CHANGE IN PARAMETER

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## COMPLICATIONS

- NUMBER OF COMPLICATIONS IN THE 255 PATIENTS REPORTED TO HAVE BEEN TREATED WITH ASE IS SMALL
  - SCLERAL VASCULITIS AND MELTING IN RA PATIENTS
  - IMMUNE COMPLEX DEPOSITION WITH 100 % SERUM
  - PERIPHERAL CORNEAL INFILTRATE AND ULCER (N=1)
  - INCREASED DISCOMFORT OR EPITHELIOPATHY (N=5)
  - MICROBIAL KERATITIS IN PATIENTS WITH EPI DEFECT (N=3)
  - TEMPORARY BACTERIAL CONJUNCTIVITIS (N=5)
  - EYELID ECZEMA (N=2)
- SOME COMPLICATIONS POSSIBLY DUE TO UNDERLYING DISEASE OR OTHER THERAPY (RETAINED SUTURE MATERIAL, BANDAGE CTL)

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**“EFFECT OF AUTOLOGOUS SERUM EYEDROPS  
IN THE TREATMENT OF SEVERE DRY EYE”**

- KOJIMA ET AL. AM J OPHTHALMOL 2005;139:242-6.
- **PROSPECTIVE RANDOMIZED CASE-CONTROL TRIAL**
- 37 EYES OF 20 SEVERE DRY PATIENTS WITHOUT PUNCTAL OCCLUSION
- AFTER 2 WEEK WASH-OUT, RANDOMLY ASSIGNED TO TWO GROUPS
  - A – ONLY PRESERVATIVE-FREE ARTIFICIAL TEARS
  - S – ONLY AUTOLOGOUS 20 % SERUM EYEDROPS 6 TIMES A DAY
- IMPROVED MEAN TBUT, F/RB STAINING SCORES, AND SUBJECTIVE SYMPTOM SCORES IMPROVED

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**FURTHER STUDY NEEDED:**

- DEVELOPMENT OF FDA-APPROVED MANUFACTURING PROTOCOL
  - STABILITY
  - STERILITY
  - STORAGE
- CLINICAL TRIALS
  - TIGHT INCLUSION AND EXCLUSION CRITERIA TO ACHIEVE HOMOGENEOUS PATIENT POPULATIONS
  - DOSE-RESPONSE INVESTIGATION
  - CROSS-OVER STUDIES
- EXPANSION OF INDICATIONS
- EVENTUALLY –
  - FRACTIONATION OF SERUM COMPONENTS TO DETERMINE ACTIVE PORTION
  - TRUE CHEMICAL SUBSTITUTION

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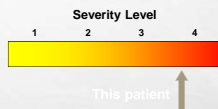
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**CASE EXAMPLE  
DIAGNOSIS AND TREATMENT**

**DIAGNOSIS**

- PRIMARY SJÖGREN'S SYNDROME



Treatment	Eye Care Professional	Rheumatology
Initial	Education Cyclosporine Topical corticosteroids Nonpreserved artificial tears	Pilocarpine Cevimeline Hydroxychloroquine Minimize anticholinergics
Follow-up	Nighttime lubricant gel Punctal plugs	Self-stopped pilocarpine (cost) Rituximab clinical trial

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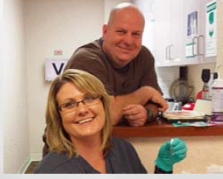
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**THANK YOU!**



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