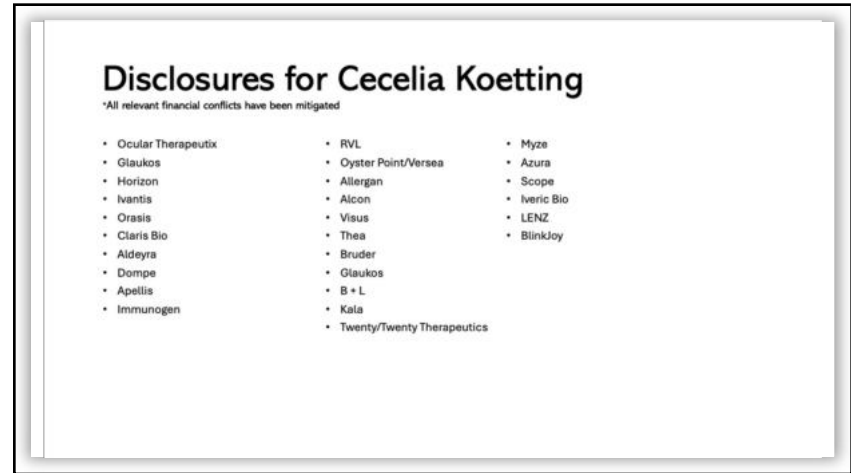
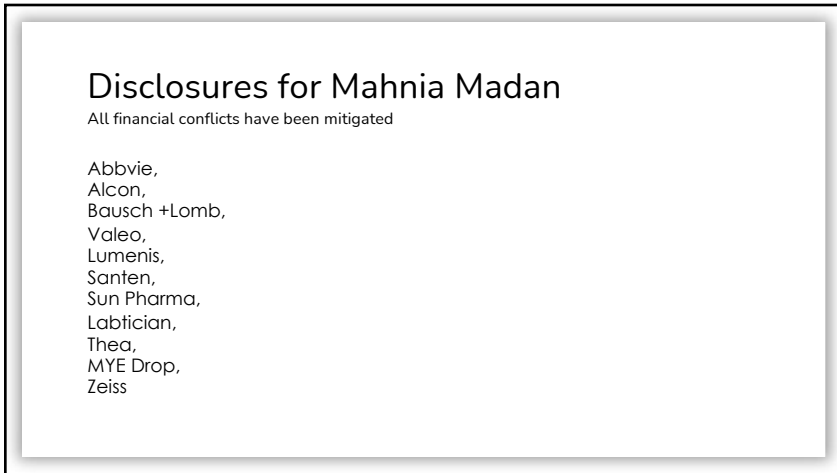


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5

**FDA warns consumers not to purchase or use EzriCare Artificial Tears due to potential contamination**

**FDA warns consumers not to purchase or use certain methylsulfonylmethane (MSM) eye drops due to contamination**

Update [8/20/2023] FDA is warning the public that these recalled products should not be used, including off-label use in animals. FDA does not have direct knowledge of veterinary use of these products or of animal adverse events that are linked to the products; however, on August 14, 2023, the New Jersey Department of Health issued a health alert to notify consumers of using for animal concerns to immediately discontinue using EzriCare Artificial Tears, Delsam Pharma Artificial Tears, and Delsam Pharma Artificial Ointment on animal patients.

If you suspect that an animal under your care contracted an infection or serious side effects from these products, please report it to FDA. Visit <https://www.fda.gov/medwatch> and <https://www.fda.gov/medwatch>.

Update [8/20/2023] FDA is warning consumers not to purchase and to immediately stop using Dr. Berne's MSM Drops 5% Solution and LightEyez MSM Eye Drops – Eye Repair due to bacterial contamination, for:

**Examples of microbial contaminants found in products:**

Product	Bacterial contamination	Fungal contamination
Dr. Berne's MSM Drops 5% Solution	Bacillus, spp.	Erspizia, sp.
LightEyez MSM Eye Drops – Eye Repair	Pseudomonas, spp.; Mycobacterium, spp.; Mycobacterium, spp.; Methylobacterium, spp.	N/A

6

**List of eye drops recalled so far in 2023/2024**

- **Dr. Berne's MSM Drops 5% Solution and LightEyez MSM Eye Drops–Eye Repair (August).**
  - The FDA issued a warning to consumers, noting that testing determined that the drops were not sterile and contained microbes. They also contained methylsulfonylmethane (MSM) as an active ingredient, which is unapproved for use in the U.S.
- **EzriCare artificial tears (March).**
  - These drops were linked to a multistate outbreak of an extensively drug-resistant strain of *Pseudomonas aeruginosa*, per the [CDC](https://www.cdc.gov).
- **Delsam Pharma's artificial tears and ointment (March).**
  - As a part of the same recall as EzriCare artificial tears, these drops were linked to a multistate outbreak of *Pseudomonas aeruginosa*, per the [CDC](https://www.cdc.gov). "The outbreak is associated with multiple types of infections, including eye infections," the CDC noted in its initial warning.
- **Purely Soothing 15% MSM Drops (March).**
  - These drops were recalled after two lots were found to not be sterile. No illnesses were tied to the recall.
- **Clear Eyes Once Daily, Eye Allergy Itch Relief (February).**
  - Teva Pharmaceuticals recalled select batches of the eye drop after they failed an impurities test. More than 700,000 bottles were recalled.
- **Brimonidine Tartrate Ophthalmic Solution, 0.15% (March).**
  - These eye drops, which are intended to be used by people with glaucoma or ocular hypertension, had faulty caps that could lead to unsterile solutions, the [FDA](https://www.fda.gov) noted.

7

**Eyedropsafe.org**

- Generic OTC Artificial tear Brands :
  - Rite aid
  - CVS
  - Cardinal Health
  - All Similisan
  - Off Brand Lumify's
  - Target Up and Up
  - Walmart Equate

8

### FDA investigations pending

- Freshkote
- RegenerEyes
- Ashland Eyecare Organic Eye Oil drops

9

### Things to consider

<p><b>DO's</b></p> <ul style="list-style-type: none"> <li>Suggest specific brands</li> <li>Give sample if possible or send Rx</li> <li>Preservative Free when appropriate</li> <li>Hyaluronic Acid</li> <li>Gels and ointments</li> <li>Lipid supplementing?</li> </ul>	<p><b>Don'ts</b></p> <ul style="list-style-type: none"> <li>Vasoconstrictors/redness relief</li> <li>BAK</li> </ul>
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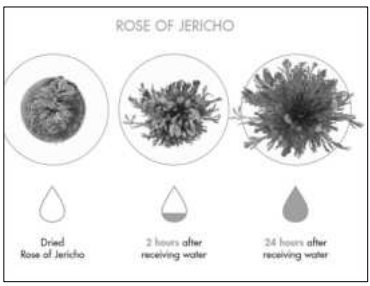
10

### Hyaluronic acid

- Glycosaminoglycan**
  - High molecular weight polysaccharide
  - In our connective tissue, synovial fluid, and AH and vitreous of the eye
- Ability to bind or retain water**
  - Bind up to 1000 times its weight
- Viscoelasticity**
  - Helps stabilize tear film
- Wound healing**
  - Aids in epithelial cell proliferation, healing and migration
- Different molecular weights**
  - Hold different amounts of water, high weight holds more

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### Trehalose



Used frequently outside US

Found in nature as a bioprotectant and osmoprotectant

Helps to protect corneal cells from desiccation and high osmolarity

- Fortifies the cell membrane
- Prevents denaturation of proteins in the absence of water

Schmidl's 2015 trehalose-containing drops increased patients' tear film thickness as measured by OCT, after instillation of only one drop, up to 240 minutes compared with drops without trehalose

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## HA + Trehalose VS. HA only

Chiambaretta's 2017 study

3-6 x day 84 days with either hyaluronic acid (HA) with trehalose vs. HA only

Questionnaires, Schirmer testing, tear film breakup time and conjunctival hyperemia scores

The authors concluded that **HA with trehalose was more effective, and gave better patient satisfaction**

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## 69 YOF - My Mom

CC: Sharp jabbing pain left forehead and scalp

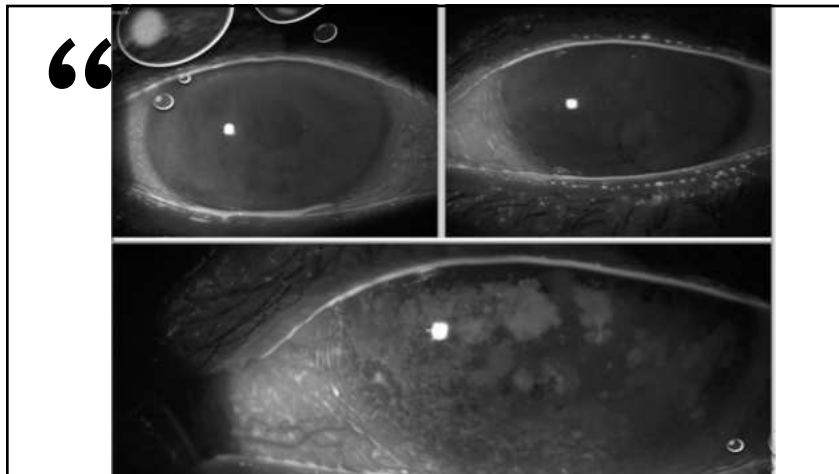
Red eye, excessive tearing, blurred vision, photophobia, and decreased visual acuity ongoing for months.

Tx: Using AT, hot compresses, Pred Forte QD, Valcyclovir, Gabapentin

Hx: Cataract surgery, HTN, High Cholesterol



14



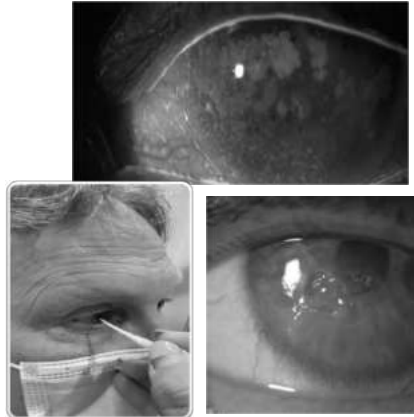
15

## Neurotrophic Keratitis

NK is a corneal disease characterized by a reduction or absence of corneal sensitivity

Impaired corneal nerve leads to

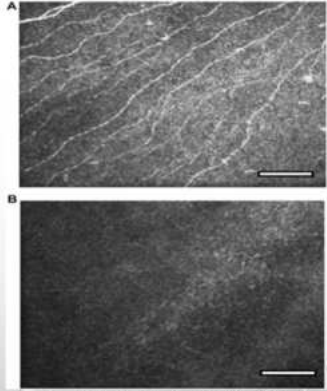
- Impaired corneal healing
- Reduced tear production
- Reduced blink rate
- Leads to non healing corneal defects



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### PREVALENCE

- 65,000 CASES IN NA
- 1-5 CASES/10,000
- RARE BUT DEVASTATING
- 6-12.8% OF **HERPETIC/ZOSTER KERATITIS**

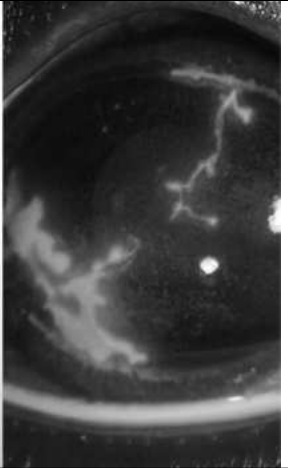


Sacchetti et al. Clinical Opth. 2014  
Dworkin et al. Clinical Opth. 2007

17

### CAUSES OF NK

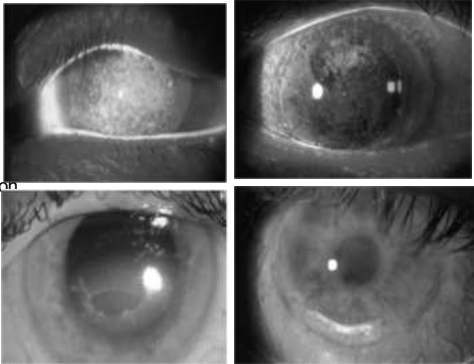
- OCULAR
  - INFECTIONS - HERPES (ZOSTER/SIMPLEX) – 12%
  - INJURY – CL MISUSE, DIRECT INJURY, OSD, EXPOSURE KERATOPATHY
  - CHEMICAL – BAK, GLAUCOMA MEDS, NSAIDS, ANESTHETIC DROPS
  - SURGERY – REFRACTIVE, GLAUCOMA, CORNEA, RETINA SURGERY (SB), PRP FOR DR, CATARACT
- SYSTEMIC
  - DIABETES
  - VIT A DEFICIENCY
  - MS
- GENETIC
- OTHER CAUSES – BRAIN SURGERY, BRAIN TUMORS, ANEURYSMS, STROKE, CNS DEGENERATION



18

### Clinical Presentation

- “Stain with out pain”
- Signs don’t match symptoms
- Lack of distress
- Reduced or absent corneal sensation
- Conjunctival injection
- Photophobia, epiphora,
- corneal neovascularization



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Table 1  
Demographic characteristics of Stage 1 NK patients

Patient	Gender	Age range (years)	Eye involvement	Etiology of NK	Contact lens use	Previous ocular surgery
1	Female	70	Both	Iatrogenic (Glaucoma drops)	+	-
2	Female	80	left	Herpetic NK	+	-
3	Female	60	left	Herpetic NK	-	Cataract
4	Male	80	Both	Dry eye syndrome	-	-
5	Female	70	Both	Romexia	-	-
6	Male	90	Both	Puck's endothelial dystrophy	-	Cataract + Puck's surgery
7	Female	90	Both	Herpetic NK	-	-
8	Female	70	Both	Dry eye syndrome	-	Cataract + Pharyngitis
9	Female	90	Both	Dry eye syndrome	+	-
10	Male	70	left	Paralytic bullous keratopathy + iatrogenic (Glaucoma drops)	+	Multiple glaucoma surgeries
11	Male	90	Both	Iatrogenic (Glaucoma drops)	-	-
12	Female	80	Both	Dry eye syndrome	-	-
13	Male	50	left	Neurosurgical cause (meningioma)	+	-
14	Male	90	Both	Previous vitrectomy + laser retinopathy	-	Radial keratotomy
15	Male	80	Both	Iatrogenic (Glaucoma drops)	-	Cataract

Ghalibafan S, Osei K, Amescua G, Sabater A. Efficacy of Plasma Rich in Growth Factors (PRGF) in Stage 1 Neurotrophic Keratitis

20



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### DRY EYE TREATMENT

- Lifestyle changes
- Modify risk factors
- AT, Omega 3
- Lid hygiene, hot compresses
- Autologous Serum/PRP
- Recombinant GF
- Amniotic Fluids
- Oral Secretagogues
- Bandage CL/Amniotic Membrane
- Scleral CL

---

- Topical steroids,
- PFAT, Gel drops
- Lifitegrast/Cyclosporin
- Topical/Oral antibiotics
- Punctal Plugs,
- Eyelid treatments
- Steroids long term
- Amniotic graft
- Surgical

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### How It All Started?

- The Ebers Papyrus 1534 BC - first reference of a blood use in the eye.
- In 1975, Ralph et al. used it in dry eye
- In 1984, Fox et al. used AS as treatment for DED

23

### PRP APPLICATIONS

PRP FOR HAIR LOSS

BEFORE

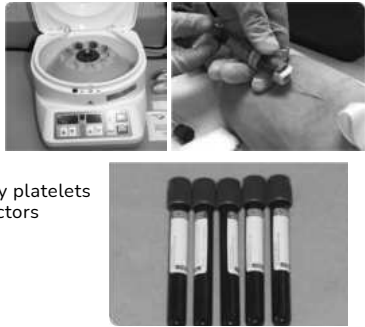
"Vampire Facial" Made Popular by Kim Kardashian

24

## BLOOD BIOLOGICS TO THE RESCUE


AS, PRP, PRGF, PRF, L-PRF, PL

- All made by centrifugation of blood
- All derived from growth factors released by platelets
- All provide different amounts of growth factors



25

In almost every form of OSD, a lubricating drop is needed



What is a good eye drop?

26

## Human Tear: 1800 Known Molecules

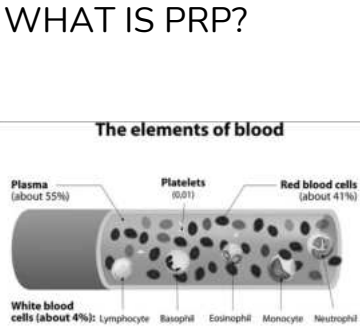
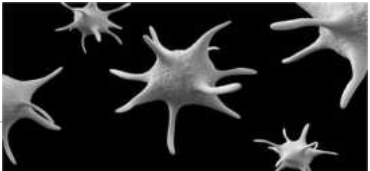
- Perfect lubricant
- Antimicrobial activity
- Anti-inflammatory activity
- Nourishing
- Maintain clarity of cornea
- **Epitheliotropic** - supports proliferation, migration & differentiation of corneal and conjunctival cells



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## WHAT IS PRP?

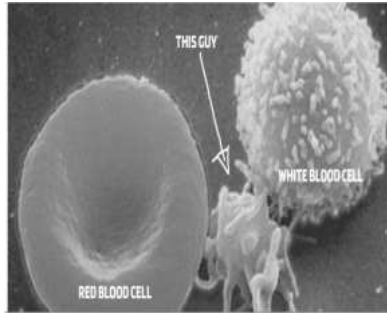
The elements of blood

PRP – 3-5x platelet concentration than whole blood

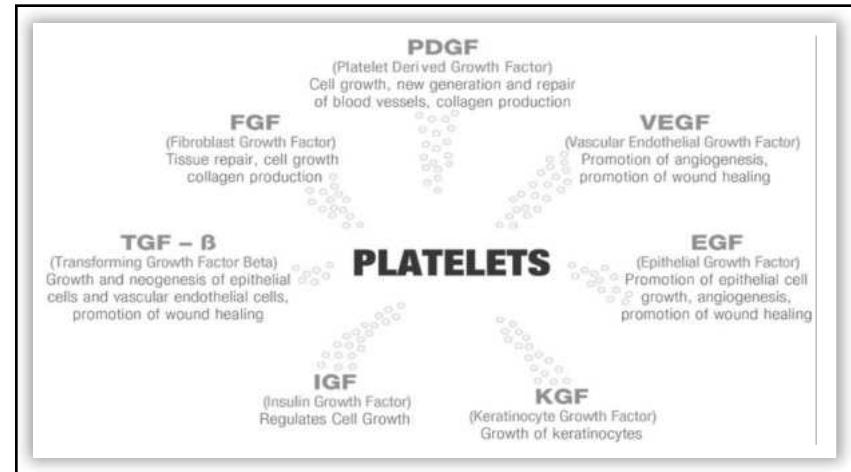
28

### WHY PLATELETS?



- Contain GROWTH FACTORS
- Considered true powerhouse for healing
- Not only involved in clot formation, play a key role in tissue repair and regeneration
- Epitheliotropic

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### PLASMA = Plasma Factors

- Makes up 55% of blood
- Proteins- albumin/fibrinogen
- Immunoglobulins – fight infections
- Electrolytes – maintain cell function



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Physico-chemical parameters (31, 57)	TEARS	PRP	
Chemistry, moles/l	5.0	25	Maintains physiological osmolarity and pH
pH	7.2-7.4	7.2-7.4	Support tear surface tension, physiological hydration of the ocular surface and ocular homeostasis
Proteins (33, 55, 56, 74)	7.37	60-70	Anti-apoptotic activity, detoxification
Total proteins, mg/ml	0.05	20-40	Adhesion protein supporting wound healing
Albumin, mg/ml	2.1	200-300	Anti-microbial
Fibrinogen, mg/ml	0.030	6-12	Endotoxin binding
IgA, mg/ml	0.41	0.5	Anti-collagenase
IgM, mg/ml	-	3-500	Anti-microbial; bacteriocidal
IgG, mg/ml	-	0.25-0.7	Anti-microbial and anti-inflammatory
Alpha 2 macroglobulin	-	2.9	Iron carrier; anti-microbial
Complement system	-	-	
Lactoferrin, mg/ml	1.01	-	
Triaxoferrin, mg/ml	-	2-3	
Lysozyme, mg/ml	1.4	6	
Growth factors (35-57, 67)			Epithelial and stromal repair processes
TGF-beta 1, ng/ml	2-10	6-50	Enhances mitosis and healing
PDGF, ng/ml	0.59-1.7	30-100	Accelerates the migration of epithelial cells; anti-apoptotic
EGF, ng/ml	0.3-3	0.5-1	Supports corneal epithelial cells
HGF, ng/ml	0.3-0.5	0.1-1	Supports conjunctival endothelial permeability
VEGF, ng/ml	0.019	1-5	
Vitamins (33)			Prevents squamous metaplasia and helps maintain the normal histology in the conjunctiva
Vitamin A, ng/ml	16-2	500-1000	Antioxidant
C, mg/ml	117	7-20	
Antioxidants (33)			
Tyrosine, µM	40	77	
Cholesterol, µM	107	NO	
Electrolytes			
Na+, mEq/L	146	135-146	
K+, mEq/L	24.1	3.5-5.0	
Ca <sup>2+</sup> , mM	1.5	1.1	
Cl <sup>-</sup> , mM	126	96-108	
HCO <sub>3</sub> <sup>-</sup> , mM	26	21-29	
HCl, mM	0.14	0.13	
PO <sub>4</sub> <sup>3-</sup> , mM	0.22	1.42	
SO <sub>4</sub> <sup>2-</sup> , mM	0.39	0.53	

32

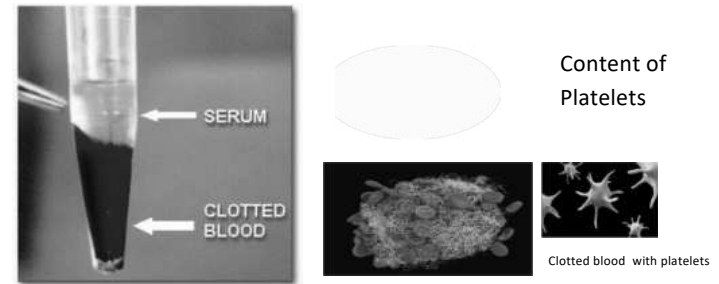


### Benefits of PRP

- Neurosensory Repair = Growth factors (Epitheliotropic)
- Anti-inflammatory = Cytokines
- Prevent Infections = Immunoglobulins/Proteins
- Repair Osmolarity = Dilute proinflammatory mediators
- Natural Analgesic Actions = Reduces pain
- Resembles biological tears = pH/osmolarity
- PRP is natural = No preservatives/stabilizers
- No side effects = No burning or stinging

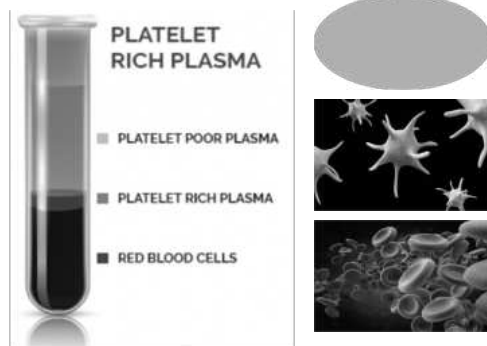
33

### Preparation - Autologous Serum



34

### Preparation - PRP



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### AS VS PRP?

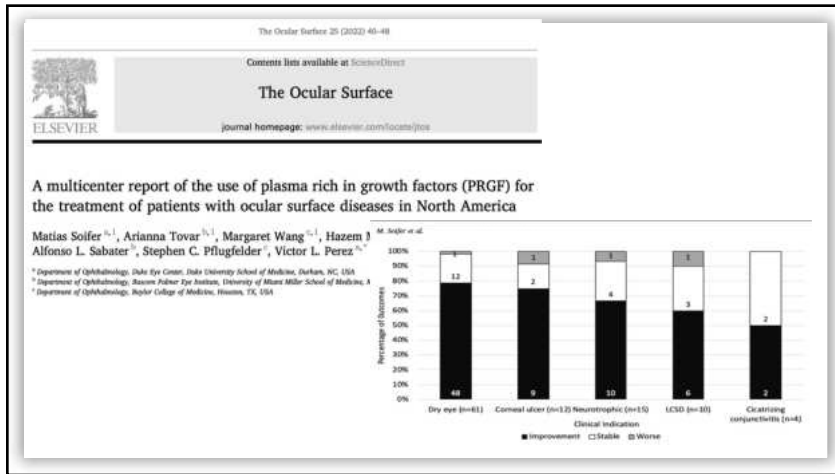
#### AS

- Does NOT contain platelets
- Less concentration of GF/Plasma factors
- Serum is not plasma
- Has inflammatory cytokines
- Contains high amounts of TGF-Beta – suppress wound healing
- Diluted with saline (20-50%) to reduce inflammatory cytokines (further dilutes GF)

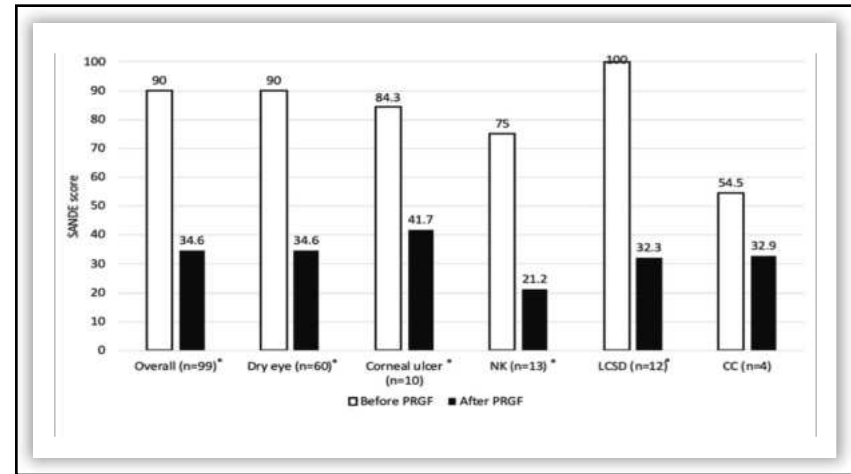
#### PRP

- Contains Platelets
- High Concentration for GF and Plasma Factors
- GF released in a biologically relevant ratio
- No inflammatory cytokines
- Not diluted
- Dispensed 100%
- Considered superior to AS
- Used in medicine

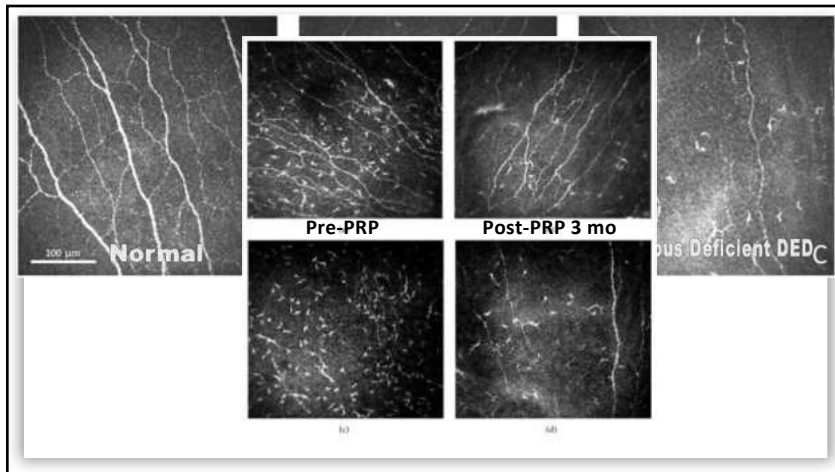
36



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### AUTOLOGOUS SERUM IN NK

- MATSUMOTO ET AL IN 2004 – AS 20%
- YOON ET AL. IN 2007 – UMBILICAL SERUM 20%
- JENG AND DUPPS 2009, 2013 – AS 50% AND 100%

<sup>1</sup> Ophthalmology. 2004; Jan;111(1):119–20. doi: 10.1016/j.ophtha.2003.10.016  
**Autologous serum application in the treatment of neurotrophic keratopathy**  
Yukihiko Matsumoto<sup>1</sup>, Masao Sugita, Eiji Goto, Yoshiko Okamoto, Takashi Kojima, Reiko Ishida, Kazuo Tsubota

<sup>2</sup> Ophthalmology. 2007; Sep;114(9):1637–42. doi: 10.1016/j.ophtha.2006.12.014. Epub 2007 Mar 26  
**Application of umbilical cord serum eyedrops for the treatment of neurotrophic keratitis**  
Kyoung-Chul Yoon<sup>1</sup>, Yi-Chuan Yoo, Seung-Kyo Im, Tae-Sun Jeong, Yeoung-Gook Park, Jin Chul

40

## PRP/PRGF IN NK

**YOU ET AL. IN 2020 – LOOKED AT 117 STUDIES ON PRP/PRGF IN OSD**

**“PRP/PRGF IS MORE EFFECTIVE ON THE REDUCTION OF OCULAR SURFACE INFLAMMATION THAN AUTOLOGOUS SERUM.”**

**Human Platelets and Derived Products in Treating Ocular Surface Diseases – A Systematic Review**

Jingling You,<sup>1,2</sup> Chris Hoopes,<sup>1,3,4,5</sup> Marina Hoopes,<sup>6</sup> Constantinos Pektouros,<sup>1,4</sup> and Gerard Suber<sup>1,3,4</sup>

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**PRGF exerts more potent proliferative and anti-inflammatory effects than autologous serum on a cell culture inflammatory model**

E. Aniza<sup>1</sup>, F. Muruzabal<sup>1</sup>, M. de la Fuente<sup>1</sup>, A. Riestra<sup>1</sup>, J. Merayo-Lloves<sup>1</sup>, G. Orive<sup>1,2,3,4,5,6,7</sup>

<sup>1</sup>Biotechnology Institute IMASD, Madrid, Spain  
<sup>2</sup>Autologous Conditioned Serum (ACS) Laboratory of Ocular, Spain  
<sup>3</sup>Research Unit, Laboratory of Pharmaceutical Sciences of the Spanish University of Pharmacy, Madrid, Spain  
<sup>4</sup>Research Unit, Research Center in Biotechnology, Biomedical and Nanomedicine (RCBUN), Madrid, Spain

41

J. Ocul Pharmacol. 2018; 2018: 3538754.  
 Published online 2018 Jun 25. doi: 10.1155/2018/3538754

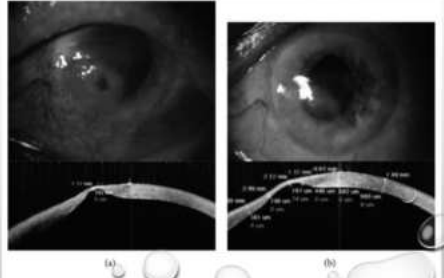
PMCID: PMC6031214  
 PMID: 30029885

**Clinical Efficacy of Platelet-Rich Plasma in the Treatment of Neurotrophic Corneal Ulcer**

Domitinka Vrhovnik-Duhovnik,<sup>1\*</sup> Jerne Jalu,<sup>2\*</sup> Anesorka Rodrovic,<sup>3</sup> Eva Svethovode-Furstenovic,<sup>4</sup> Erika Krasnar-Jancic,<sup>5</sup> Beata Petrovacki-Jancic,<sup>6</sup> Anesorka Cerinjak-Hranica,<sup>7</sup> and Jurek Zecirovic<sup>1</sup>

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- 97.4% ACHIEVED THE COMPLETE RESOLUTION OF CORNEAL DEFECT/ULCER
- MEAN RESOLUTION TIME WAS 11.4 WEEKS
- REDUCTION IN OSDI (60.9%)
- BCVA (52.8%) WAS OBSERVED



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## EMERGING THERAPIES FOR NK

ClinicalTrials.gov

Home • Search Results • Study Record

UNKNOWN STATUS

ClinicalTrials.gov Identifier: NCT02707130

**Efficacy and Safety of Plasma Rich in Growth Factors (PRGF-Endoret) Eye-drops in the Treatment of Neurotrophic Keratitis**


Information provided by Biotechnology Institute IMASD (Responsible Party)  
 Last Update Posted: 2017-07-14

- INSULIN (INSULIN GROWTH FACTOR) + SUBSTANCE P NEUROTRANSMITTER
- VARENICLINE
- NGF MIMETICS
- THYMOSIN

Kody D. Larkin DFP, Karappa. Front Pharmacol. 2022 Mar 22.

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## Who Can Benefit From PRP?




- Mild/moderate/severe DED
- Aqueous and Evaporative
- LASIK/PRK induced
- Neuropathic/Neurotropic
- Corneal ulcers/RCE
- Persistent Epi defects
- Autoimmune (SS) dry eye
- Patients want natural options

44

“

And when clinicians do recommend blood derivatives, they are implemented only as an end-stage therapy, when patients could have benefitted from them much earlier.”

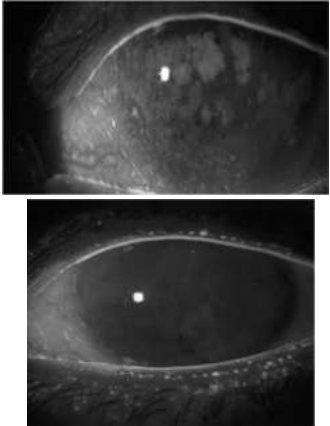
*Ophthalmology Times*



45


### Management Plan

- PRP TID - QID OD
- PF steroids QD
- Cyclosporine BID
- Antihistamine/Mast Cell
- Stabilizer PF - QD



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### OTHER APPLICATIONS OF PRP



Patient Treated with PRP Insert

1 Month RLL      3 Month F

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- How does autologous serum compare to PRP to PRGF and PRF?
- What type of patients would benefit from PRP?
- Do patients have to be on PRP for ever? Do you taper?
- Do you draw the blood?
- What equipment do you need?
- How much does it cost the patient? Doctor?

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## THANK YOU



**Mahnia Madan, OD, FAAO**  
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Co-founder MYE Drop  
Vancouver Eye Dr

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University of Colorado School of Medicine  
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