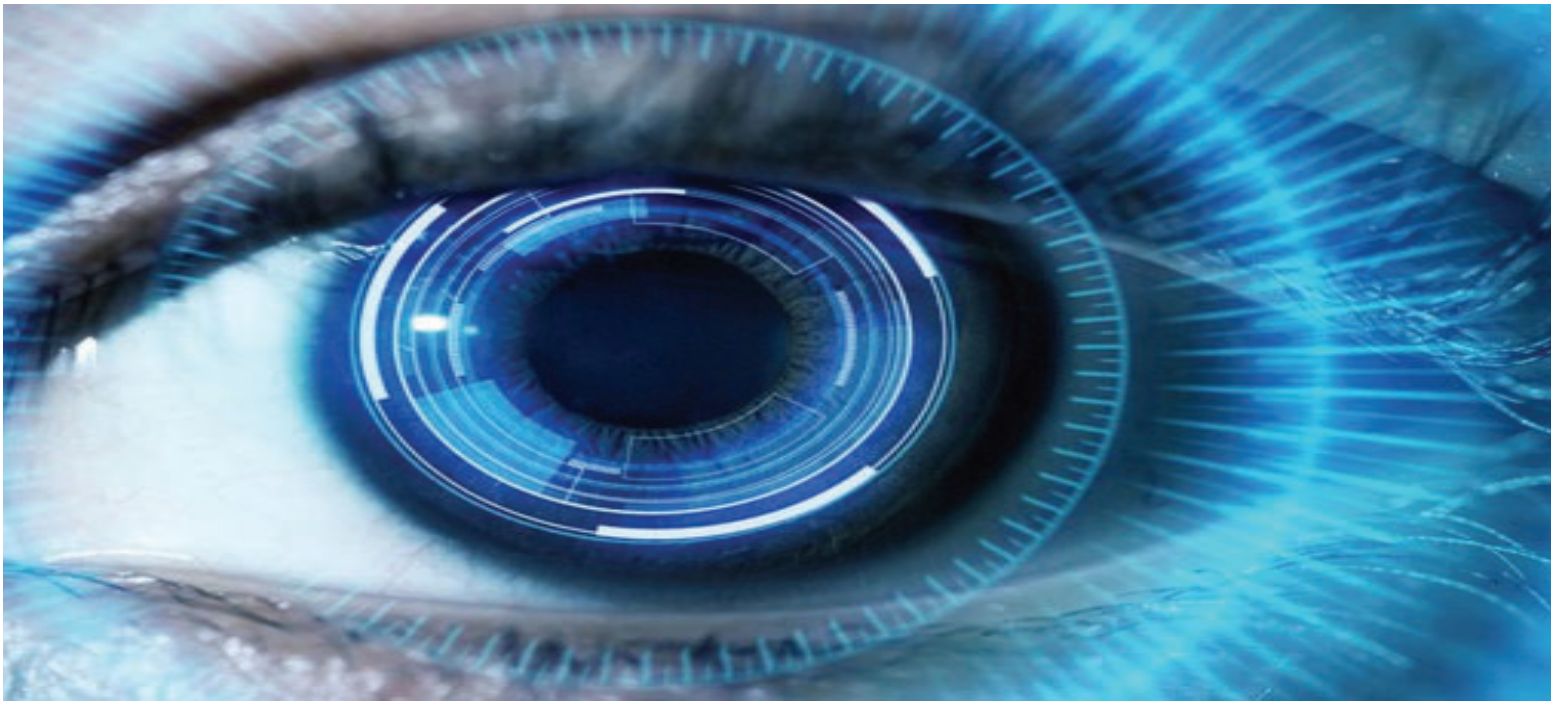
DRY EYE INNOVATIONS: FROM PRP TO IPL



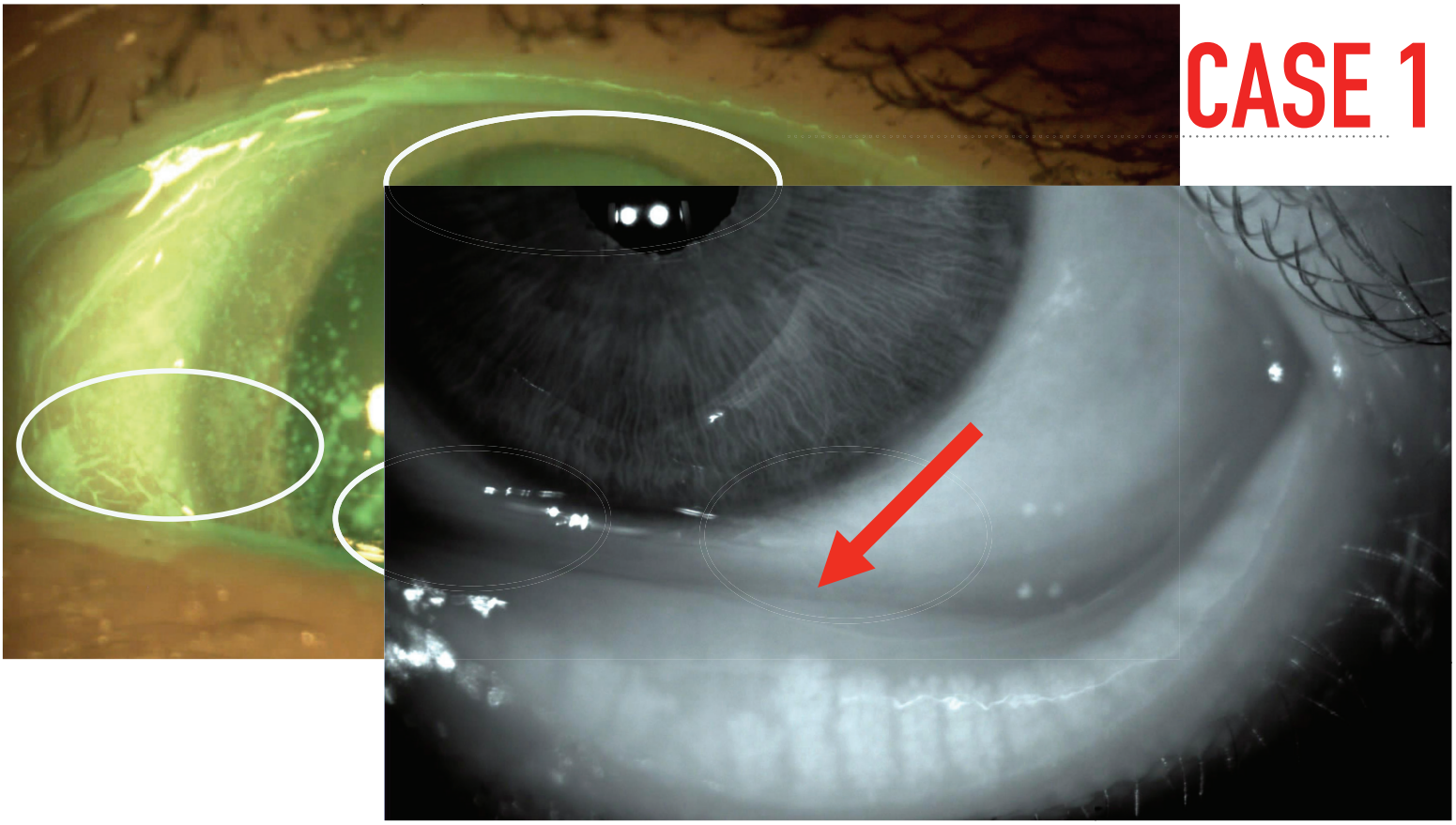
Mahnia Madan, OD, FAAO. Adjunct Faculty Pacific University College of Optometry. Vice President BC Doctors of Optometry. www.vancouvereyedr.ca

PATIENT – SARA

- 55 YOWF
- CC: Referral for dry eyes
  - Burning, redness
  - Sand or gravel in the eyes
  - "Eyes feel so tired, I just want to close them"
  - Constantly using drops
- VA: OD: 20/25- OS: 20/25-

HISTORY

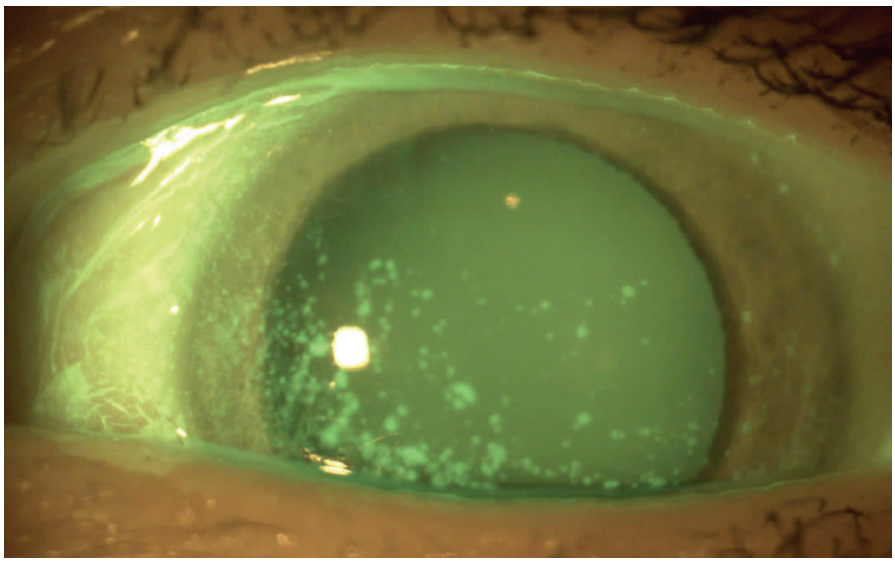
- Dry Eyes
  - Hylo Gel QID
  - Xiidra BID
  - Omega 3/Bruder
  - Moisture goggles
- Medical
  - Sjogren's Syndrome
  - Breast Cancer
  - Sarcoidosis (no Tx)

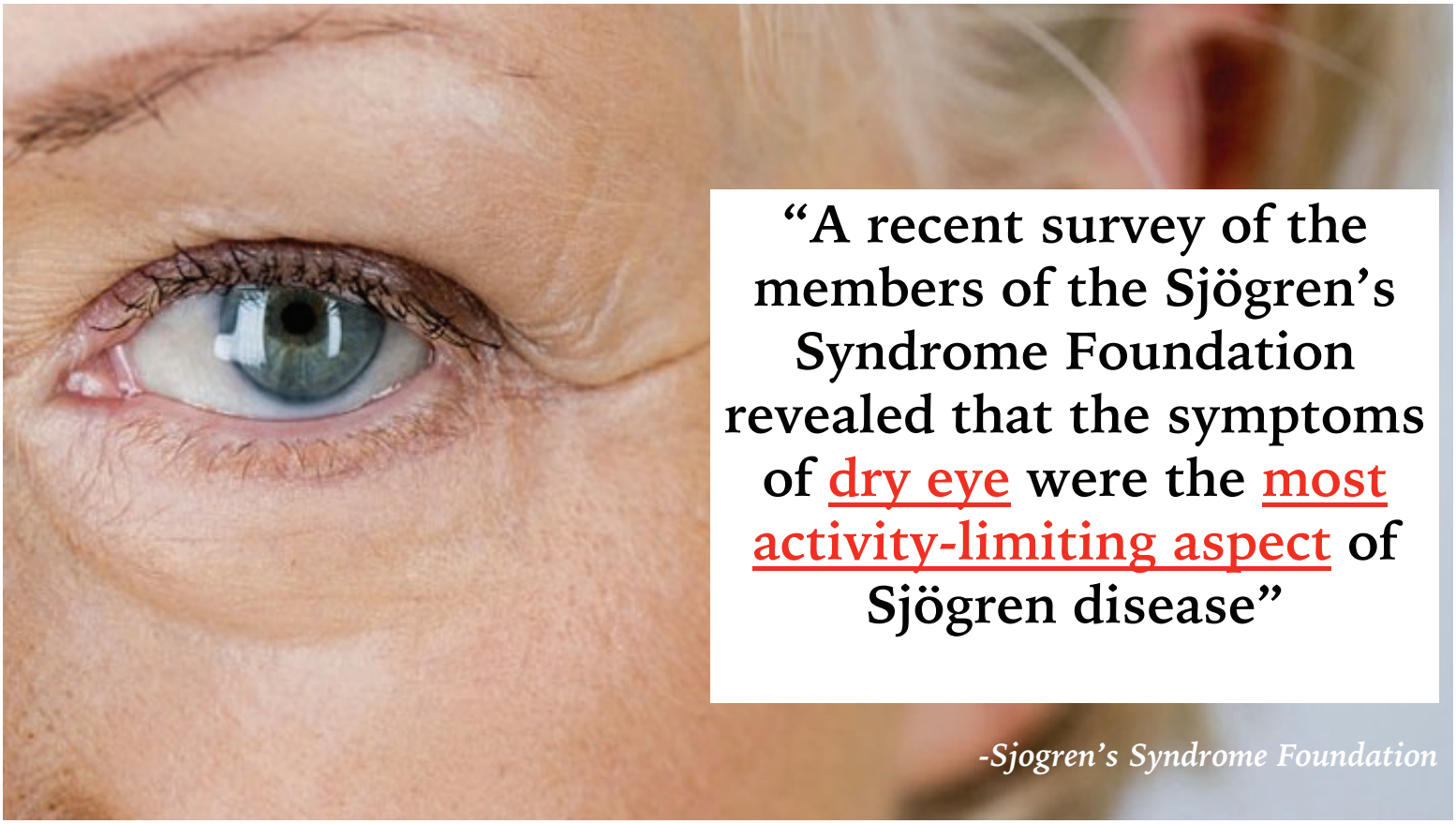


CASE 1

SJOGREN'S SYNDROME (SS)

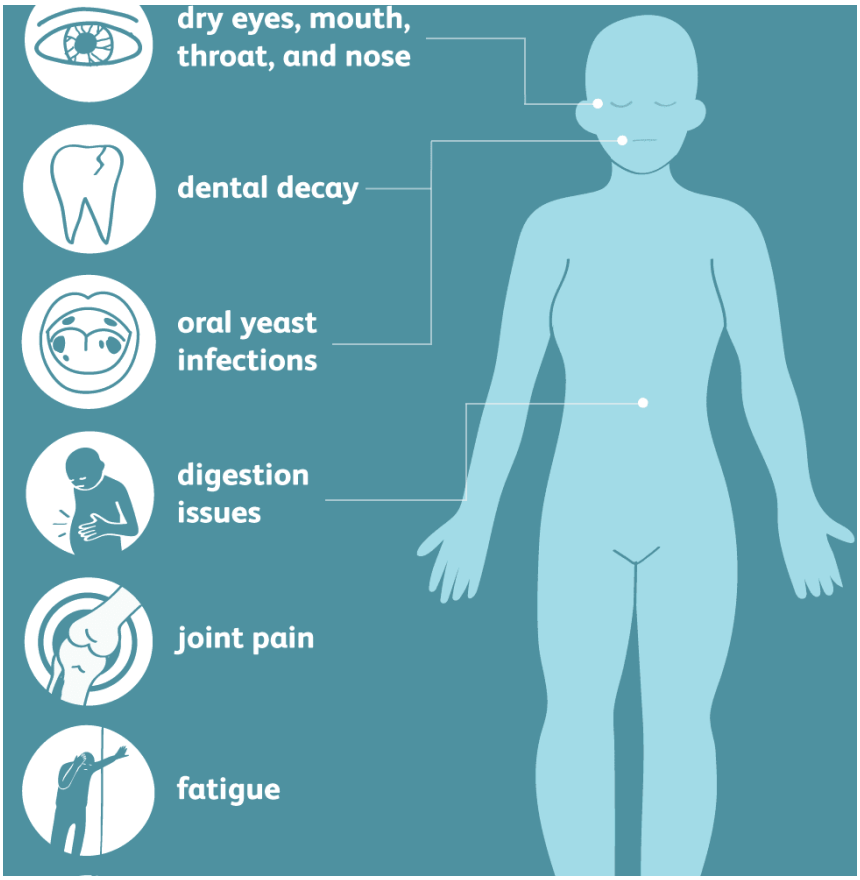
- 2nd most common autoimmune rheumatic disease
- 9 to 1 - women
- Dry eye diagnosis can precede systemic diagnosis by 3 years
- Eye doctors - first line of detection for SS
- Primary and Secondary





"A recent survey of the members of the Sjögren's Syndrome Foundation revealed that the symptoms of dry eye were the most activity-limiting aspect of Sjögren disease"

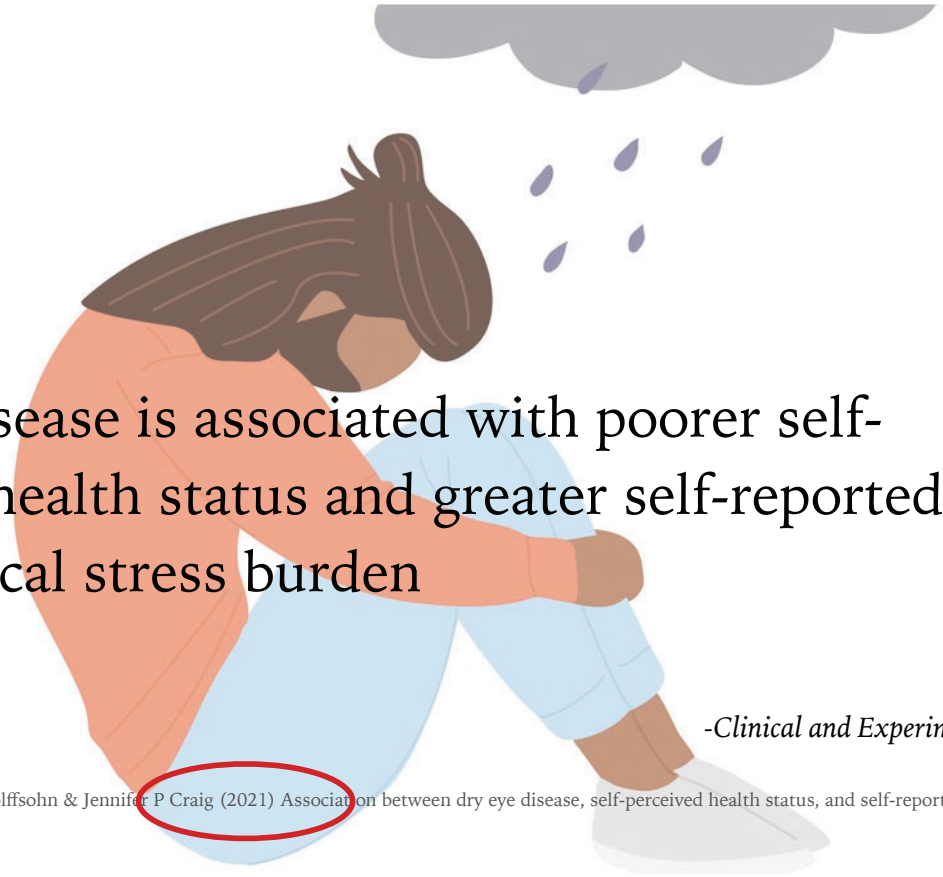
-Sjogren's Syndrome Foundation



- Debilitating fatigue
- Peripheral neuropathy
- Lymphoma


"Once viewed as a painful nuisance, dry eye disease (DED) today is considered a critical and significant public health issue."
-Ophthalmology Times

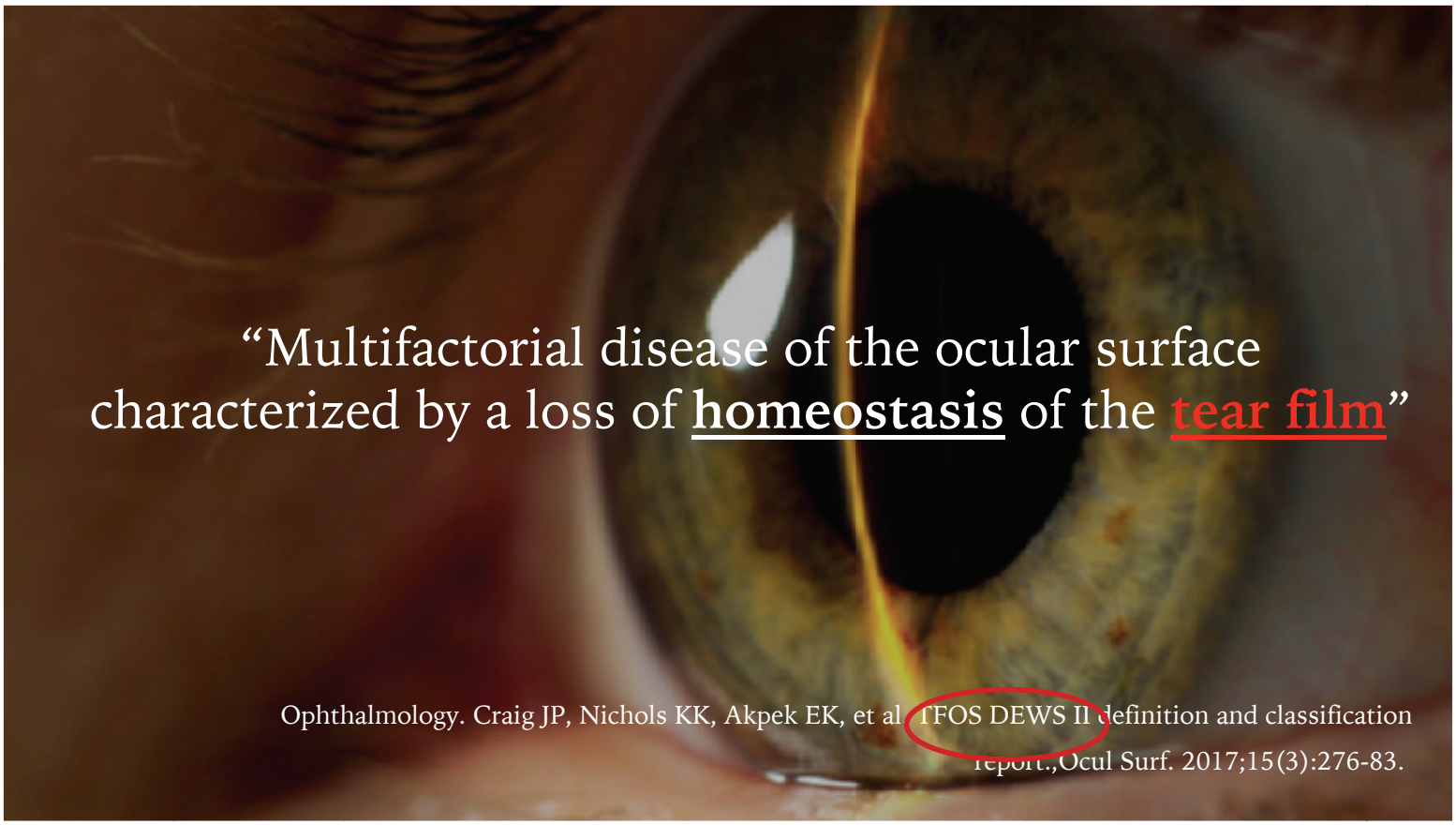

"Patients who have moderate to severe dry eye disease, the impact of their disease on their lives is similar to having angina or being on hospital dialysis"
Buchholz P, Steeds CS, Stern LS, et al. Utility assessment to measure the impact of dry eye disease. Ocul Surf. 2006; 4:155–61. [PubMed: 16900272]



Dry eye disease is associated with poorer self-perceived health status and greater self-reported psychological stress burden

-Clinical and Experimental Optometry

Michael TM Wang, Alex Muntz, James S Wolffsohn & Jennifer P Craig (2021) Association between dry eye disease, self-perceived health status, and self-reported psychological stress burden, : 10.1080/08164622.2021.1887580



"Multifactorial disease of the ocular surface characterized by a loss of **homeostasis** of the **tear film**"

Ophthalmology. Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II definition and classification report.,Ocul Surf. 2017;15(3):276-83.

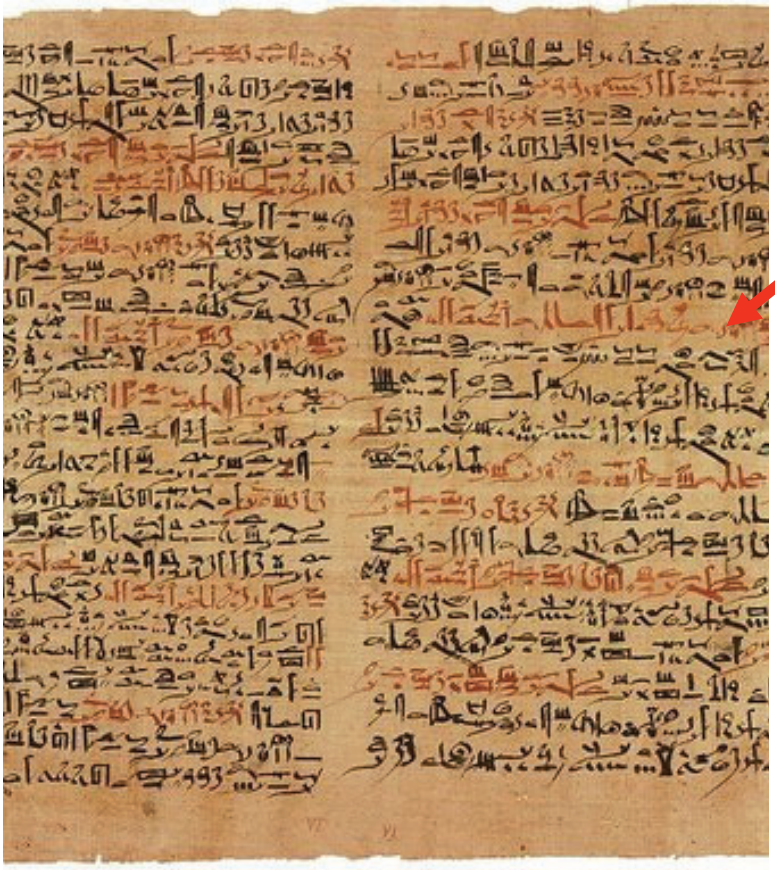
DRY EYE TREATMENT NOW

- *Lifestyle changes*
- *Modify risk factors*
- *AT, Omega 3*
- *Lid hygiene*

- *Topical steroids,*
- *PFAT, Gel drops*
- *Lifitegrast/Cyclosporin*
- *Punctal Plugs,*
- *Eyelid treatments*
- *Topical/Oral antibiotics*

- *Autologous Serum/PRP*
- *Bandage CL*
- *Oral Secretagogues*
- *Amniotic Membrane*
- *Scleral CL*

- *Steroids long term*
- *Amniotic graft*
- *Surgical*



HOW IT 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. and Tsubota** used AS as treatment for DED

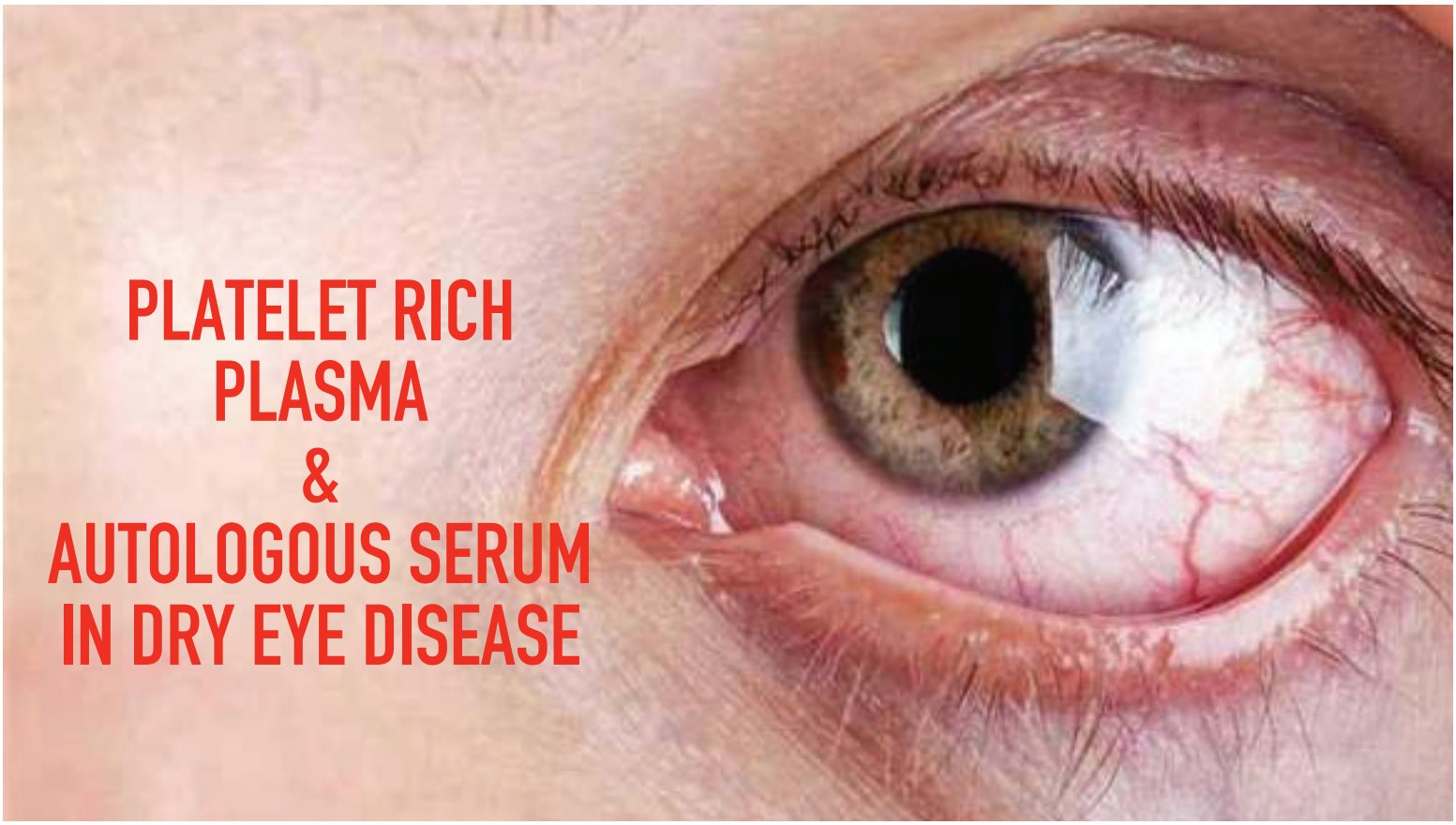
PRP APPLICATIONS

PRP APPLICATIONS

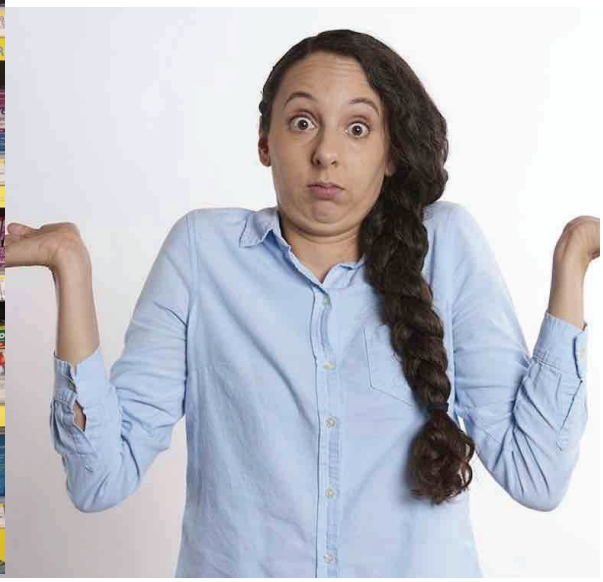
BLOOD BIOLOGICS IN MEDICINE

AS, PRP, PRGF, PRF, L-PRF, PRL....

- All derived from components of blood after RBCs discarded
- All made by centrifugation of blood
- All provide different amounts of GF!



"In almost every form of DED, a lubricating drop is still needed"



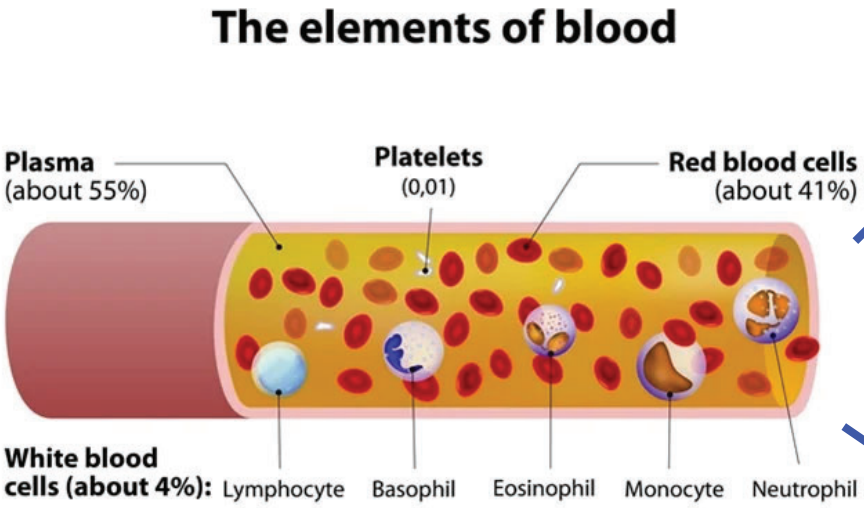
WHAT IS A GOOD EYE DROP?

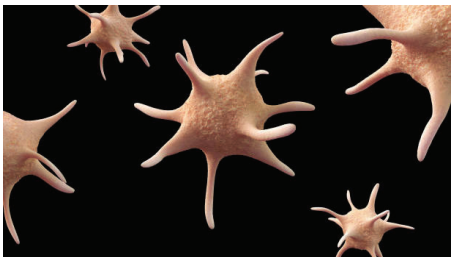
HUMAN TEARS: "MAGIC DROPS" – 1800 KNOWN MOLECULES

- ➤Perfect lubricant
- ➤Antimicrobial activity
- ➤Anti-inflammatory activity
- ➤Nourishing
- ➤Maintain clarity of cornea
- ➤**Epitheliotrophic - They support proliferation, migration, and differentiation of corneal and conjunctival cells!**

Willcox MDP, Argüeso P, Georgiev GA, et al. TFOS DEWS II Tear Film Report. Ocul Surf. 2017;15(3):366-403

WHAT IS PRP ?



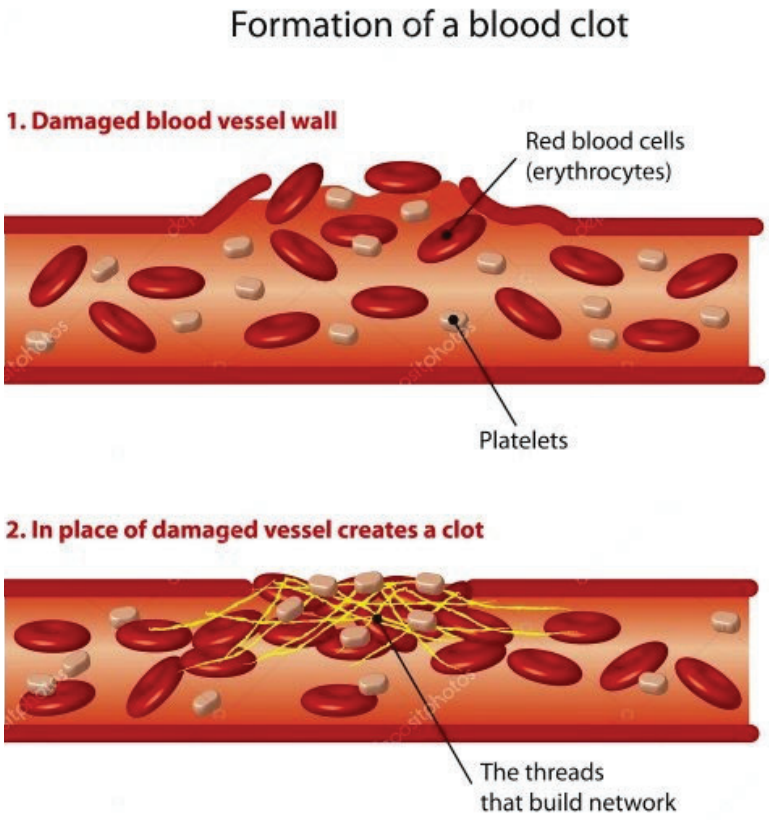


Platelets

+

Plasma

PRP = 3-5x platelet concentration than whole blood



WHY PLATELETS?

- PLATELETS:
  - Clot formation
  - *Repair damaged tissue*
  - Healing
  - Anti-analgesic
  - Antimicrobial
- Contain over 800 molecules

TRUE POWER HOUSES FOR HEALING

Boswel, Stacie G. Platelet-Rich Plasma: A Milieu of Bioactive Factor

PLASMA

- Makes up 55% of blood
- Main function is to take ***nutrients, hormones,*** *and* ***proteins*** *to the parts of the* ***body*** *that need it.*
- Contains:
  - Proteins (albumin and fibrinogen)
  - Immunoglobulins - fight infections
  - Electrolytes - maintain cell function
- Over 600 active molecules in plasma to support cellular healing.

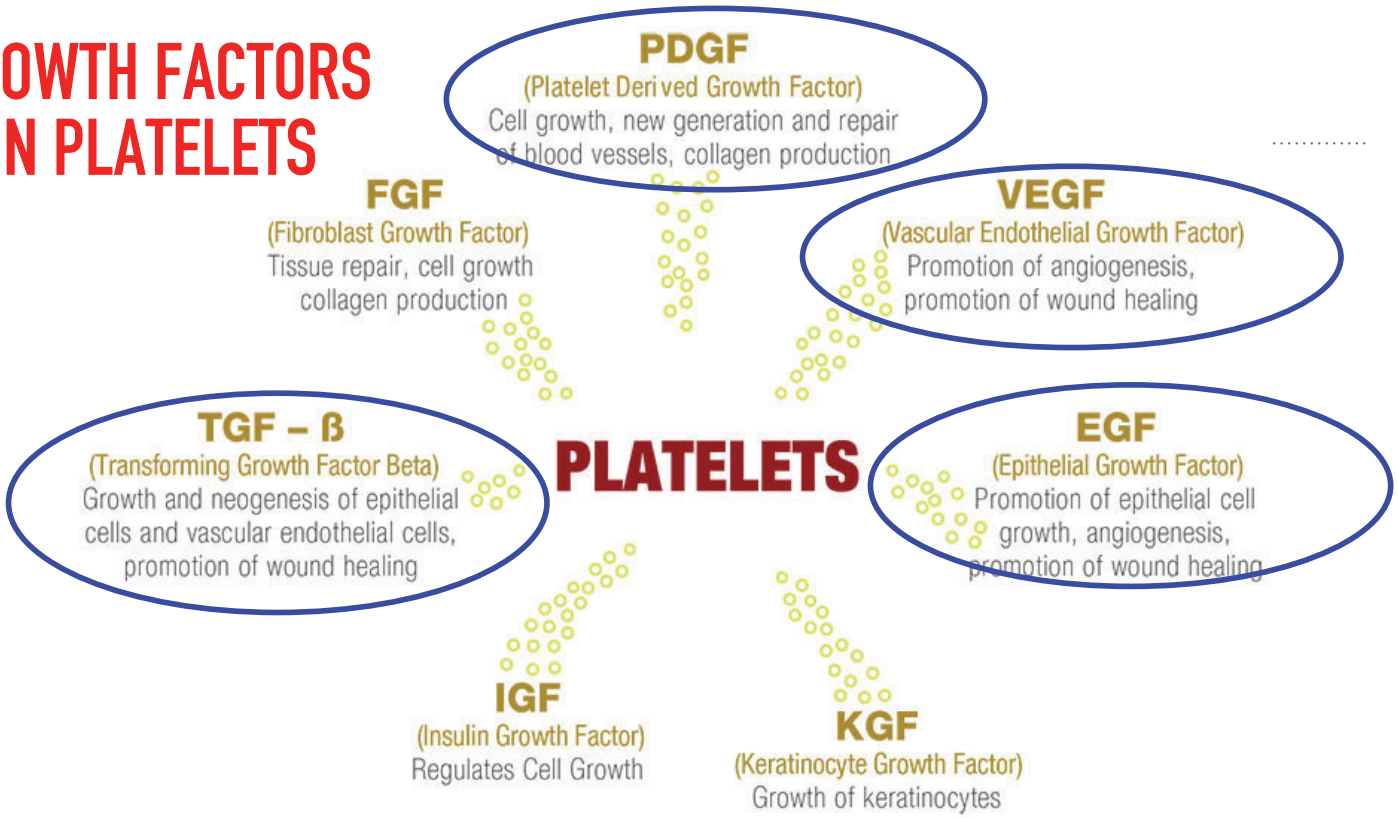
Platelet-Rich Plasma: A Milieu of Bioactive Factors

Stacie G. Boswell, D.V.M., Brian J. Cole, M.D., M.B.A., Emily A. Sundman, B.S., Vasili Karas, B.S., and Lisa A. Fortier, D.V.M., Ph.D.

PRP – COMPOSITION

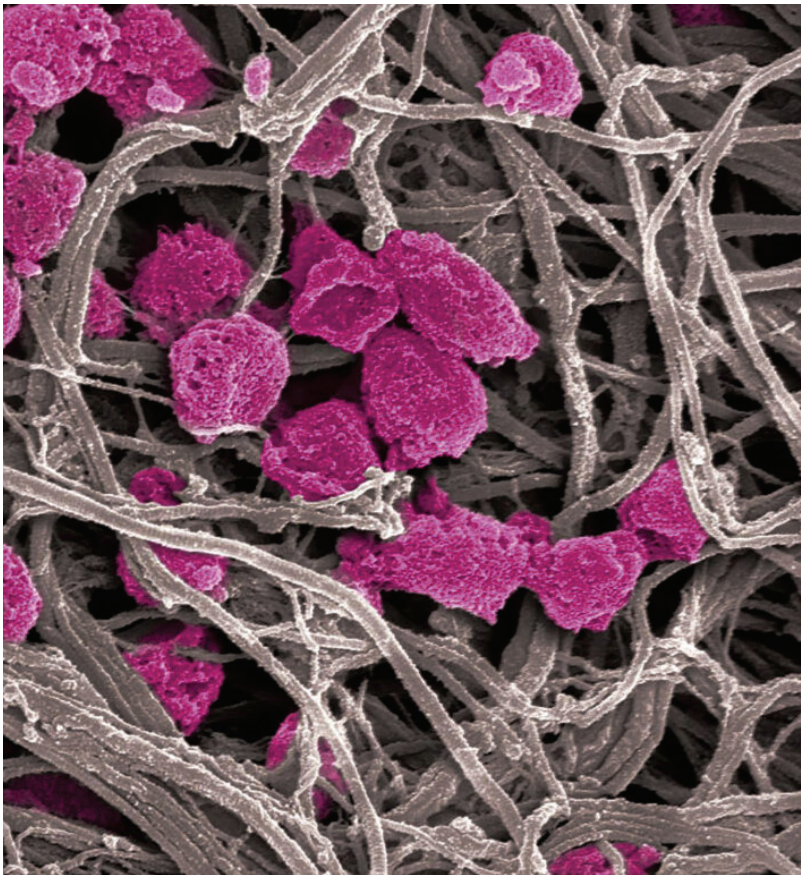
GROWTH FACTORS	Key role in tissue repair Epitheliotrophic - Support proliferation/migration/differentiation of corneal/conjunctival cells. Have anti-inflammatory actions
VITAMINS	Important for maturation of epithelium Prevents metaplasis of epithelium
FIBRONECTIN	Promotes cell migration and adhesion of epithelium to stroma Has “clearing” responsibilities to remove infectious agents/cellular debris.
CYTOKINES LYSOZYMES	Anti-inflammatory cytokines to reduce tissue inflammation
ALBUMIN/IMMUNOGLOBULINS	Has anti-apoptotic activity Albumin - most important protein in plasma. Reduces degradation of

GROWTH FACTORS IN PLATELETS



Dominika Wróbel-Dudzińska, Jorge Alio,"Clinical Efficacy of Platelet-Rich Plasma in the Treatment of Neurotrophic Corneal Ulcer", *Journal of Ophthalmology*, vol. 2018, Article ID 3538764, 7 pages, 2018. https://doi.org/10.1155/2018/3538764

	TEARS	PRP	
Physico-chemical parameters (33, 57)			
Osmolality, mosm/l	302	300	Maintains physiological osmolality and pH
pH	7.2–7.4	7.2–7.4	
Proteins (33, 5			
Total proteins, m			sion, physiological hydration of the ocular surface, and ocular homeostasis
Albumin, mg/mL		35–40	Anti-apoptotic activity, toxification
Fibronectin, µg/		200–300	Adhesion protein supporting wound healing
IgG, mg/mL		8–12	Anti-microbial
IgA, mg/mL			Anti-microbial
IgM, mg/mL		0.5	Endotoxin binding
IgD, µg/mL			
IgE, µg/mL			
Alpha 2-macrog			Anti-collagenase
Complement sy			Anti-microbial; bacteriostatic
Lactoferrin, mg/			Anti-microbial and anti-inflammatory
Transferrin, mg/			Iron-carrier; anti-microbial
Lysozyme, mg/			Iron carrier; anti-microbial
Growth factors			
TGF-β1, ng/mL			Epithelial and stromal repair processes
PDGF, ng/mL			Enhances mitosis and scarring
EGF, ng/mL			Accelerates the migration of epithelial cells; anti-apoptotic
HGF, ng/mL			Supports corneal epithelial cells
VEGF, ng/mL			Reduces conjunctival endothelial permeability
Vitamins (33)			
A, ng/mL			Prevents hyperplasia and helps maintain the normal histology
C, µg/mL			Antioxidant
Antioxidants (3			
Tyrosine, µM	45	77	
Glutathione, µM		ND	
Electrolytes (3			
Na+, mEq/L	145	135–146	
K+, mEq/L	24.1	3.5–5.0	
Ca^{2+}, mM	1.5	1.1	
Cl^-, mM	128	96–108	
HCO_3^- mM	26	21–29	
NO_3^- mM	0.14	0.19	
PO_4^{3-} mM	0.22	1.42	
SO_4^{2-} mM	0.39	0.53	

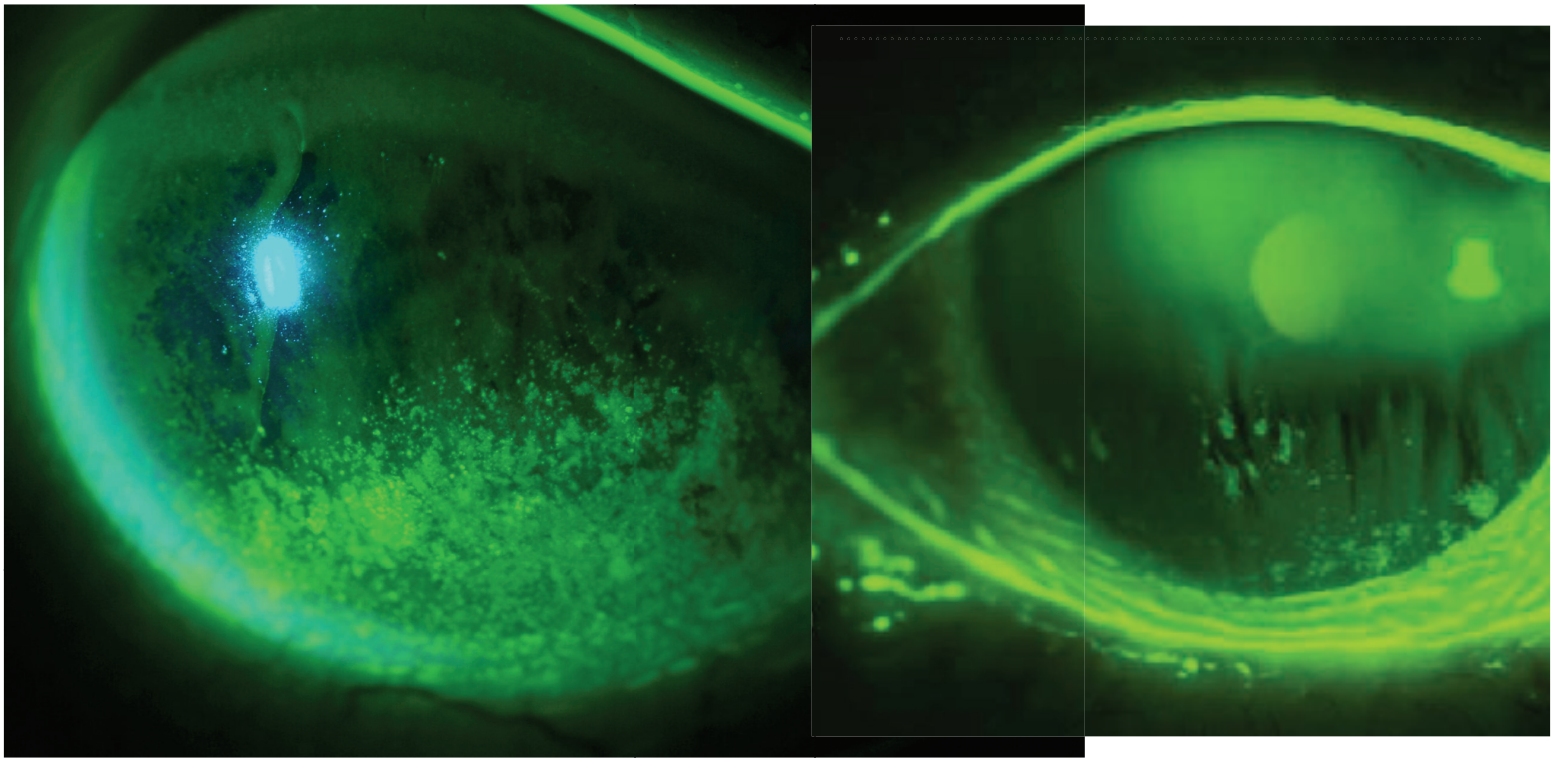


BENEFITS OF PRP

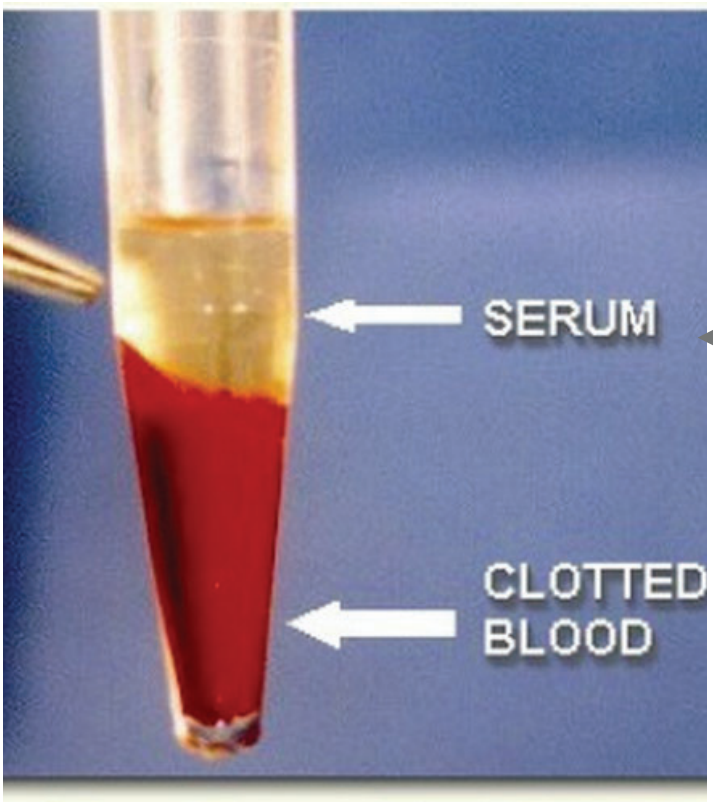
- Tissue Repair = Growth factors (Epitheliotrophic)
- Anti-inflammatory = Cytokines
- Prevent Infections = Immunoglobulins/Proteins
- Repair Osmolarity = Dilute proinflammatory mediators
- Natural Analgesic Actions = reduce pain
- Resembles biological tears = pH/Osmolarity

- PRP is natural = NO preservatives/stabilizers
- No side effects = no stinging or burning

PRE/POST PRP EYE DROPS



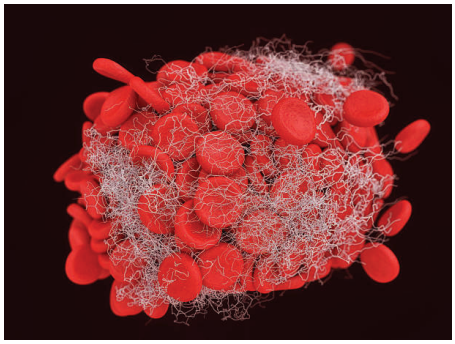
PREPARATION – AS



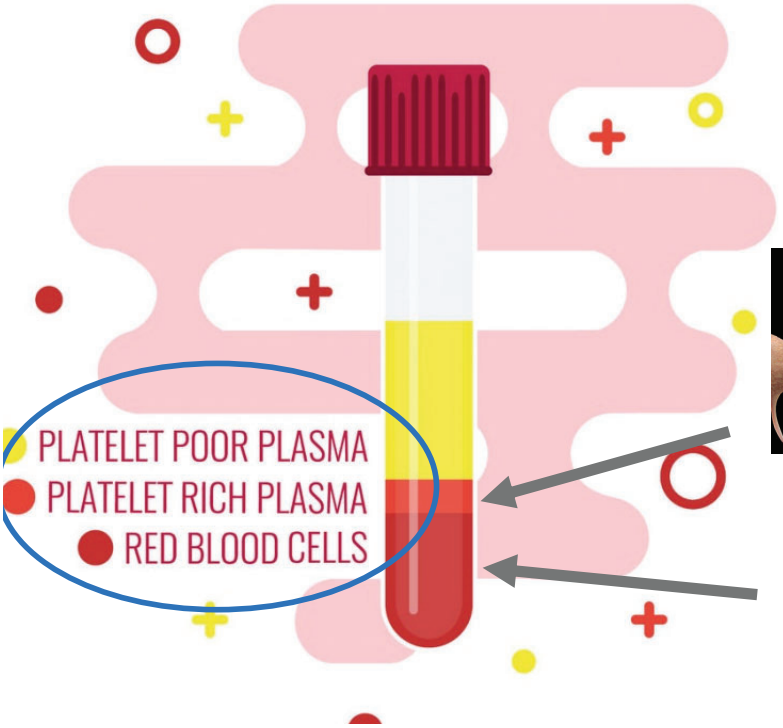
- Uses Clotted Blood

Autologous Serum

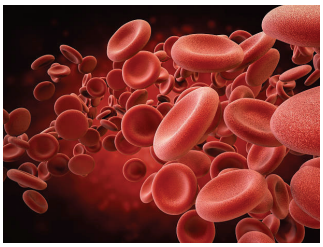
Clotted RBC with Platelets



PREPARATION – PRP



- Uses Un-clotted Blood
- In-fact, blood is prevented from clotting with an anticoagulant



Keeping platelets in their true form

AS VS PRP

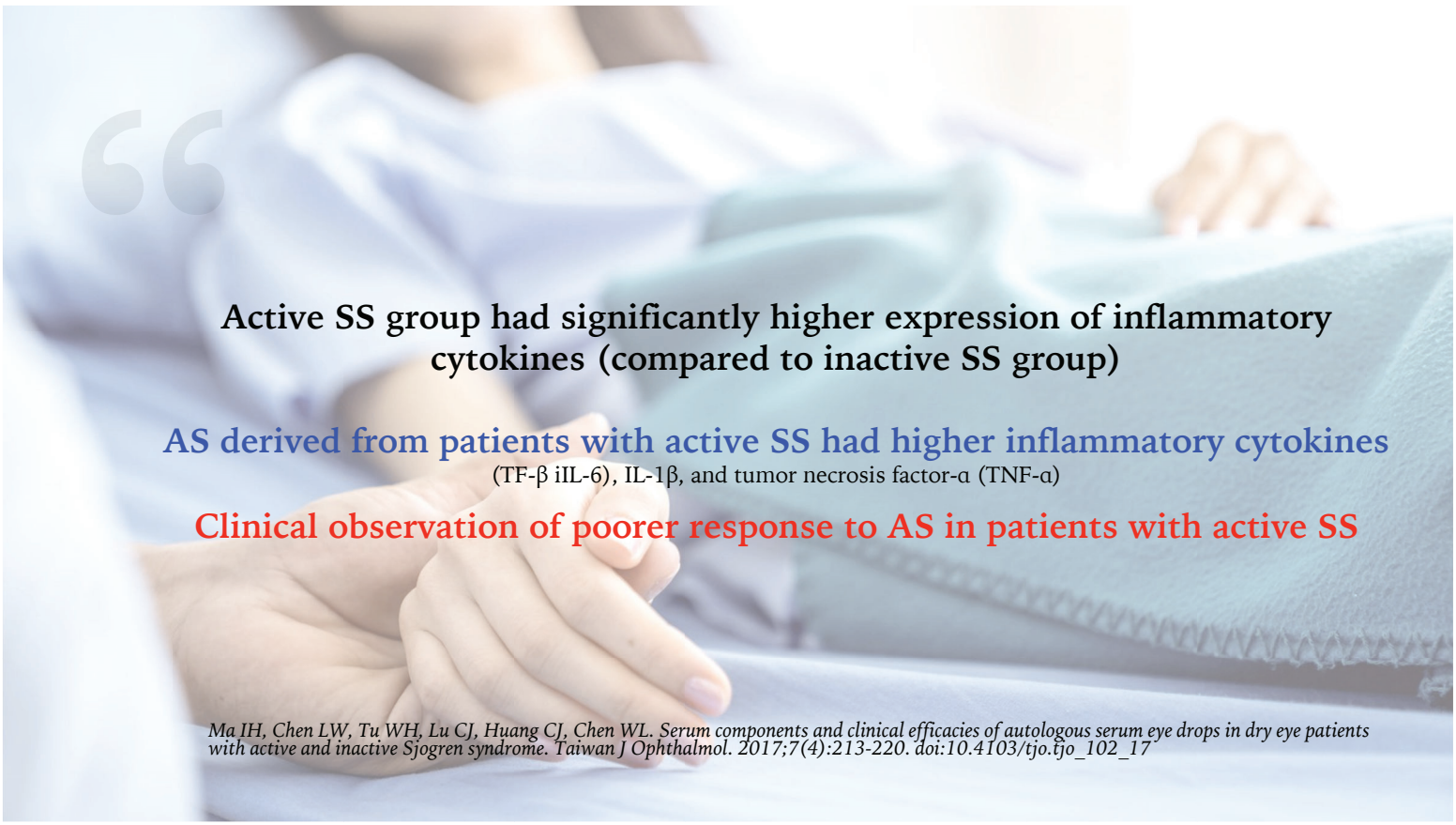
AS

- Does NOT contain PLATELETS
- Less concentration of GF/Plasma factors
- Serum is not plasma.
- Has inflammatory cytokines from monocytes and leukocytes
- Inflammatory cytokines are deleterious in patients with immune diseases
- Contains high amounts of TGF-β - can suppress wound healing
- Often diluted with saline (20-50%) to reduce cytokine load (which further dilutes GF/Plasma factors)

PRP

- Contains PLATELETS
- High concentration of GF/Plasma factors
- GF released in a biologically relevant ratio
- No inflammatory cytokines
- Not diluted
- Dispensed 100%
- PRP is considered superior to AS
- Used in medicine

The Use of Platelet-Rich Plasma in Dry Eye Disease
By Marina Viegas Moura Rezende Ribeiro, Eurica Adélia Nogueira Ribeiro and Luiz Feliciano Ribeiro



Active SS group had significantly higher expression of inflammatory cytokines (compared to inactive SS group)

AS derived from patients with active SS had higher inflammatory cytokines
(TF-β iIL-6), IL-1β, and tumor necrosis factor-α (TNF-α)

Clinical observation of poorer response to AS in patients with active SS

Ma IH, Chen LW, Tu WH, Lu CJ, Huang CJ, Chen WL. Serum components and clinical efficacies of autologous serum eye drops in dry eye patients with active and inactive Sjogren syndrome. Taiwan J Ophthalmol. 2017;7(4):213-220. doi:10.4103/tjo.tjo_102_17

PRP STUDY

Treatment of Dry Eye Disease with Autologous Platelet-Rich Plasma: A Prospective, Interventional, Non-Randomized Study

Jorge L. Alio,[1,2] Alejandra E. Rodriguez,[3] Renan Ferreira-Oliveira,[1,3] Dominika Wróbel-Dudzińska,[1,3] and Ahmed A. Abdelghany[1,2,4]

Abstract Go to:

Introduction

The objective of this study was to evaluate the use of autologous platelet-rich plasma (PRP) eye drops as monotherapy for the treatment of moderate to severe cases of dry eye disease.

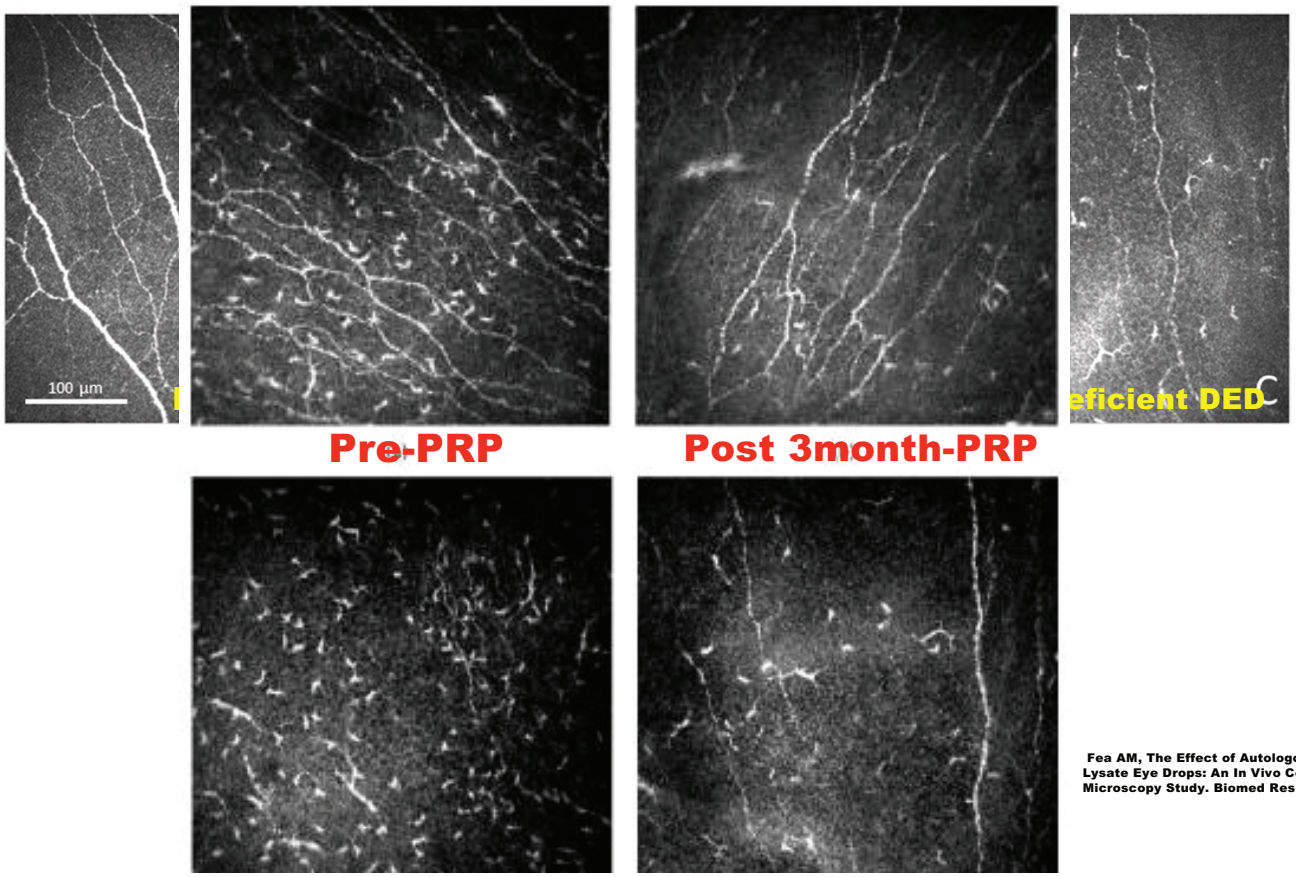
Methods

Three hundred and sixty-eight patients with moderate to severe dry eye disease (DED) were included in this prospective case series. Subjects were classified as evaporative DED (EDED) or aqueous deficient DED (ADDED). Improvement of the DED subjective symptoms, corneal fluorescein staining (CFS), and corrected distance visual acuity (BCVA) were evaluated. We also analysed how many rounds of PRP therapy were used.

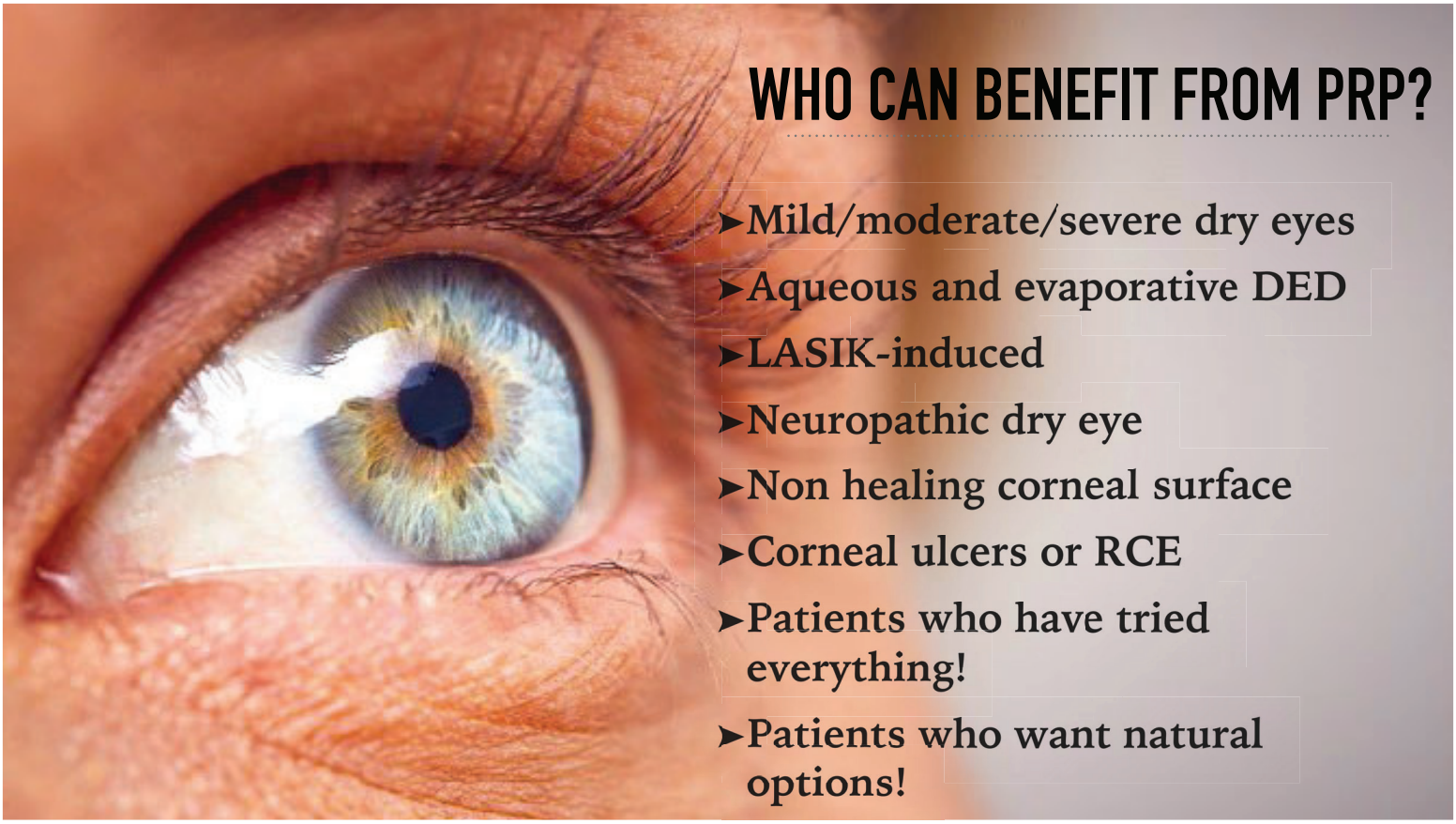
- **87.5%** - subjective improvement (OSDI)
- **76.1%** had decreased corneal staining (6 weeks)
- **64.4%** received only one round of PRP (mono-therapy)
- **28.8%** experienced an increase of one or more lines of vision

	Conventional treatment group (n = 20)	PRP treatment group (n = 27)	*p*-value*
Follow-up (mon)	15.2 ± 17.4 (6-64)	14.6 ± 12.0 (6-42)	0.900
BCVA at final visit	0.84 ± 0.14	0.87 ± 0.14	0.400
Recurrences (total no. of episodes)			
Major	23	7	0.001
Minor	50	10	0.001
Mean frequency of recurrences	0.39 ± 0.24	0.06 ± 0.08	0.003

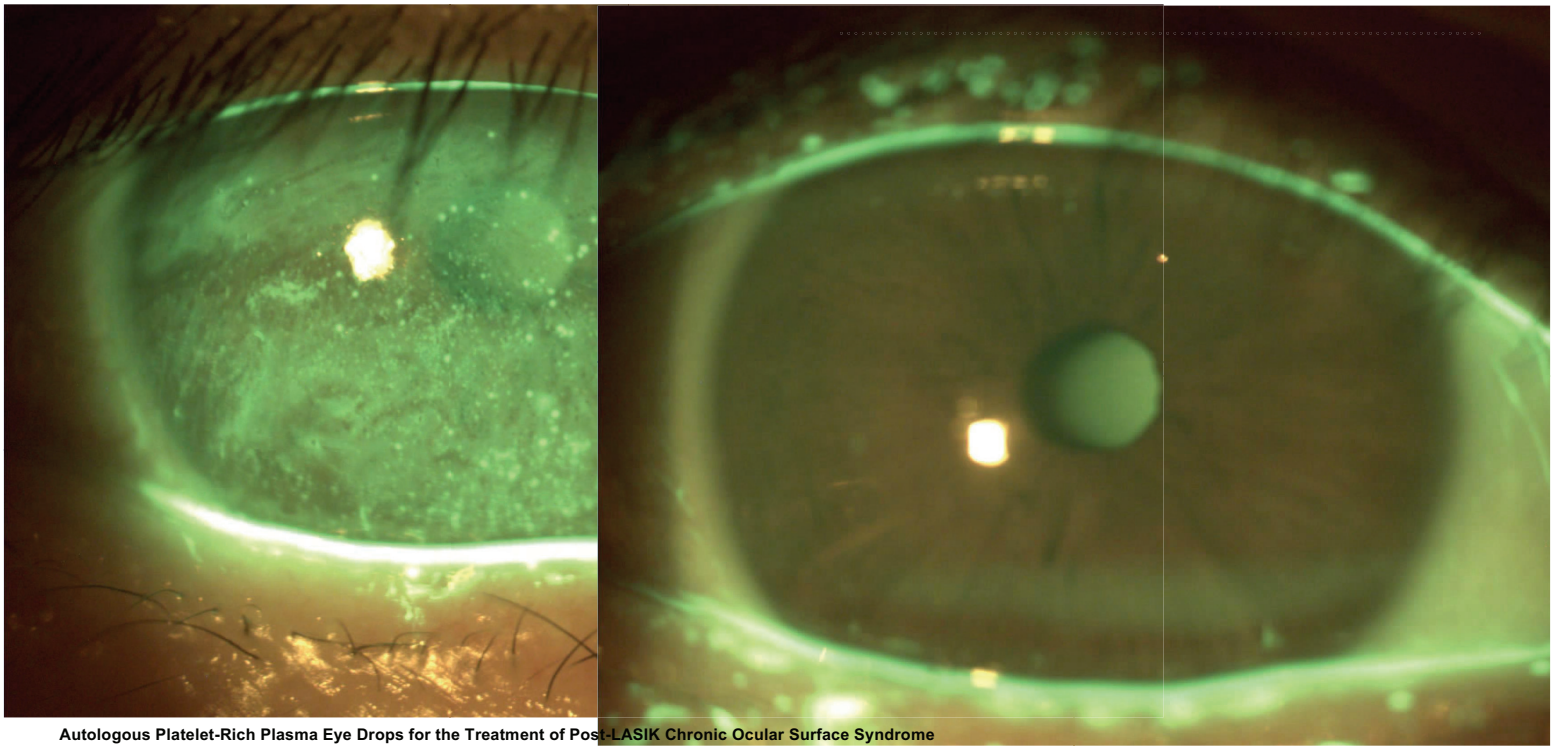
Lee JH, Kim MJ, Ha SW, Kim HK. **Autologous Platelet-rich Plasma Eye Drops in the Treatment of Recurrent Corneal Erosions**. *Korean J Ophthalmol*. 2016;30(2):101-107. doi:10.3341/kjo.2016.30.2.101



Fea AM, The Effect of Autologous Platelet Lysate Eye Drops: An In Vivo Confocal Microscopy Study. Biomed Res Int.

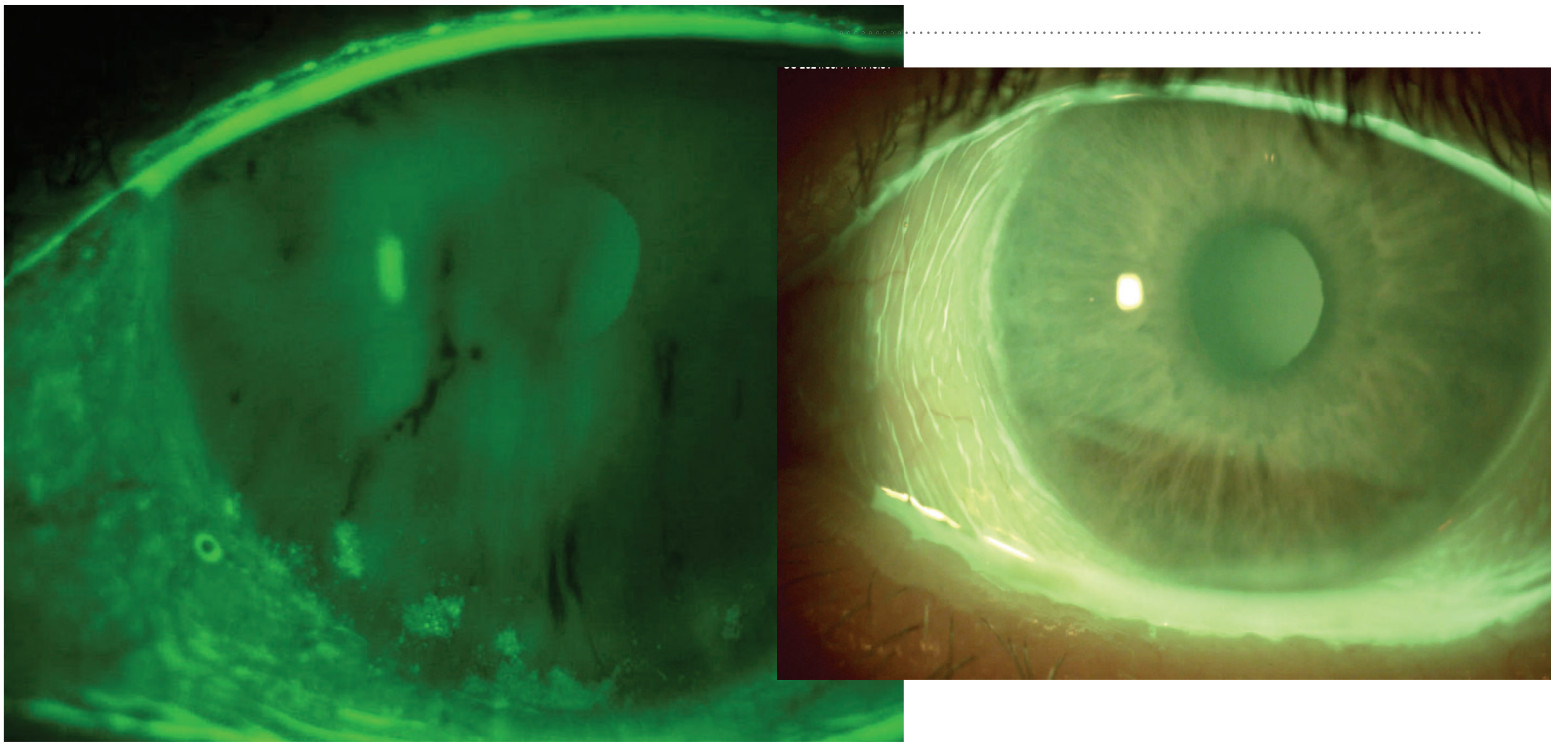


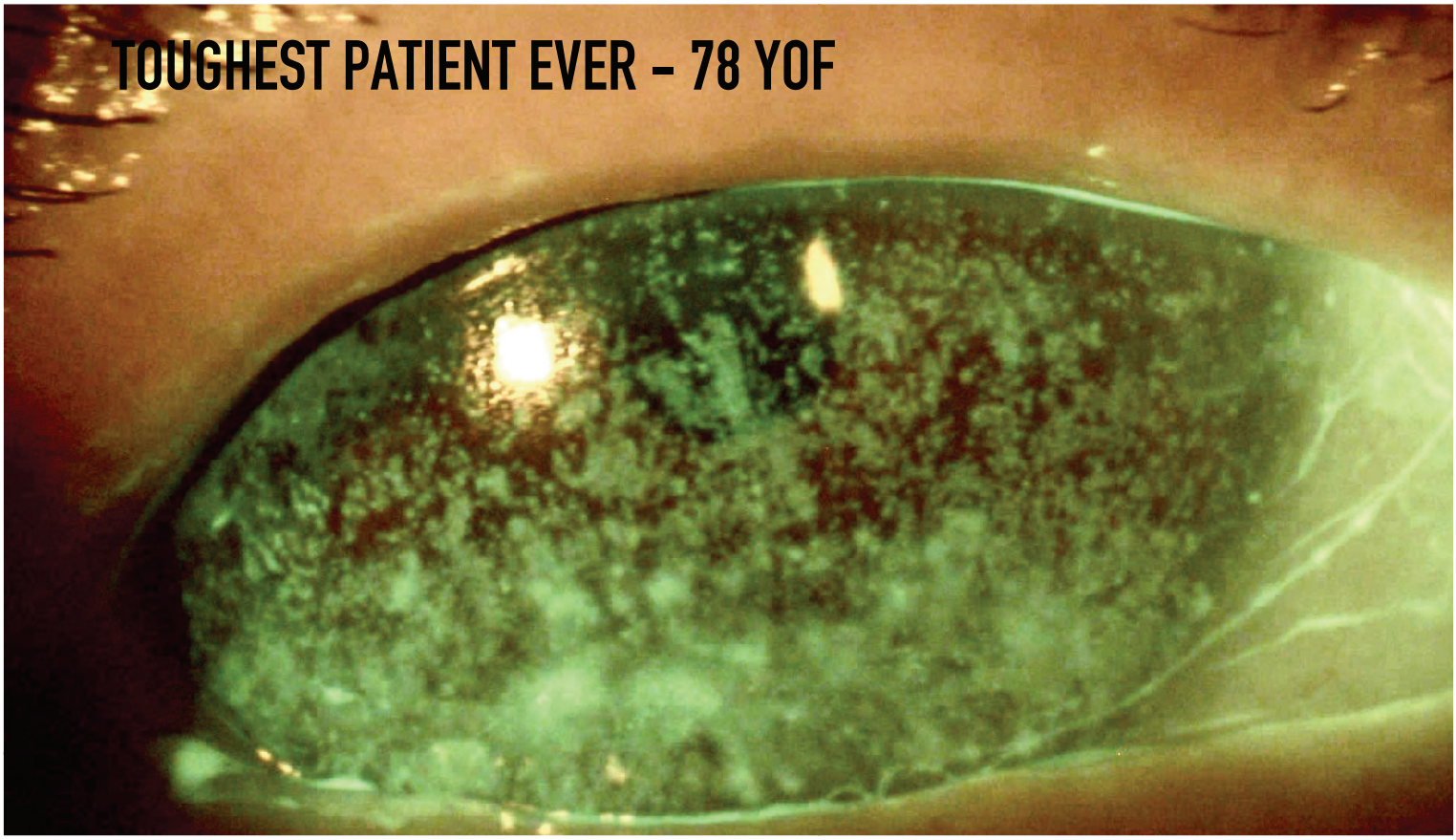
POST LASIK – PRP EYE DROPS

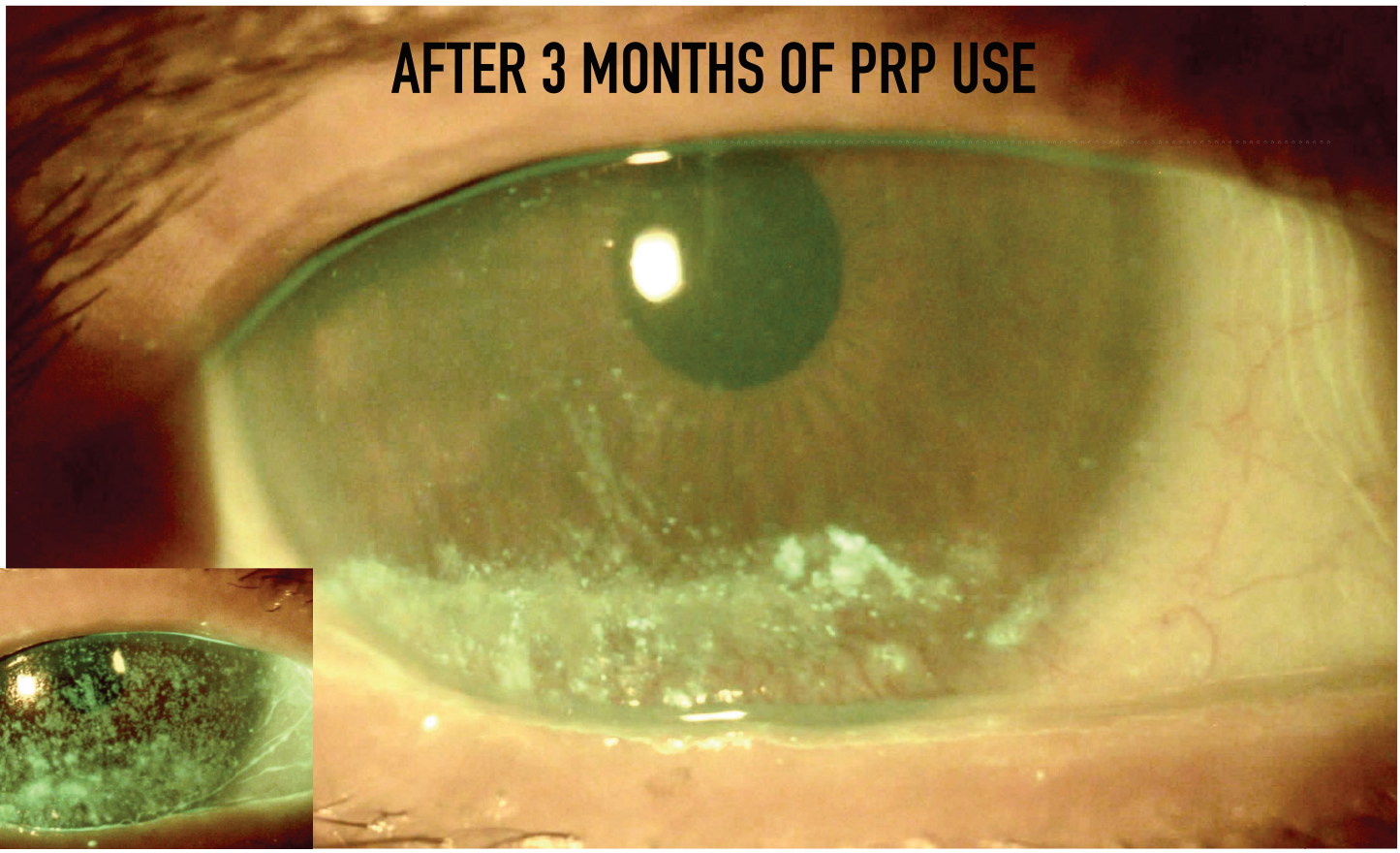


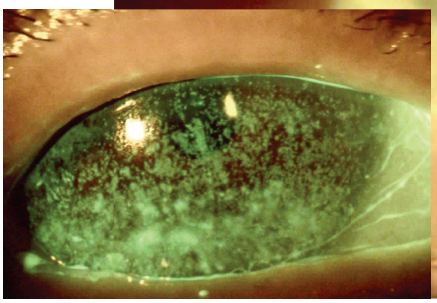
Autologous Platelet-Rich Plasma Eye Drops for the Treatment of Post-LASIK Chronic Ocular Surface Syndrome

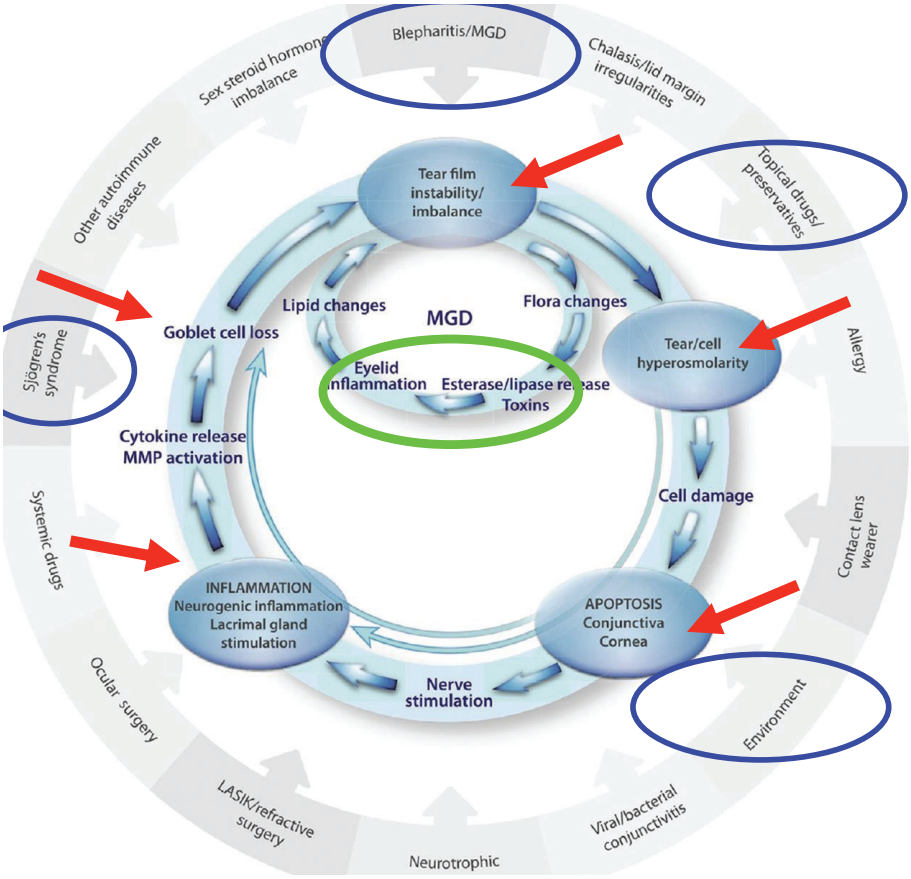
GLAUCOMA THERAPY INDUCED DED– PRP EYE DROPS




TOUGHEST PATIENT EVER – 78 YOF


AFTER 3 MONTHS OF PRP USE





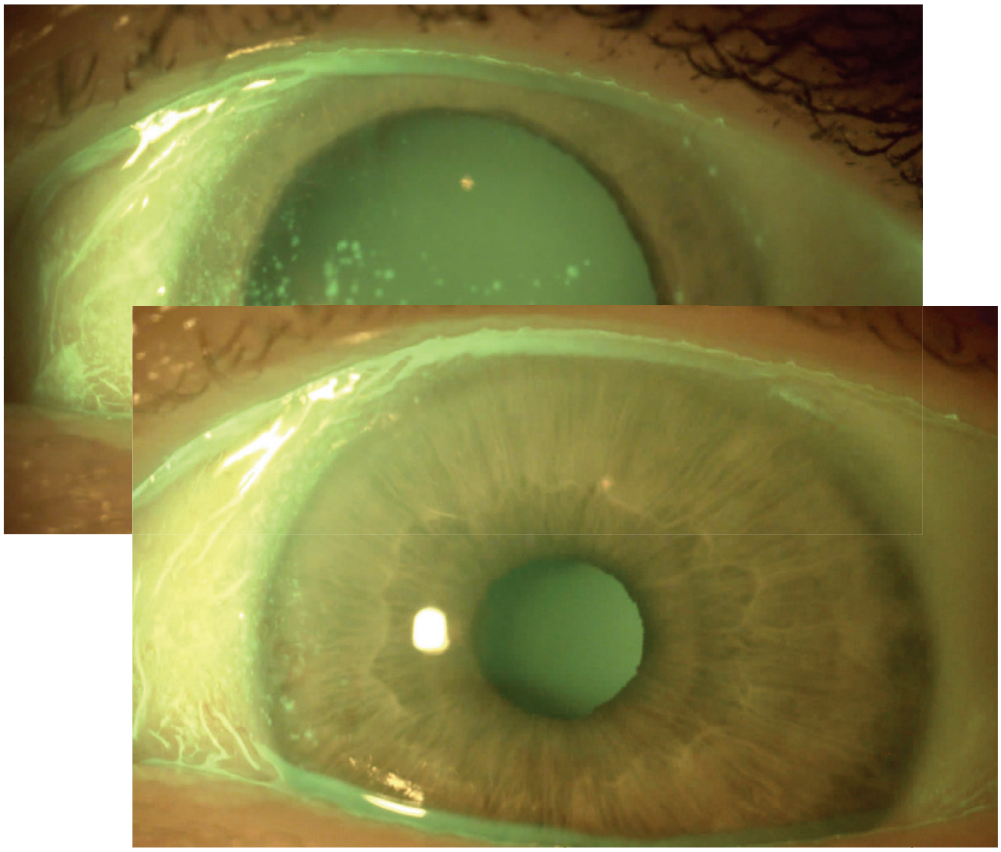
PRP CAN HELP THE CIRCLE OF DED

- Manage the entry points
- PRP promotes tissue healing
- Layer treatments
- Can see real results

Baudouin C, Messmer EM, Aragona P, *et al*Revisiting the vicious circle of dry eye disease: a focus on the pathophysiology of meibomian gland dysfunction*British Journal of Ophthalmology* 2016;**100**:300-306

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

-Ophthalmology Times



CASE 1

- ➤Lifestyle modifications
- ➤Treat the lid disease
- ➤Use immuno-modualators
- ➤Use PRP to “re-set” the ocular surface

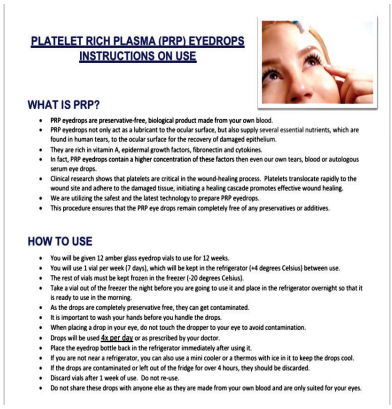
PRP IN MY CLINIC

- ➤ We make PRP Eye Drops in my Vancouver clinic
- ➤Blood draw/strict sterilization techniques
- ➤ 45 minute appointment
- ➤ 3 month supply of PRP to use QID

HOW CAN YOUR PATIENTS GET PRP?

- Access to PRP is increasing
- Over 40 different systems in medicine available
- Can implement a system in your own practice
- Work with local labs

INSTRUCTIONS – HOW TO USE



PLATELET RICH PLASMA (PRP) EYEDROPS INSTRUCTIONS ON USE

WHAT IS PRP?

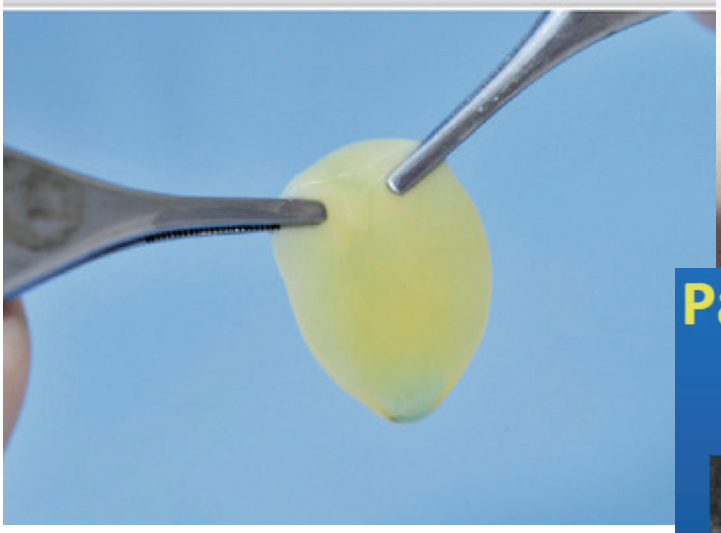
- PRP eyedrops are preservative-free, biological product made from your own blood.
- PRP eyedrops not only act as a lubricant to the ocular surface, but also supply several essential nutrients, which are found in human tears, to the ocular surface for the recovery of damaged epithelium.
- They are rich in vitamin A, epidermal growth factors, fibronectin and cytokines.
- In fact, PRP eyedrops contain a higher concentration of these factors then even our own tears, blood or autologous serum eye drops.
- Clinical research shows that platelets are critical in the wound-healing process. Platelets translocate rapidly to the wound site and adhere to the damaged tissue, initiating a healing cascade promotes effective wound healing.
- We are utilizing the safest and the latest technology to prepare PRP eyedrops.
- This procedure ensures that the PRP eye drops remain completely free of any preservatives or additives.

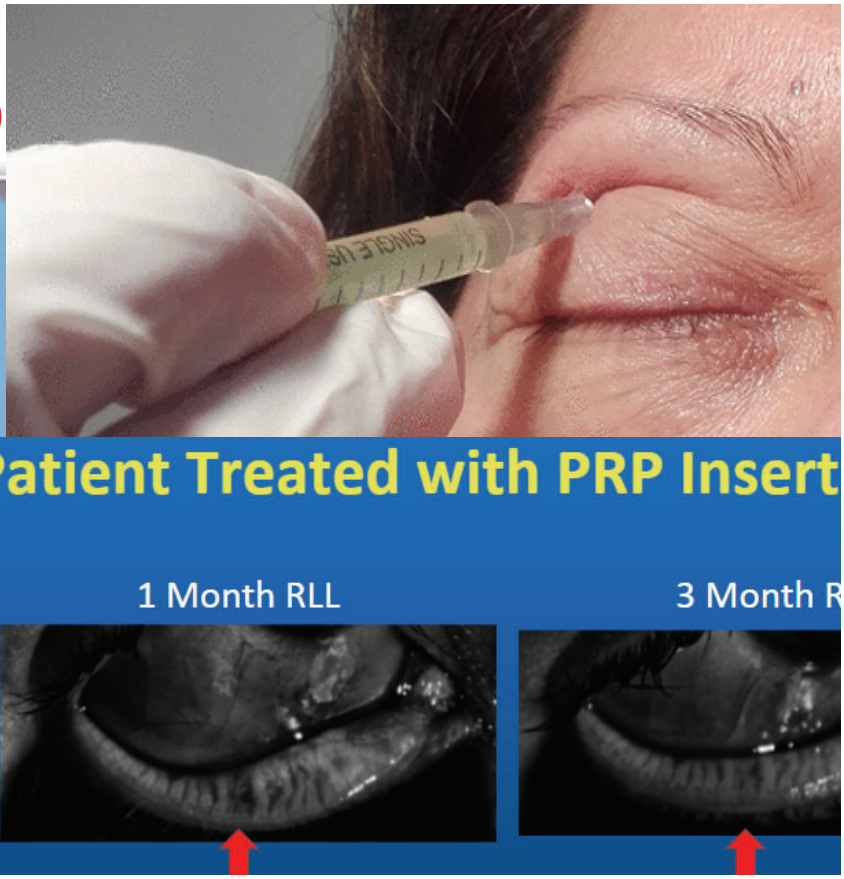
HOW TO USE

- You will be given 12 amber glass eyedrop vials to use for 12 weeks.
- You will use 1 vial per week (7 days), which will be kept in the refrigerator (+4 degrees Celsius) between use.
- The rest of vials must be kept frozen in the freezer (-20 degrees Celsius).
- Take a vial out of the freezer the night before you are going to use it and place in the refrigerator overnight so that it is ready to use in the morning.
- As the drops are completely preservative free, they can get contaminated.
- It is important to wash your hands before you handle the drops.
- When placing a drop in your eye, do not touch the dropper to your eye to avoid contamination.
- Drops will be used 4x per day or as prescribed by your doctor.
- Place the eyedrop bottle back in the refrigerator immediately after using it.
- If you are not near a refrigerator, you can also use a mini cooler or a thermos with ice in it to keep the drops cool.
- If the drops are contaminated or left out of the fridge for over 4 hours, they should be discarded.
- Discard vials after 1 week of use. Do not re-use.
- Do not share these drops with anyone else as they are made from your own blood and are only suited for your eyes.

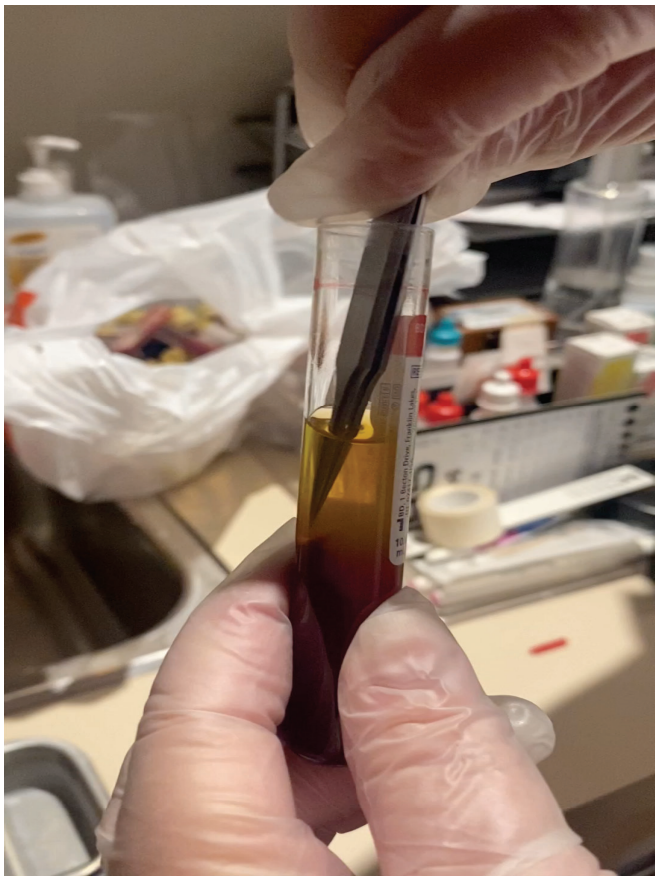
- 1 gtt PRP QID OU x 3 months
- Keep in refrigerator between use
- Rest keep frozen in the freezer (-20C)

OTHER APPLICATIONS OF PRP





PRF – PLATELET RICH FIBRIN



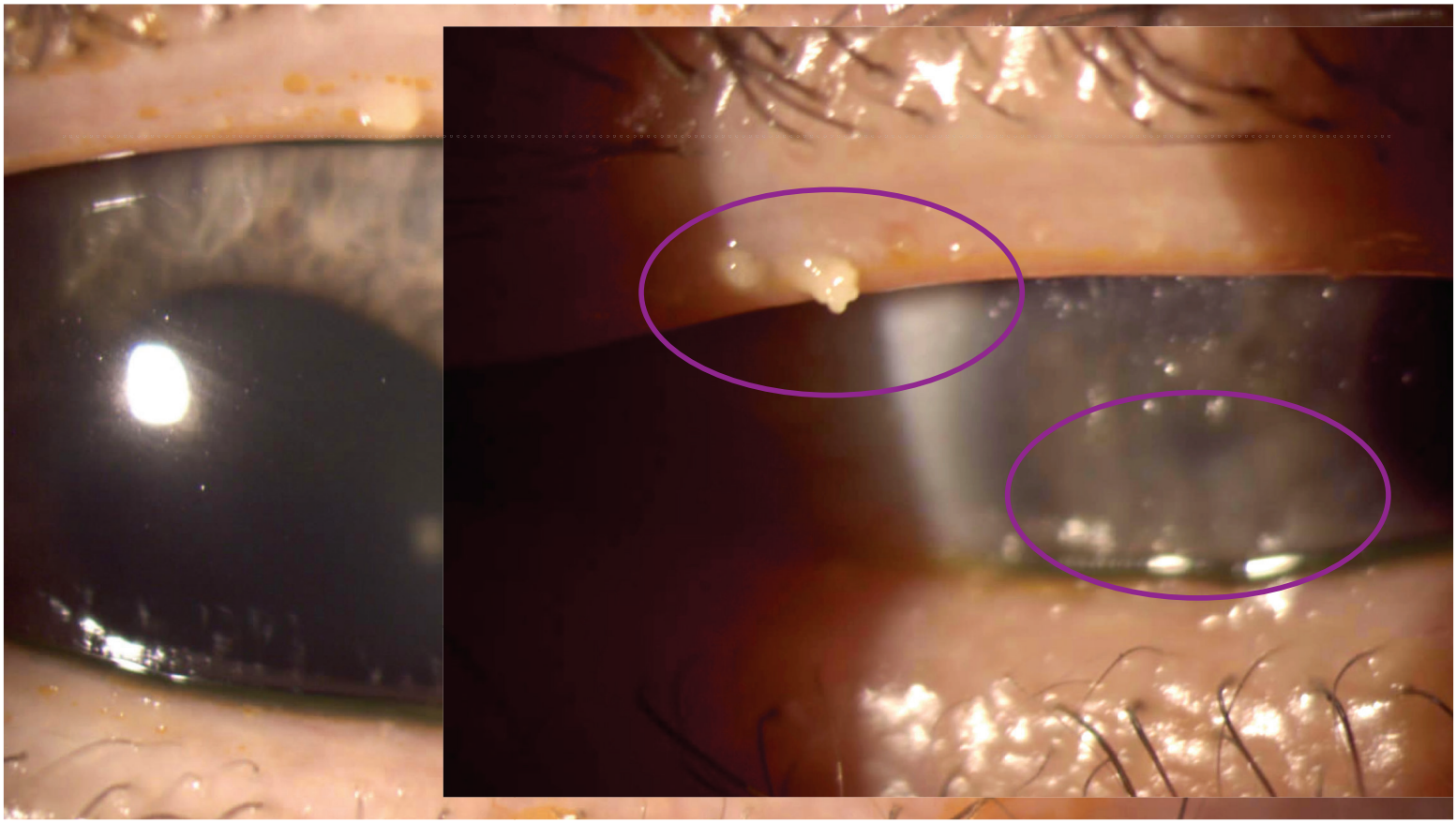
CASE: RYAN

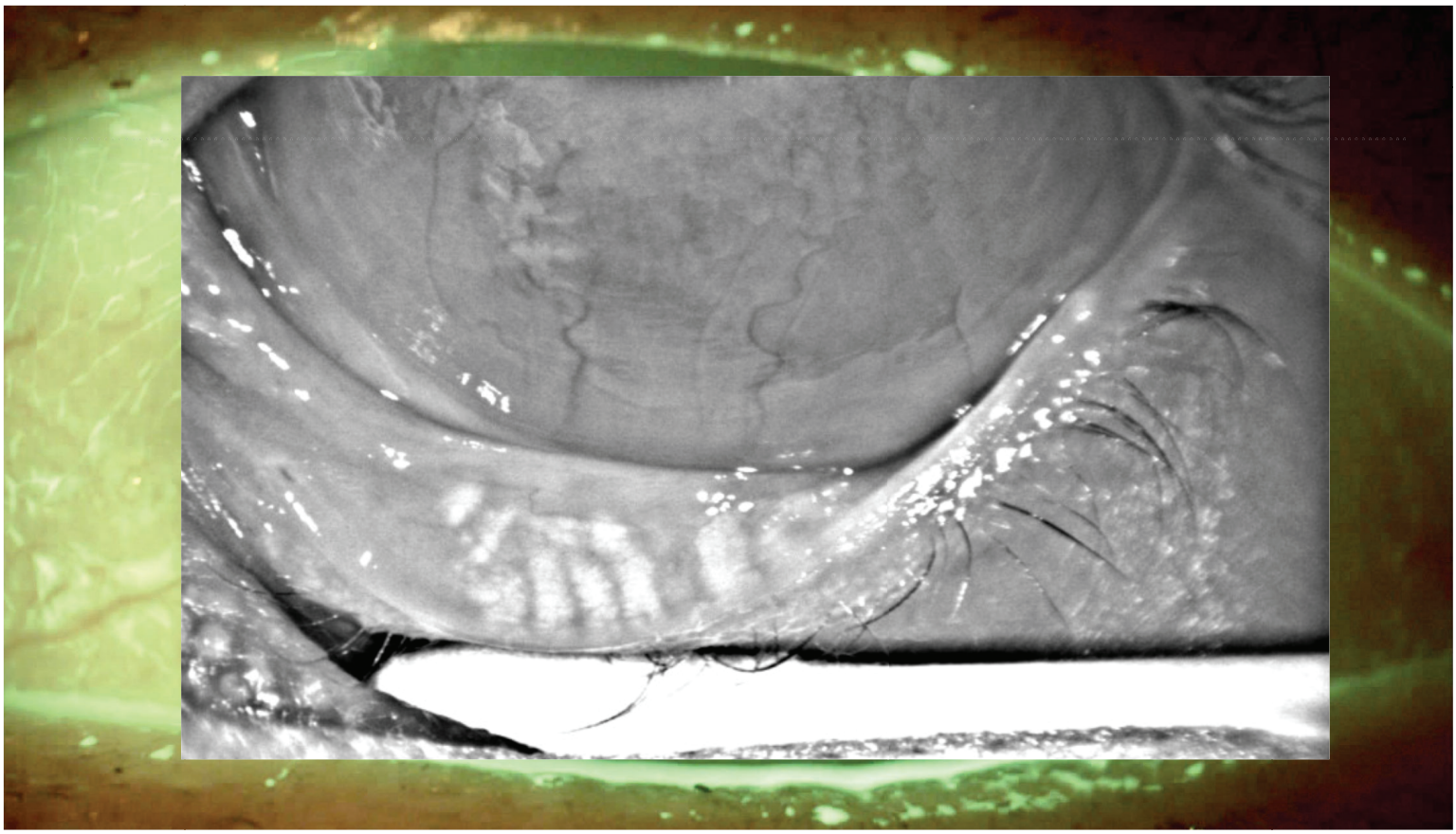
- 37 YOWM
- CC:
  - Referred for dry eye consult
  - Rosacea and MGD
  - Consideration for IPL treatment

PATIENT HISTORY

- History:
  - Rosacea Dx 2020
  - Accutane use
  - Computer programmer
- Current Treatment:
  - Xiidra BID
  - Doxycycline 100mg QD x 2 months
  - Omega 3, hot compresses, lid hygiene
  - Several lubricating drops
  - Anti-inflammatory diet
  - Punctal plug use

OSDI SCORE >38 (SEVERE)





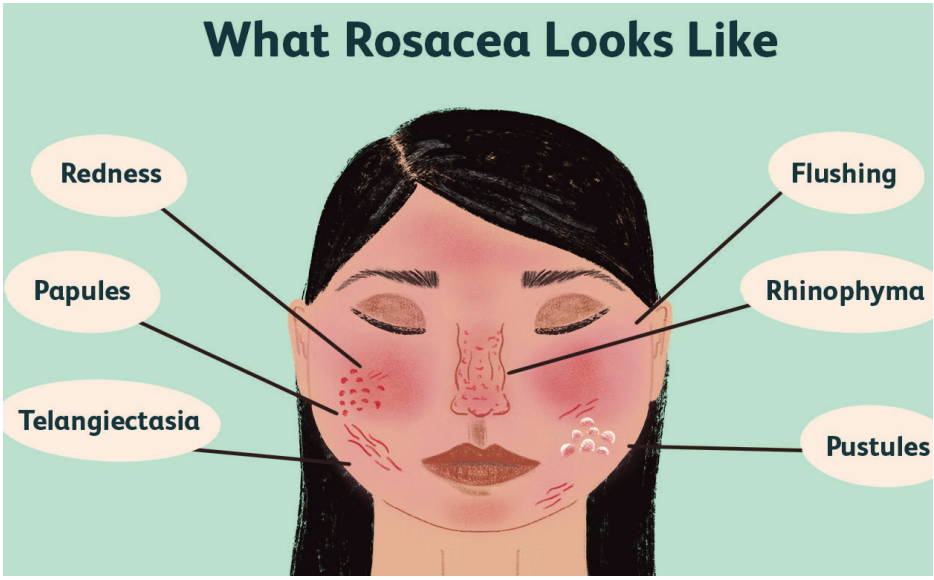
Rosacea, a common disorder that is **under recognized & under treated.**

Prevalence figures indicate that it is present in **2 of every 10 adults** in a *primary care waiting room.*

-John Baldwin HE. Diagnosis and treatment of rosacea: state of the art. J Drugs Dermatol. 2012 Jun;11(6):725-30. PMID: 22648219.ny Appleseed

DIAGNOSIS IS CHALLENGING . . . ..

- Inflammatory dermatosis affecting face and eyes
- Increased *Demodex & Helicobacter pylori* infestation
- Elevated MMP-2/9 on skin
- Symptoms triggered by environmental factors



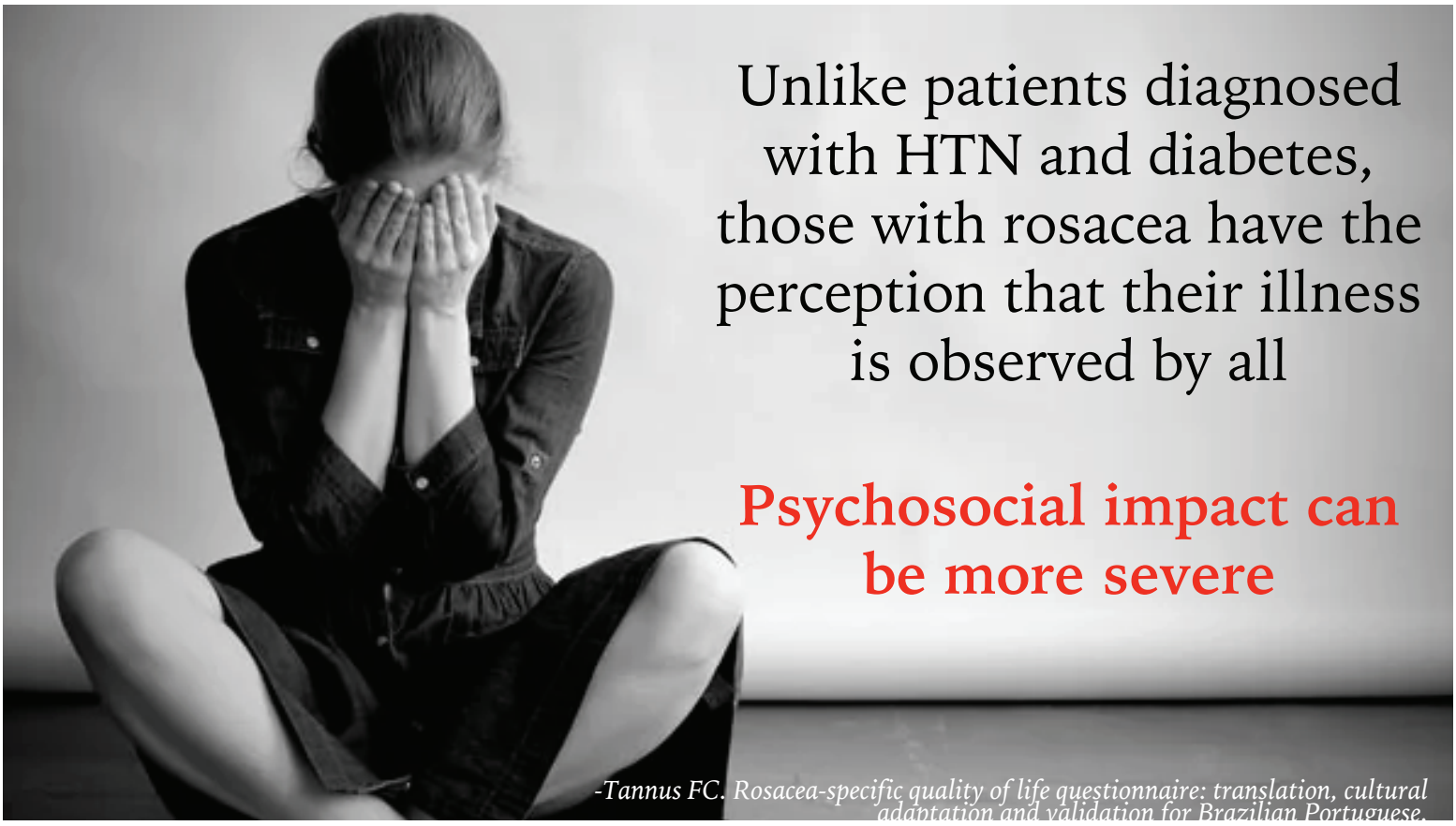
Peak age is 30 - 60

1. I worry that my rosacea may be serious	Emotion
2. My rosacea burns or stings	Symptom
3. I worry about getting scars from my rosacea	Emotion
4. I worry that my rosacea may get worse	Emotion
5. I worry about side effects from rosacea medications	Emotion
6. My rosacea is irritated	Symptom
7. I am embarrassed by my rosacea	Emotion
8. I am frustrated by my rosacea	Emotion
9. My rosacea makes my skin sensitive	Symptom
10. I am annoyed by my rosacea	Emotion
11. I am bothered by the appearance of my skin (redness, blotchiness)	Emotion
12. My rosacea makes me feel self-conscious	Emotion
13. I try to cover up my rosacea (with makeup)	Function
14. I am bothered by persistence/reoccurrence of my rosacea	Emotion
15. I avoid certain foods or drinks because of my rosacea	Function
16. My skin feels bumpy (uneven, not smooth, irregular)	Symptom
17. My skin flushes	Symptom
18. My skin gets irritated easily (cosmetics, aftershaves, cleansers)	Symptom
19. My eyes bother me (feel dry or gritty)	Symptom
20. I think about my rosacea	Emotion

ROSA QOL

- Clinical parameters often poorly related to impact on QoL
- Can provide valuable insight into the QoL of patients with rosacea
- Personalized treatments
- Contradict the perception that rosacea is a cosmetic issue

Global ROSacea Consensus 2019 panel



OCULAR ROSACEA

- Overlooked by dermatologists
- >80% of facial rosacea patients have ocular involvement
- Lid involvement
  - Blepharitis
  - *0.7/cm2 vs 12.8 mites*
  - MGD
  - Eyelid telangiectasias

Rainer BM, Kang S, Chien AL. Rosacea: epidemiology, pathogenesis, and treatment. *Dermatoendocrinol* 2017

OCULAR ROSACEA IMPACTS CORNEA

- >40% have corneal involvement
- Conjunctival hyperaemia
- SPK
- Corneal vascularization/pannus
- Infiltrates/ulcers
- Phlyctenules
- Scarring
- Limbal stem cell deficiency

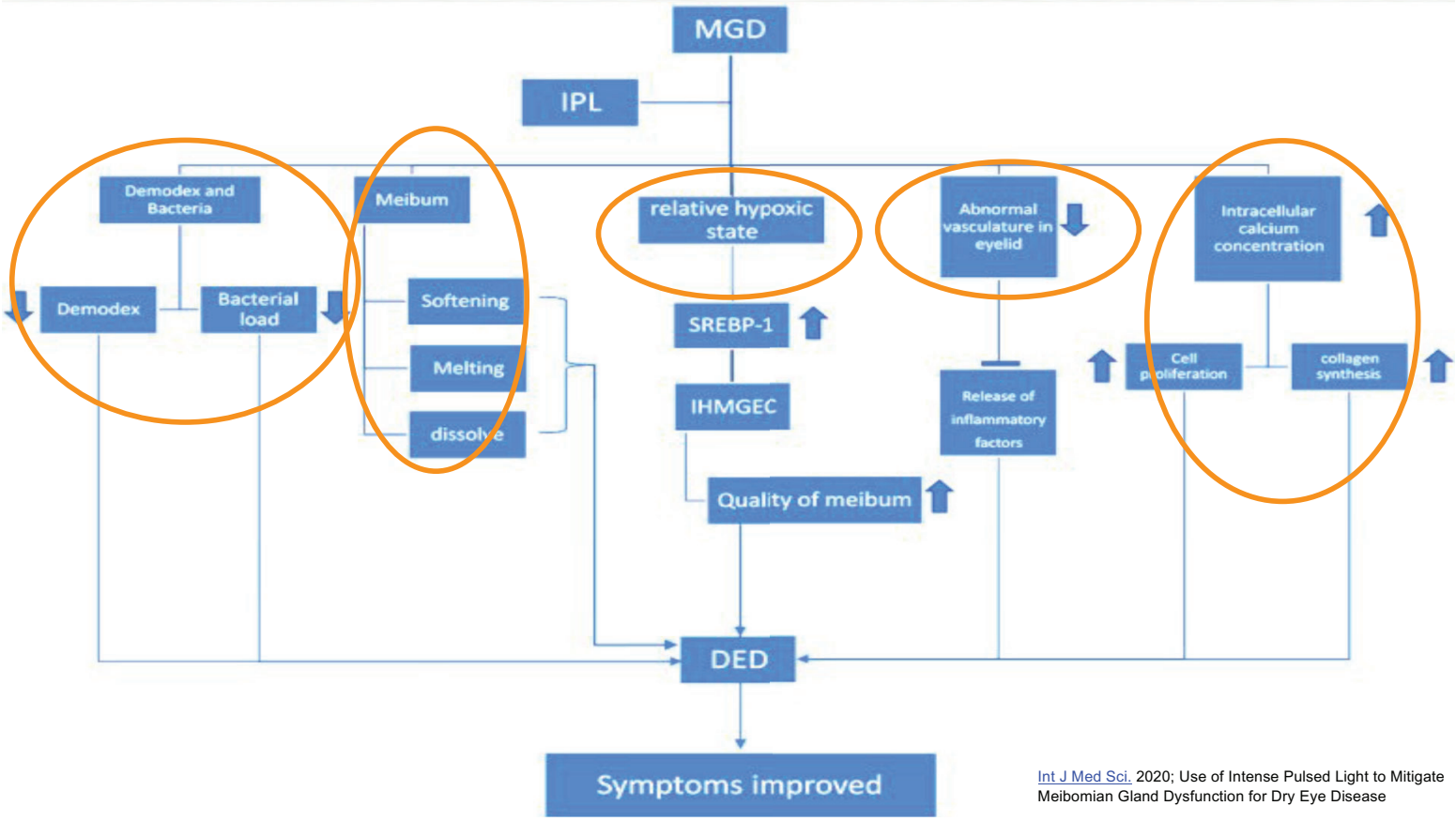
Goals of combining treatments in rosacea include:

- Help achieve skin clear of rosacea
- Help patients achieve treatment goals more quickly
- Maximize remission periods
- Minimize burden of disease

ROSACEA TREATMENT UPDATE

- Skincare/ SPF
- Topical therapies
  - Brimonidine/oxymatazoline/ ivermectin/metronidazole/benzyl benzoate
- Oral therapies
  - Doxycylcine/Beta Blockers Hydroxychloroquine
- Laser and IPL
- Injections
  - Botox /IL 17 inhibitors

Dermatol Ther (Heidelb). 2021 Feb;Rosacea Treatment: Review an



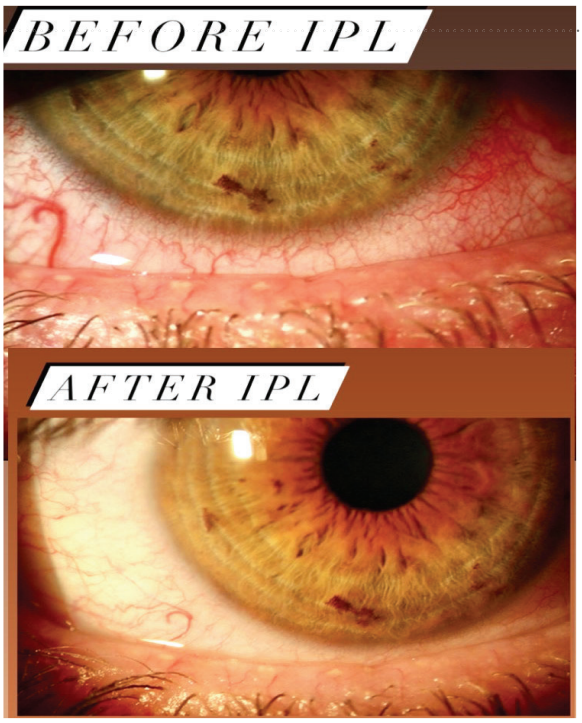
Int J Med Sci. 2020; Use of Intense Pulsed Light to Mitigate Meibomian Gland Dysfunction for Dry Eye Disease

Summary of studies on IPL for DED Therapy

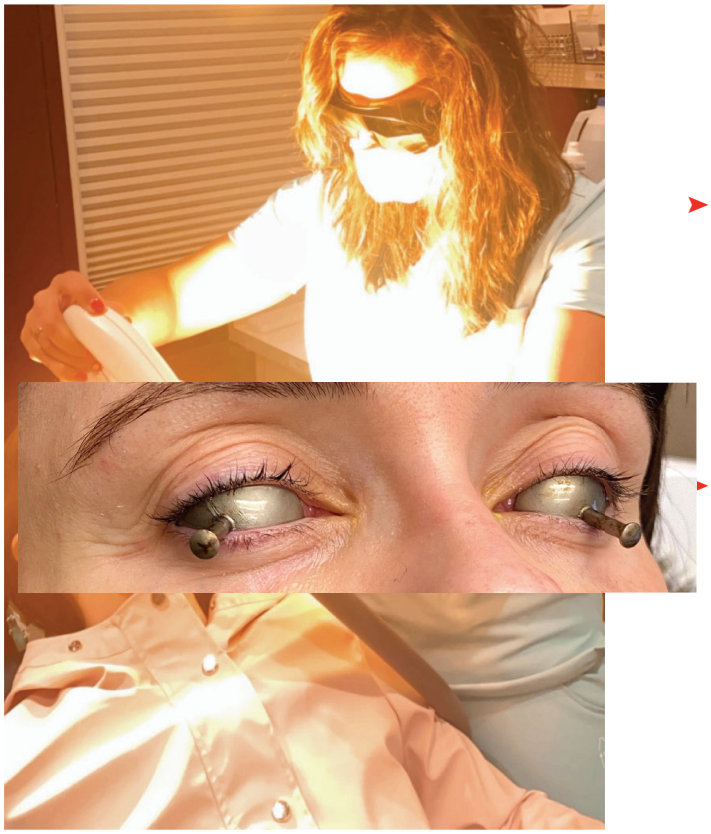
Year	Design	Patients (n)	IPL sessions	Dry eye symptom	BUT	Meibomian function
2020	Prospective	58	5	Improved	Improved	Improved
	randor					
	double					
	placeb					
2020	Prospe					
	randor					
	double					
	sham-(					
2020	Prospe					
	contro					
	randor					
2020	Retros					
2019	Prospe					
	contro					
	randor					
2019	Prospe					
	controlled					

2019	Prospective controlled	12	1	Improved OSDI	Improved	-
2019	Prospective comparative	40	3	Improved OSDI	Improved	-
2019	Pro					
2019	Pro					
2019	Cas					
2019	Ret					
2019	Ret					
2018	Pro					
2018	Pro					
2017	Prospective, randomized, double-masked, controlled	44	3	Improved OSDI, SPEED	Improved	Improved
2017	Prospective, randomized, double-masked, controlled	44	3	Improved SPEED with no statistical difference	Improved	Improved
2017	Prospective interventional noncomparative	40	4	Improved SPEED	Improved	Improved
2017	Prospective noncomparative	36	4	-	Improved	-
2016	Prospective, open label	40	4	Subjective symptoms improved	Improved	Improved
2016	Retrospective	100	4	Improved OSDI	Improved	Improved
2015	Prospective controlled	28	3	Improved OSDI, SPEED	Improved	-
2015	Retrospective noncomparative case series	91	7	Subjective symptoms improved	Improved	-

IPL WORKS

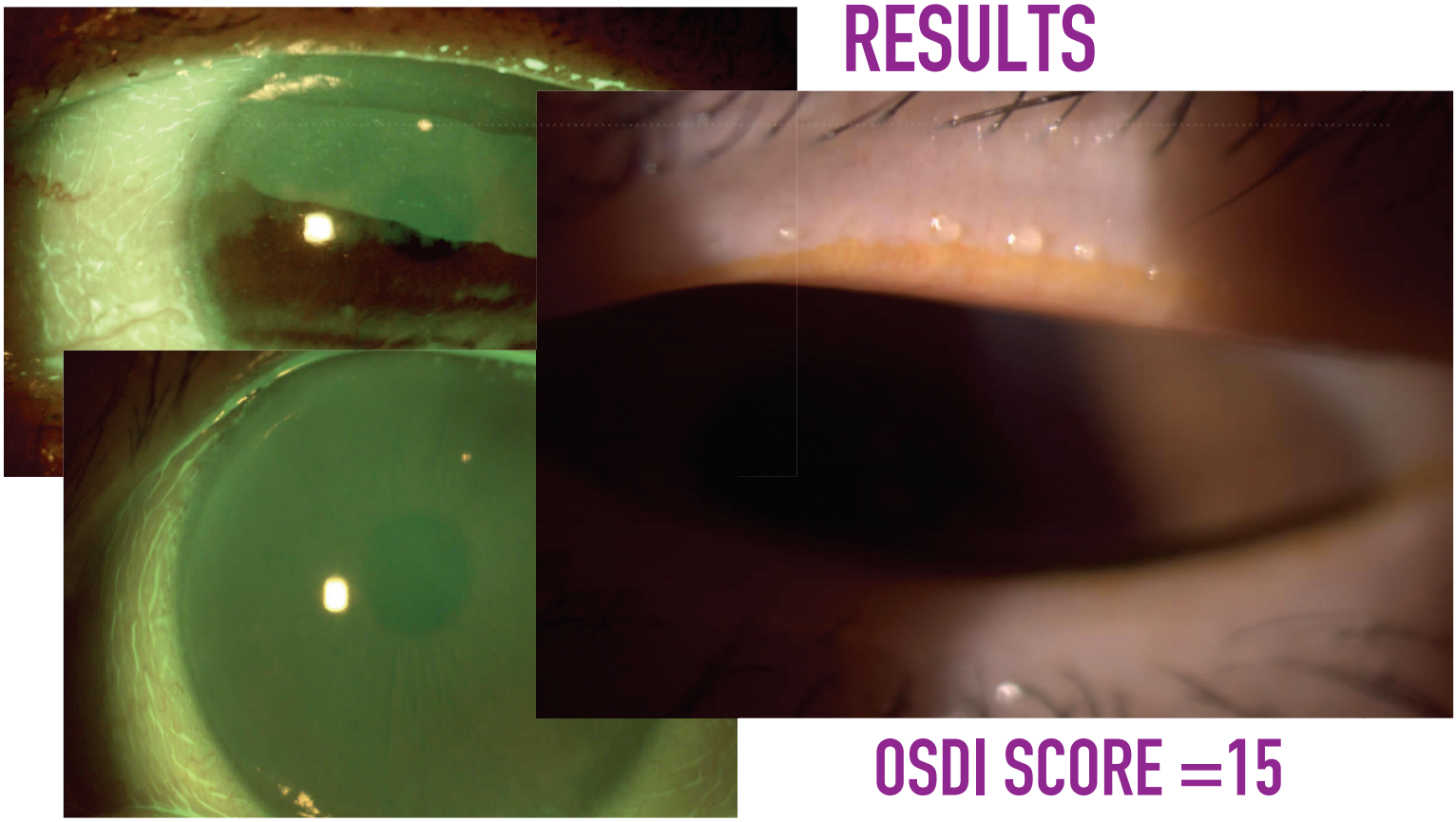


Int J Med Sci. 2020; Use of Intense Pulsed Light to Mitigate Meibomian Gland Dysfunction for Dry Eye Disease



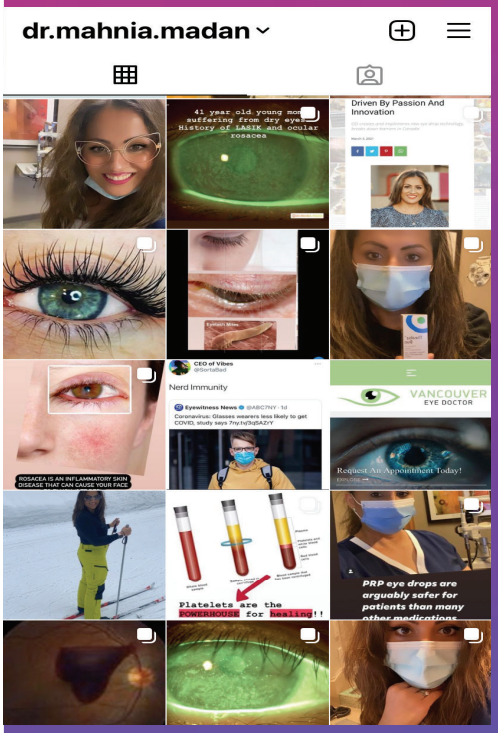
TREATMENT PLAN

- Dx: Obstructive MGD with underlying ocular/facial rosacea
  - IPL therapy (5x)
  - iLux (2x)
  - PRP (2x)
  - FML x 2 months
- Maintain with:
  - Lid hygiene (HoCL, Zocufoam)
  - Omega 3/Curcumin
  - Xiidra BID OU
  - Topical Ivermectin
  - Thealoz TID OU
  - Reduce rosacea triggers + dermatology consult



RESULTS

OSDI SCORE =15



THANK YOU!!
CONNECT WITH ME

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