California State Board of Optometry
BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY • GAVIN NEWSOM, GOVERNOR
DEPARTMENT OF CONSUMER AFFAIRS • CALIFORNIA STATE BOARD OF OPTOMETRY
2450 Del Paso Road, Suite 105, Sacramento, CA 95834
P (916) 575-7170 | Toll-Free (866) 585-2666 | www.optometry.ca.gov

# ISSUE MEMORANDUM

| | |
|---|---|
| **DATE** | May 31, 2024 |
| **TO** | Members, California State Board of Optometry (CSBO) |
| **FROM** | Gregory Pruden, Executive Officer |
| **SUBJECT** | Agenda Item #6 – Presentation from Dr. Melissa Barnett, OD, FAAO, FSLA, FBCLA, Director of Optometry, University of California, Davis, Regarding Ocular Surface Disease: Exploring the Impact of Hormonal Influence |

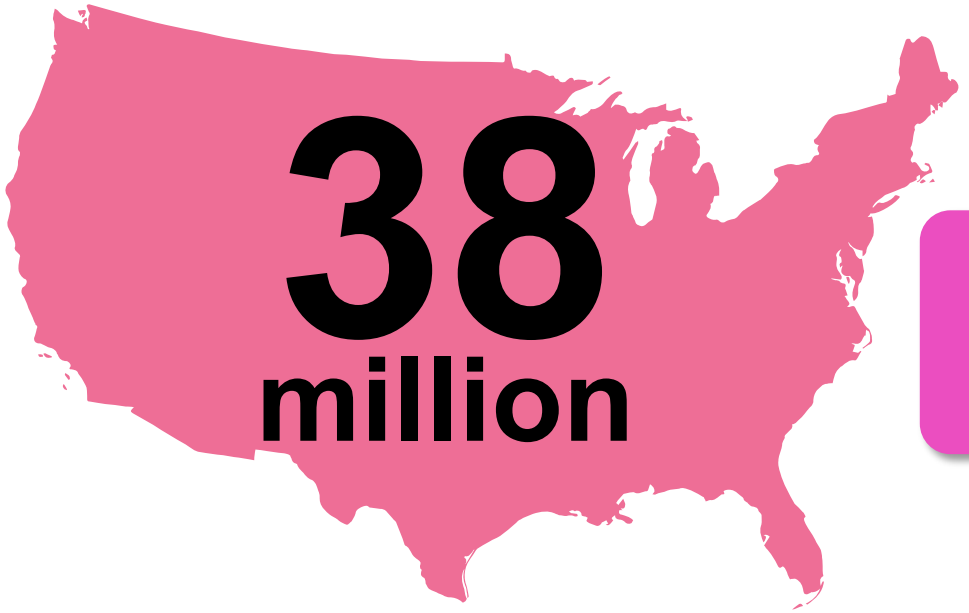
The Board will receive a presentation from Dr. Melissa Barnett, OD, FAAO, FSLA, FBCLA, Director of Optometry, University of California, Davis, Regarding Ocular Surface Disease: Exploring the Impact of Hormonal Influence.

Attachment: Presentation slides

# *Ocular Surface Disease: Exploring the Impact of Hormonal Influence*

MELISSA BARNETT, OD, FAAO,
FSLS, FBCLA

# *DED Is one of the Most Common Eye Diseases in the United States*[1]




= **1 out of every 7 American adults***[4]

**American adults suffer from symptoms of DED**[1-3]

* Aged 18+



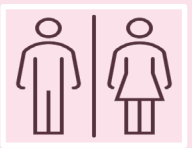
1. Karpecki PM, et al. *Am J Manag Care*. 2023;29(13)(suppl):S237-S247. 2. Paulsen AJ, et al. *Am J Ophthalmol*. 2014;157(4):799-806. 3. Farrand KF, et al. *Am J Ophthalmol*. 2017;182:90-98. 4. US Census Bureau. December 2022. Accessed December 5, 2023. https://www2.census.gov/programs-surveys/popest/tables/2020-2022/state/detail/SCPRC-EST2022-18+POP.xlsx

# *Risk Factors for DED*

Systemic Medications

Topical Medications

Age

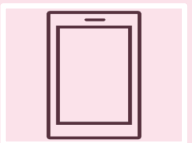


Sex

Contact Lens Wear

Ocular Surgery

Environment



Digital Devices

Systemic Disease

Smoking

Certain Anterior Segment Diseases



Sheppard J, et al. *Ann Med.* 2023;55(1):241-252. Moss SE, et al. *Arch Ophthalmol.* 2000;118(9):1264-1268.

# DED: TFOS DEWS II Definition – 2017

*Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.*

**Loss of tear film homeostasis characterizes DED**

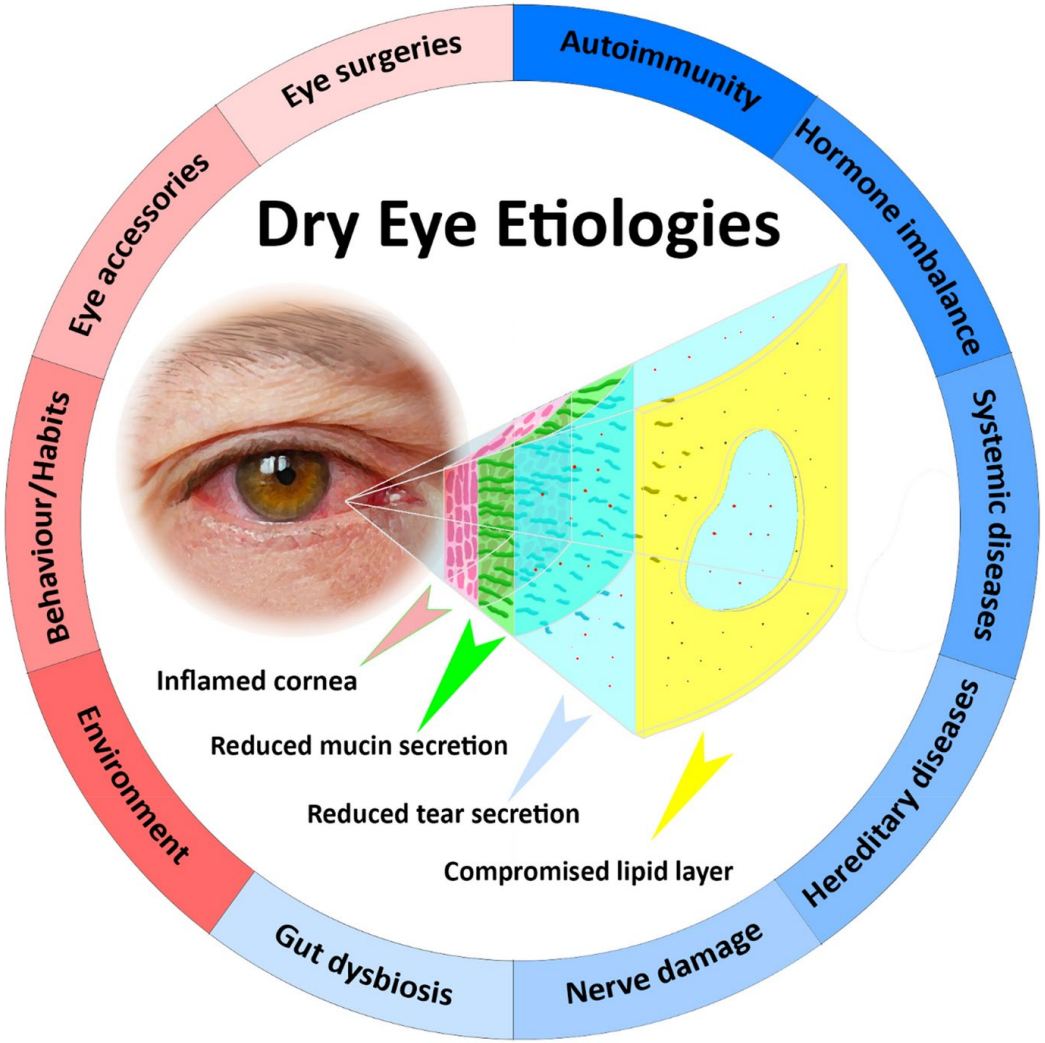
**Tear film instability in DED leads to increased evaporation and hyperosmolarity, which leads to inflammation**



Craig JP, et al. *Ocul Surf*. 2017;15(3):276-283.

DEWS, Dry Eye WorkShop; TFOS, Tear Film & Ocular Surface Society.

# *Evaporation spins the vicious cycle of inflammation*



# *Dry Eye Syndrome*

- Prevalence is much higher among women
- Aging is a risk factor
- Sex hormones are key factors
- Changing hormone levels / decreased androgens are contributory

# DED

The Ocular Surface 15 (2017) 284–333

Contents lists available at ScienceDirect

The Ocular Surface

journal homepage: www.theocularsurface.com

TFOS DEWS II Sex, Gender, and Hormones Report

David A. Sullivan, PhD [a, 1, *], Eduardo M. Rocha, MD, PhD [b], Pasquale Aragona, MD, PhD [c], Janine A. Clayton, MD [d], Juan Ding, OD, PhD [e], Blanka Golebiowski, PhD [f], Ulrike Hampel, MD [g], Alison M. McDermott, PhD [h], Debra A. Schaumberg, ScD, OD [i, j], Sruthi Srinivasan, PhD [k], Piera Versura, BSD [l], Mark D.P. Willcox, PhD, DSc [f]

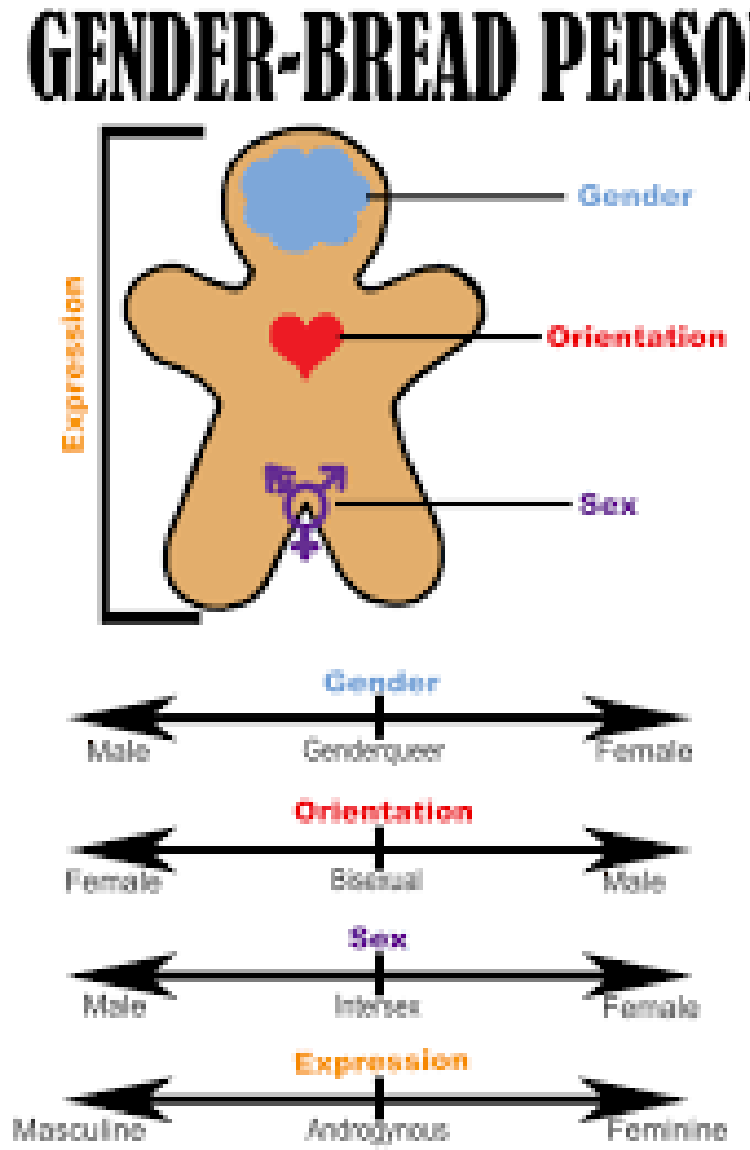
- Occurs more frequently in women than men
- Significant risk factor for the development of DED is female sex
- Sex-related difference in DED prevalence greatly attributed to the effects of
  - Sex steroids
    - Androgens, estrogens, hypothalamic-pituitary hormones, glucocorticoids, insulin, insulin-like growth factor 1 and thyroid hormones
  - Sex chromosome complement, sex-specific autosomal factors and epigenetics (e.g. microRNAs)

# *Gender and DED*

- Gender is a risk factor for DED
- Gender and sex have different meanings, although often used interchangeably
- Gender – Person's self-representation as a man or woman
- Sex – Distinguishes males and females based on their biological characteristics
- Both gender and sex affect
  - DED risk
  - Presentation of the disease
  - Immune responses
  - Pain
  - Care-seeking behaviors, etc.

# *Sex, gender and hormones*

- Sex, gender and hormones play a major role in the regulation of ocular surface and adnexal tissues
- Difference in DED prevalence between women and men



# Hormones

- Hormone change during menopause could worsen DES
- Previously thought sex hormone replacement therapy (SHRT) may improve DES
- Epidemiologic studies
  - DES incidence in women on SHRT is GREATER than women not on SHRT
  - Specifically, higher incidence of DES of older women on SHRT, especially using estrogen alone

Jensen AA, Higginbotham EJ, Guzinski GM, *et al*. A survey of ocular complaints in postmenopausal women. J Assoc Acad Minor Phys 2000; 11:44–49. Okon A, Jurowski P, Gos R. The influence of the hormonal replacement therapy on conjunctival epithelium morphology among peri- and postmenopausal women. Klinika oczna 2001; 103:183–186. Chia EM, Mitchell P, Rochtchina E, *et al*. Prevalence and associations of dry eye syndrome in an older population: the Blue Mountains Eye Study. Clin Exp Ophthalmol 2003; 31:229–232. Nagler RM, Pollack S. Sjögren's syndrome induced by estrogen therapy. Semin Arthritis Rheum 2000; 30:209–214. Erdem U, Ozdegirmenci O, Sobaci E, *et al*. Dry eye in postmenopausal women using hormone replacement therapy. Maturitas 2007; 56:257–262. Uncu G, Avci R, Uncu Y, *et al*. The effects of different hormone replacement therapy regimens on tear function, intraocular pressure and lens opacity. Gynecol Endocrinol 2006; 22:501–505.

# *Hormones*

- Increase in dry eye frequency and symptoms with longer SHRT use
- Findings disagree with other studies
  - Menopause was a risk factor for DES, but SHRT was beneficial
- Other studies
  - Estrogen therapy in women triggered or worsened the onset of DES and / or Sjögren's syndrome

# SHRT


- Theory for conflicting conclusions
- Outcome of SHRT depends on
  - 1. Estrogen dosage
  - 2. Age of the individuals when therapy is first initiated
    - Estrogen may only benefit younger women
    - Estrogen detrimental and / or pro-inflammatory in postmenopausal women
  - 3. Type and combination of SHRT applied
    - Estrogen at physiological doses – early ages
      - Supportive of lacrimal gland function and preservation of anterior ocular surface health
    - At higher doses and/or in combination with other hormonal supplements would be harmful and/or induce inflammation
    - Elderly women would be more susceptible

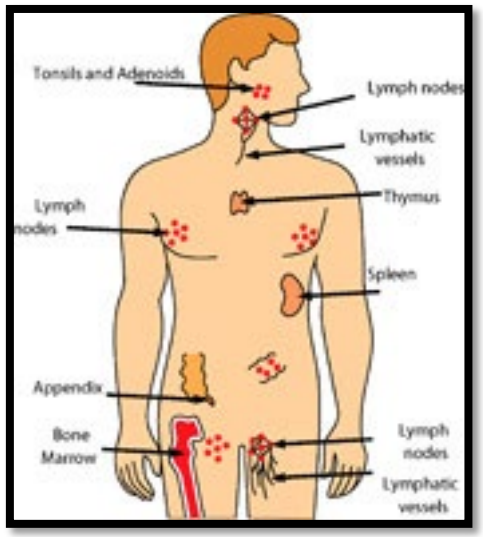
# Androgens

- Androgens impact structure and function of meibomian and lacrimal glands
- Important in regulating the ocular surface and adnexa
- Mediate many of the sex-related differences in these tissues
- Androgen deficiency is associated with both aqueous-deficient and evaporative DED

Sex hormones and the dry eye. Truong, S, Cole N, Stapleton F, et al. Clin Exp Optom. 2014 Apr 1. doi: 10.1111/cxo.12147. Knop E, Knop N, Millar T, Obata H, Sullivan DA. The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland. Invest Oph- thalmol Vis Sci 2011;52:1938e78. Sullivan DA, Wickham LA, Krenzer KL, Rocha EM, Toda I. Aqueous tear deficiency in Sjo€gren's syndrome: Possible causes and potential treatment. In: Pleyer U, Hartmann C, Sterry W, editors. Oculodermal Diseases - Immunology of Bullous Oculo-Muco-Cutaneous Disorders. Buren, The Netherlands: Aeolus Press; 1997. p. 95e152. Truong S, Cole N, Stapleton F, Golebiowski B. Sex hormones and the dry eye. Clin Exp Optom 2014;97:324e36.

# *Hormones and Dry Eye*

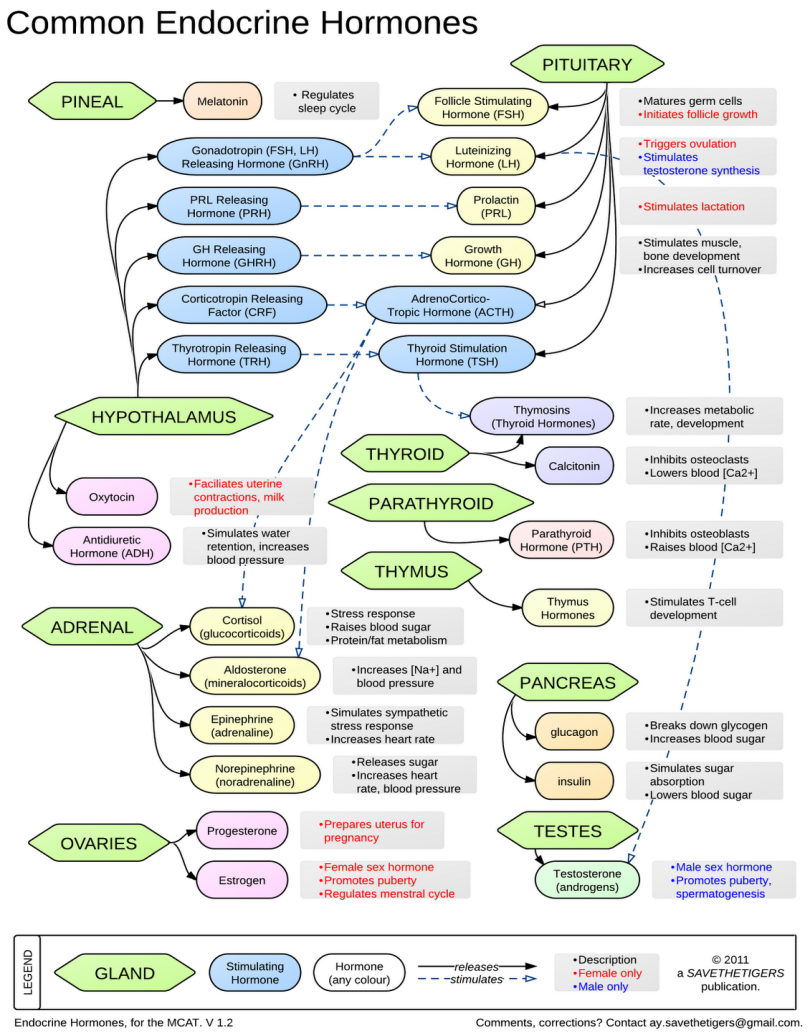
- Sex hormones influence the immune system
- Suggesting that estrogen may modulate a cascade of inflammatory events, which underlie dry eye




Sex hormones and the dry eye. Truong, S, Cole N, Stapleton F, et al. Clin Exp Optom. 2014 Apr 1. doi: 10.1111/cxo.12147.

# Endocrine system

- Hormones include
- Androgens
- Estrogens
- Progestins
- Hypothalamic-pituitary hormones
- Glucocorticoids
- Insulin
- Insulin like growth factor 1 (IGF-1)
- Thyroid hormones



# *Endocrine system*

- Plays a significant role in the regulation and sex-related differences of the ocular surface and adnexa
- Endocrine system hormones are involved in the development and/or treatment of aqueous-deficient and evaporative DED

## Endocrine Hormones

| Gland | Hormones | Functions |
|---|---|---|
| Thyroid | Thyroxine | Regulates metabolism and temperature |
| | Calcitonin | Inhibits release of calcium from the bones |
| Parathyroid | Parathyroid hormone | Stimulates the release of calcium from the bones. |
| Islet cells (in the pancreas) | Insulin | Decreases blood sugar by promoting uptake of glucose by cells. |
| | Glucagon | Increases blood sugar by stimulating breakdown of glycogen in the liver. |
| Testes | Testosterone | Regulates sperm cell production and secondary sex characteristics. |
| Ovaries | Estrogen | Stimulates egg maturation, controls secondary sex characteristics. |
| | Progesterone | Prepares the uterus to receive a fertilized egg. |
| Adrenal medulla | Epinephrine - fight<br>Norepinephrine - flight | Stimulates "fight or flight" response. |
| Adrenal cortex | Glucocorticoids | Part of stress response, increase blood glucose levels and decrease immune response.<br>Example: Cortisol - helps regulate metabolism and helps your body respond to stress |
| | Aldosterone | Regulates sodium content in the blood. |
| Pineal gland | Melatonin | Sleep cycles, reproductive cycles in many mammals. |

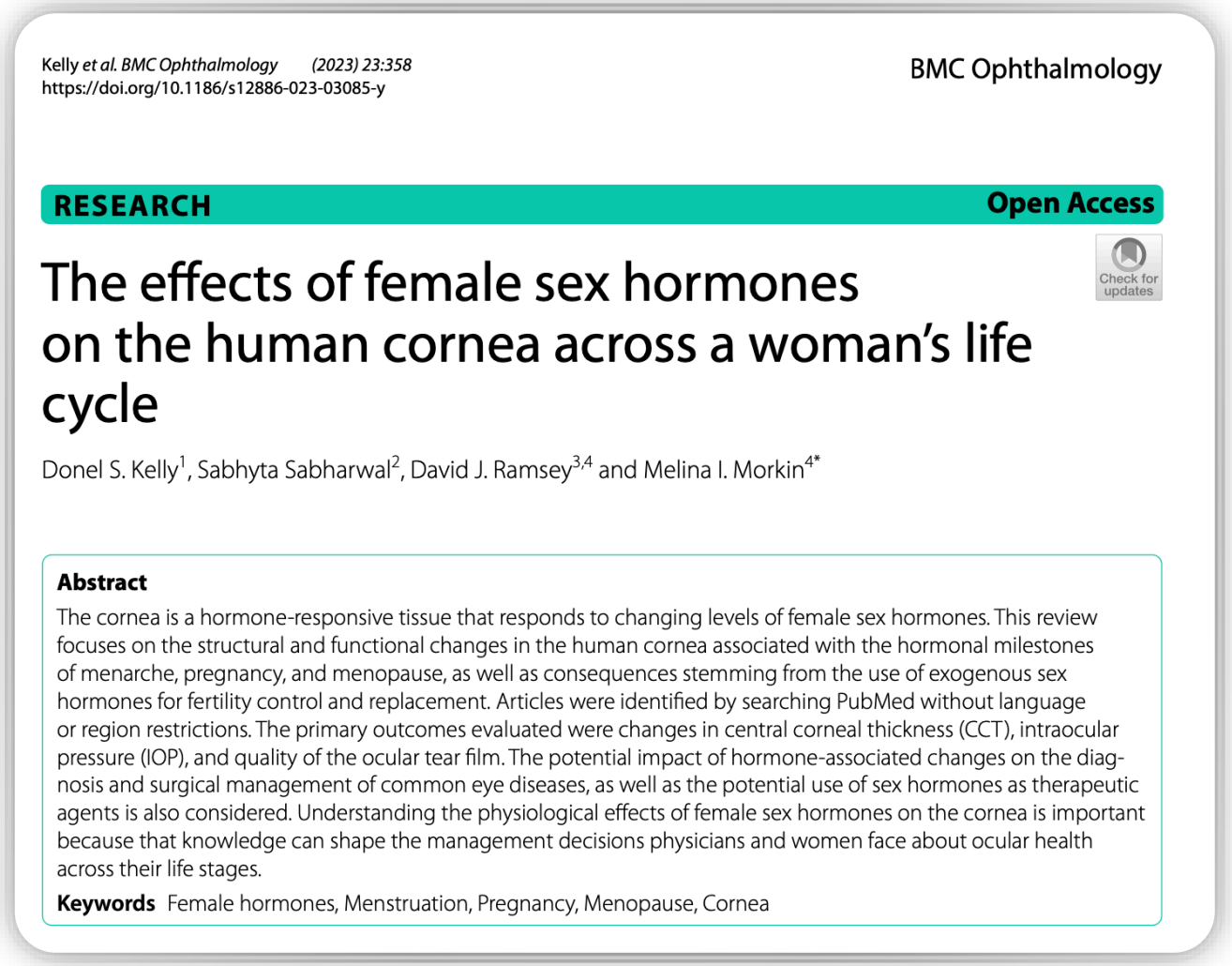
Sullivan DA, Rocha ER, Aragona P, et al. TFOS DEWS II Sex, Gender and Hormones Report. The Ocular Surface. 2017 284-333.

# *Androgen deficiency*

- Associated with corneal and conjunctival damage
- Patients on anti-androgen therapy have
  - Significant decrease in (TBUT)
  - Significant increase in corneal fluorescein and rose bengal staining
  - Significant increase in inferior bulbar conjunctival rose bengal staining

Cermak JM, Krenzer KL, Sullivan RM, Dana MR, Sullivan DA. Is complete androgen insensitivity syndrome associated with alterations in the meibomian gland and ocular surface? Cornea 2003;22:516e21.

- Cornea - hormone-responsive tissue that responds to changing levels of female sex hormones.
- Review of structural and functional changes in the human cornea associated with the hormonal milestones of menarche, pregnancy, and menopause.
- Review of consequences stemming from the use of exogenous sex hormones for fertility control and replacement.
- Articles identified by a PubMed search.



Kelly *et al. BMC Ophthalmology* (2023) 23:358
https://doi.org/10.1186/s12886-023-03085-y

BMC Ophthalmology

RESEARCH Open Access

# The effects of female sex hormones on the human cornea across a woman's life cycle

Donel S. Kelly[1], Sabhyta Sabharwal[2], David J. Ramsey[3,4] and Melina I. Morkin[4*]

**Abstract**

The cornea is a hormone-responsive tissue that responds to changing levels of female sex hormones. This review focuses on the structural and functional changes in the human cornea associated with the hormonal milestones of menarche, pregnancy, and menopause, as well as consequences stemming from the use of exogenous sex hormones for fertility control and replacement. Articles were identified by searching PubMed without language or region restrictions. The primary outcomes evaluated were changes in central corneal thickness (CCT), intraocular pressure (IOP), and quality of the ocular tear film. The potential impact of hormone-associated changes on the diagnosis and surgical management of common eye diseases, as well as the potential use of sex hormones as therapeutic agents is also considered. Understanding the physiological effects of female sex hormones on the cornea is important because that knowledge can shape the management decisions physicians and women face about ocular health across their life stages.

**Keywords** Female hormones, Menstruation, Pregnancy, Menopause, Cornea

# Primary Outcomes Evaluated Were

- Changes in central corneal thickness (CCT)
- Changes in intraocular pressure (IOP)
- Tear film quality

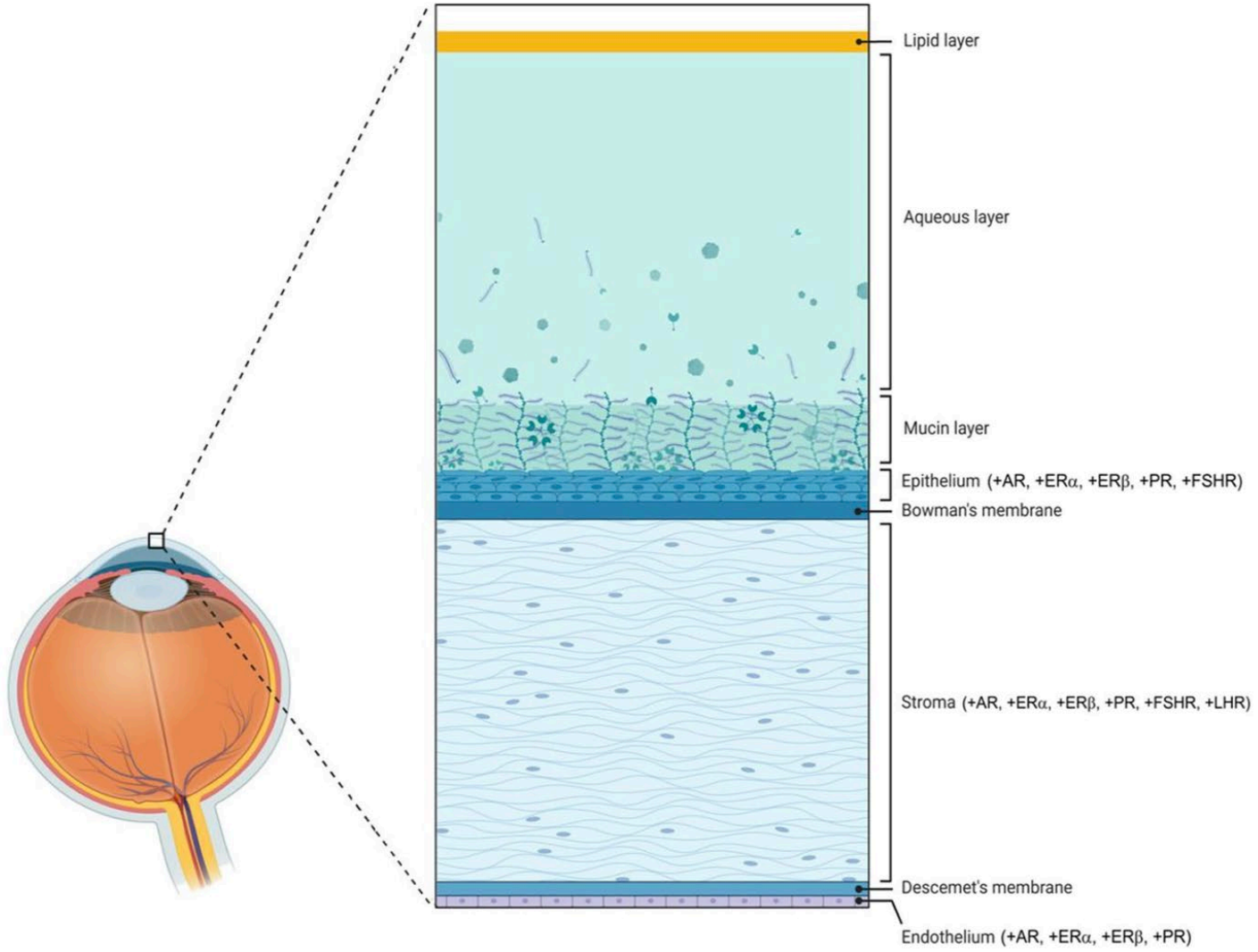



**Fig. 1** Diagram illustrating the layers of the human cornea and location of hormonal receptors. Notations: AR (androgen receptor); ER (estrogen receptor); PR (progesterone receptor); LHR (luteinizing hormone receptor); FSHR (follicle-stimulating hormone receptor). A plus-sign ( +) indicates evidence of receptor or enzyme mRNA expression in that respective layer. Figure was made in ©BioRender-biorender.com

# *The effects of female sex hormones on the human cornea across a woman's life cycle*

- Tear film changes during pregnancy may impact the function of the ocular surface
- Hormonal shifts in menopause follow a pattern opposite to those in pregnancy
- IOP tends to ↑ after menopause
- CCT tends to ↓ after menopause
- Higher incidence of DED among postmenopausal women
- The cornea responds to external hormonal treatments, such as HRT and hormonal preparation for IVF

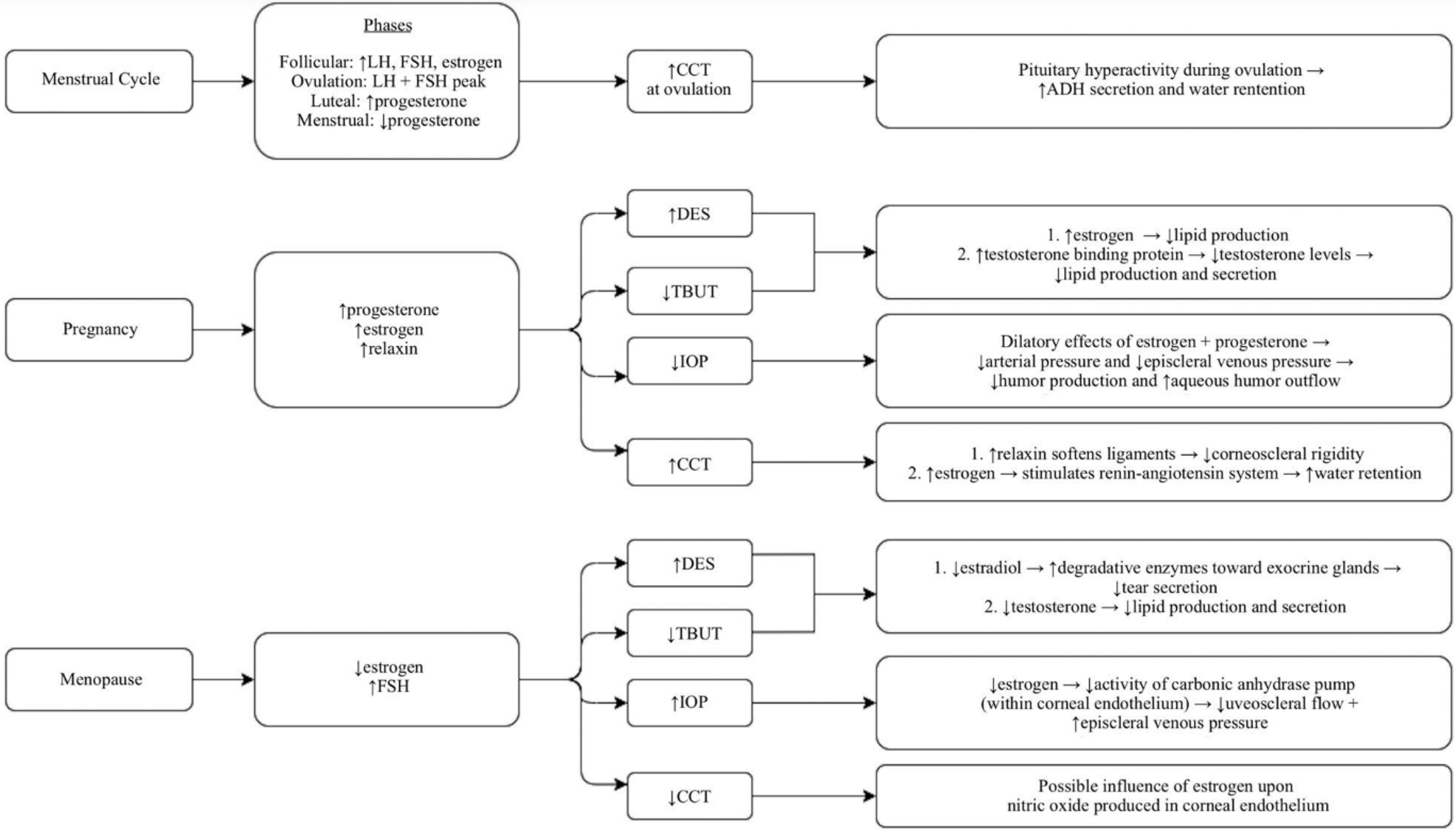
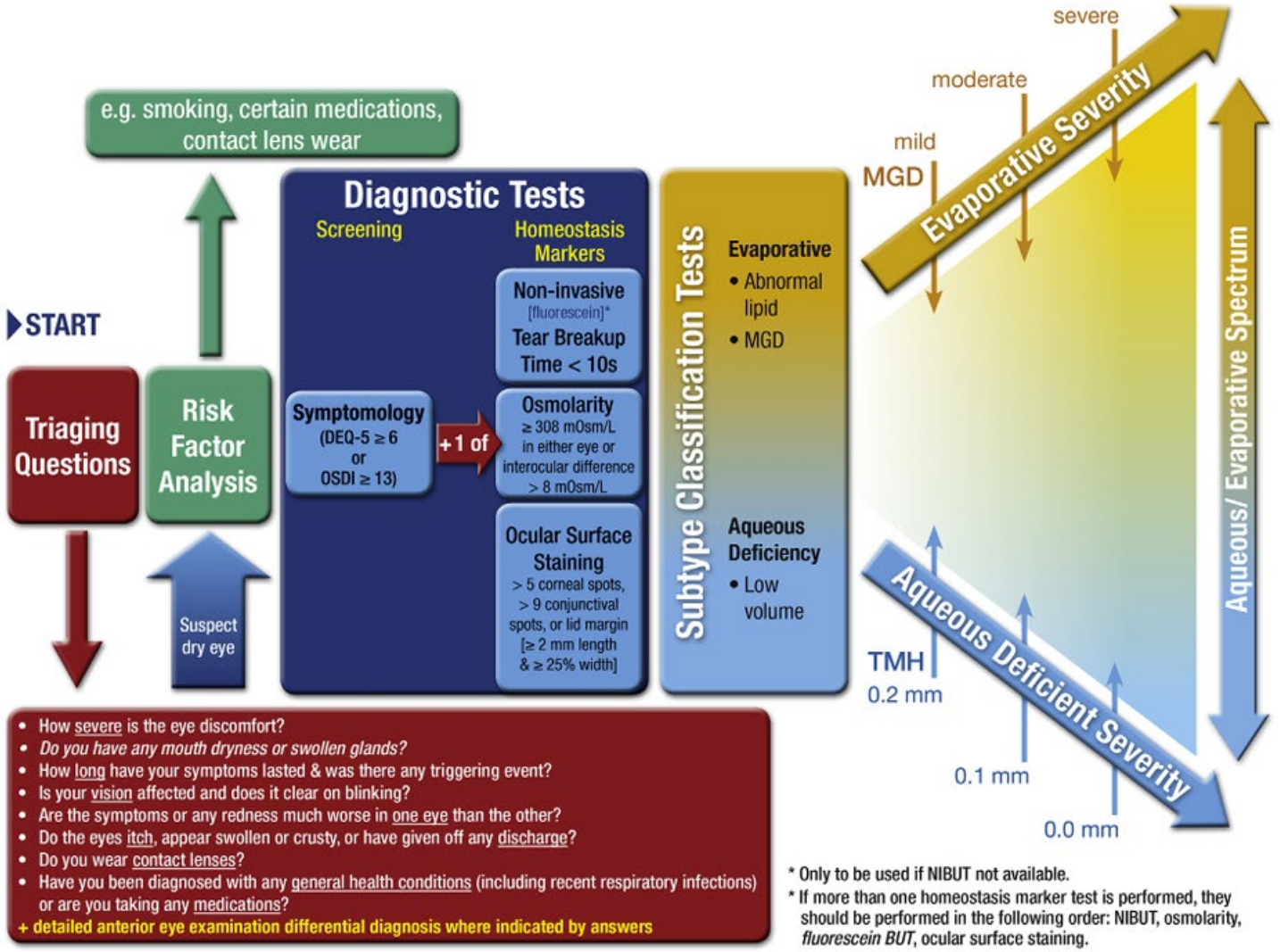



**Fig. 2** Schematic diagram of hormonal changes across the different stages of a woman's life, illustrating their impact on IOP, CCT, TBUT, and DES, as well as the proposed etiologies for each of these changes. Notations: CCT (central corneal thickness); IOP (intraocular pressure); TBUT – Tear Break-Up Time; DES – Dry Eye Symptoms; LH – Luteinizing Hormone; FSH – Follicle-Stimulating Hormone; ↑—increase; ↓—decrease; →—

- Potential use of sex hormones as therapeutic agents
  - Treatment of refractive errors
  - Topical application of estrogen eye drops resulted in a 0.6-diopter myopic shift that regressed with treatment cessation

- "Understanding the physiological effects of female sex hormones on the cornea is important…knowledge can shape the management decisions physicians and women face about ocular health across their lifetimes."

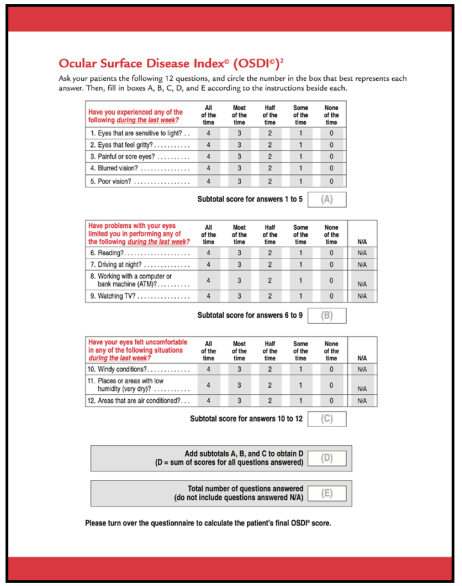
# DEWS II Diagnostic APPROACH: Subtype Classification TESTS



# *Dry Eye Diagnosis: signs and symptoms*

- Validated dry eye questionnaire

- One of the following:
  - Hyperosmolarity
    - Elevated: > 308 mOsm/L OR ± 8 intereye difference
  - (+) Vital dye staining
    - Fluorescein and/or lissamine
  - TBUT
    - < 10 seconds



Ocular Surface Disease Index® (OSDI®)[2]

Ask your patients the following 12 questions, and circle the number in the box that best represents each answer. Then, fill in boxes A, B, C, D, and E according to the instructions beside each.

| Have you experienced any of the following *during the last week*? | All of the time | Most of the time | Half of the time | Some of the time | None of the time | |
|---|---|---|---|---|---|---|
| 1. Eyes that are sensitive to light? | 4 | 3 | 2 | 1 | 0 | |
| 2. Eyes that feel gritty? | 4 | 3 | 2 | 1 | 0 | |
| 3. Painful or sore eyes? | 4 | 3 | 2 | 1 | 0 | |
| 4. Blurred vision? | 4 | 3 | 2 | 1 | 0 | |
| 5. Poor vision? | 4 | 3 | 2 | 1 | 0 | |

Subtotal score for answers 1 to 5 (A)

| Have problems with your eyes limited you in performing any of the following *during the last week*? | All of the time | Most of the time | Half of the time | Some of the time | None of the time | N/A |
|---|---|---|---|---|---|---|
| 6. Reading? | 4 | 3 | 2 | 1 | 0 | N/A |
| 7. Driving at night? | 4 | 3 | 2 | 1 | 0 | N/A |
| 8. Working with a computer or bank machine (ATM)? | 4 | 3 | 2 | 1 | 0 | N/A |
| 9. Watching TV? | 4 | 3 | 2 | 1 | 0 | N/A |

Subtotal score for answers 6 to 9 (B)

| Have your eyes felt uncomfortable in any of the following situations *during the last week*? | All of the time | Most of the time | Half of the time | Some of the time | None of the time | N/A |
|---|---|---|---|---|---|---|
| 10. Windy conditions? | 4 | 3 | 2 | 1 | 0 | N/A |
| 11. Places or areas with low humidity (very dry)? | 4 | 3 | 2 | 1 | 0 | N/A |
| 12. Areas that are air conditioned? | 4 | 3 | 2 | 1 | 0 | N/A |

Subtotal score for answers 10 to 12 (C)

Add subtotals A, B, and C to obtain D (D = sum of scores for all questions answered) (D)

Total number of questions answered (do not include questions answered N/A) (E)

Please turn over the questionnaire to calculate the patient's final OSDI® score.

© Outcomes Research Group


© TearLab

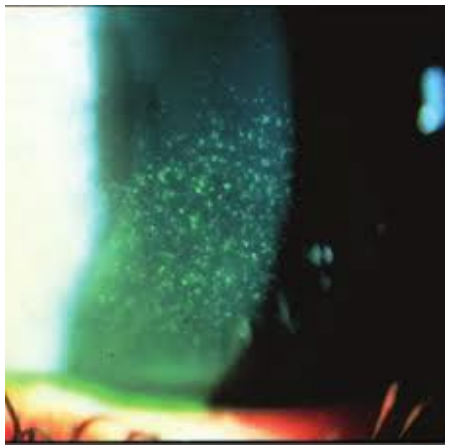


*Image courtesy of Leslie O'Dell, OD*

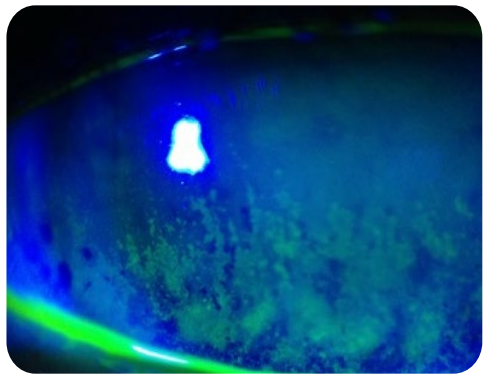


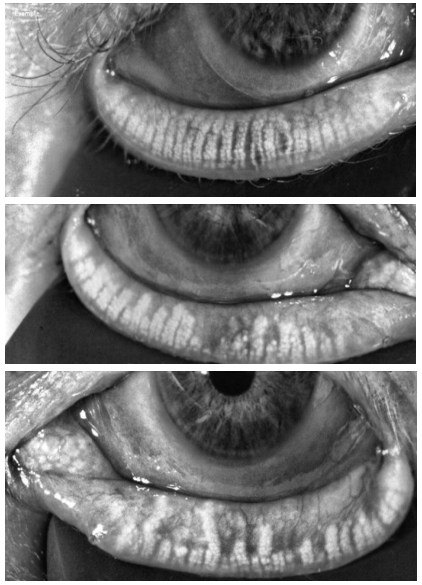
*Image courtesy of Karl Stonecipher, MD*

Tomlinson A, et al. *Invest Ophthalmol Vis Sci*. 2011;52(4):2006-2049. Lemp MA, el, *Am J Ophthalmol*. 2011; 151(5):792-798.e1 Wolffsohn JS, et al. *Ocul Surf*. 2017;15(3):539-574. Milner MS, et al. *Curr Opin Ophthalmol*. 2017;27(suppl 1):3-47.

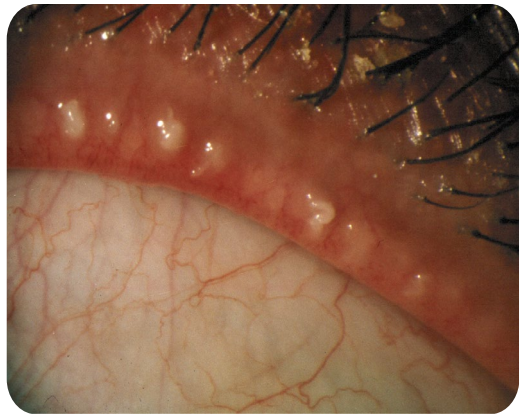
# *Subtyping to aid in the diagnosis of EDE*

- TBUT
- Meibography (structure)
- Lid margin, expressibility, and quality and quantity of meibum (function)

© TearLab



*Images courtesy of Alice T. Epitropoulos, MD, FACS*



© 1994 American Academy of Ophthalmology

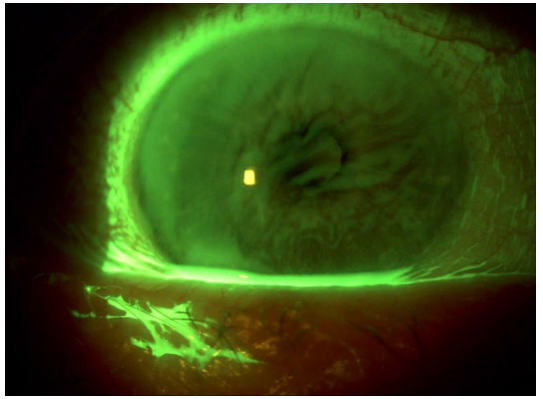
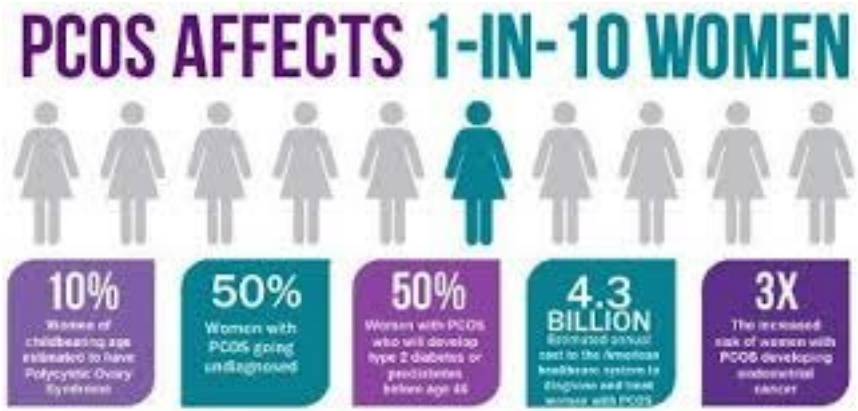


*Image courtesy of Alice T. Epitropoulos, MD, FACS*

Tomlinson A, et al. *Invest Ophthalmol Vis Sci*. 2011;52(4):2006-2049.
Wolffsohn JS, et al. *Ocul Surf*. 2017;15(3):539-574.
Milner MS, et al. *Curr Opin Ophthalmol*. 2017;27(suppl 1):3-47.

# *Effects of Sex Hormones on Ocular Surface Epithelia: Lessons Learned from Polycystic Ovary Syndrome (PCOS)*

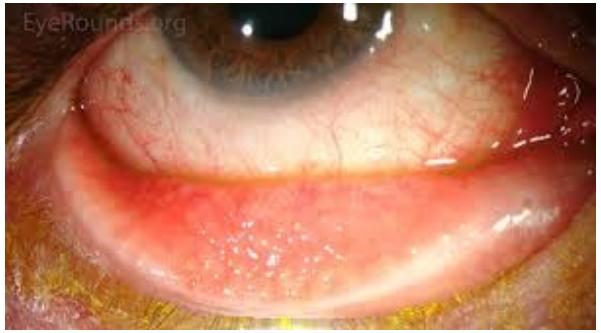
- PCOS most common endocrine abnormality in women of reproductive age
- Associated with
  - Type 2 diabetes
  - Obesity
  - Ocular surface disease




Mantelli F, Moretti C, Macchi I, et al. J Cell Physiol. October 2015

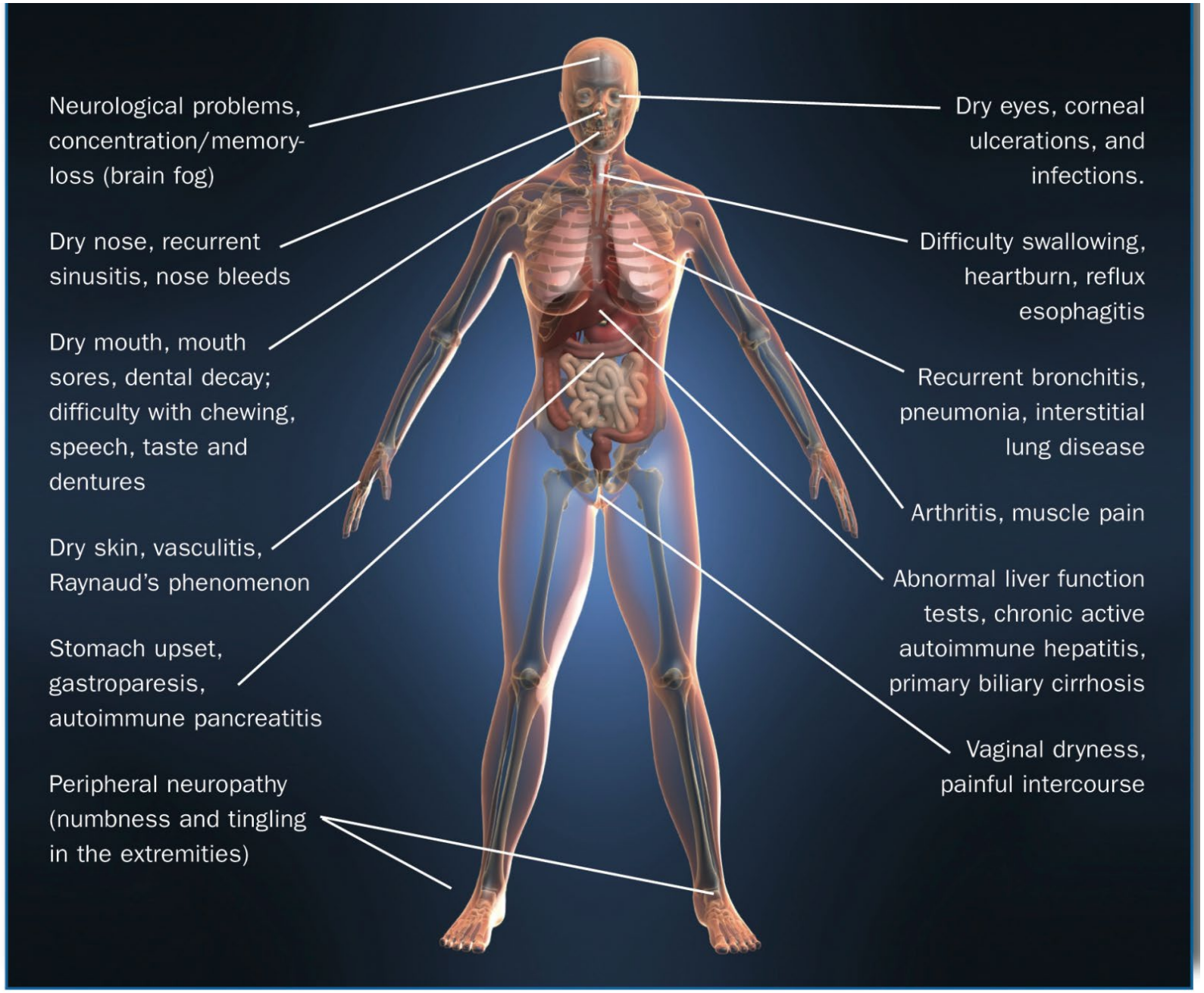
# PCOS

- Study evaluated
- Signs and symptoms related to ocular allergy and dry eye in young women with PCOS
- IDEA = Itchy-Dry Eye Associated with PCOS
  - Conjunctival hyperemia
  - Follicular reaction
  - Abundant mucous secretion
  - Occasional epithelial punctate keratitis

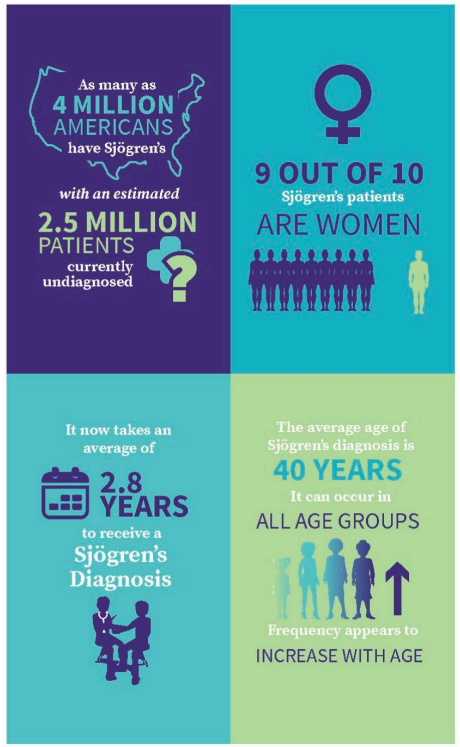



| | Involved Hormones | Receptor distribution sites | Affected functions |
|---|---|---|---|
| Cornea | Estrogens<br>Androgens<br>Progesterone | Epithelial cells<br>Stromal cells<br>Endothelial cells | Corneal thickness<br>Corneal curvature<br>Corneal sensitivity |
| Conjunctiva | Estrogens<br>Androgens | Epithelial cells<br>Goblet cells | MUC1 and MUC5AC expression and maturation index of conjunctival epithelium |
| Meibomian Glands | Androgens | Acinar cells | Production of fatty acids and lipids |
| Lacrimal Glands | Androgens (M>F) | Epithelial cells | Lacrimal gland secretory activity |

Table from Effects of Sex Hormones on Ocular Surface Epithelia: Lessons Learned from Polycystic Ovary Syndrome (PCOS)
Mantelli F, Moretti C, Macchi I, et al. J Cell Physiol. October 2015



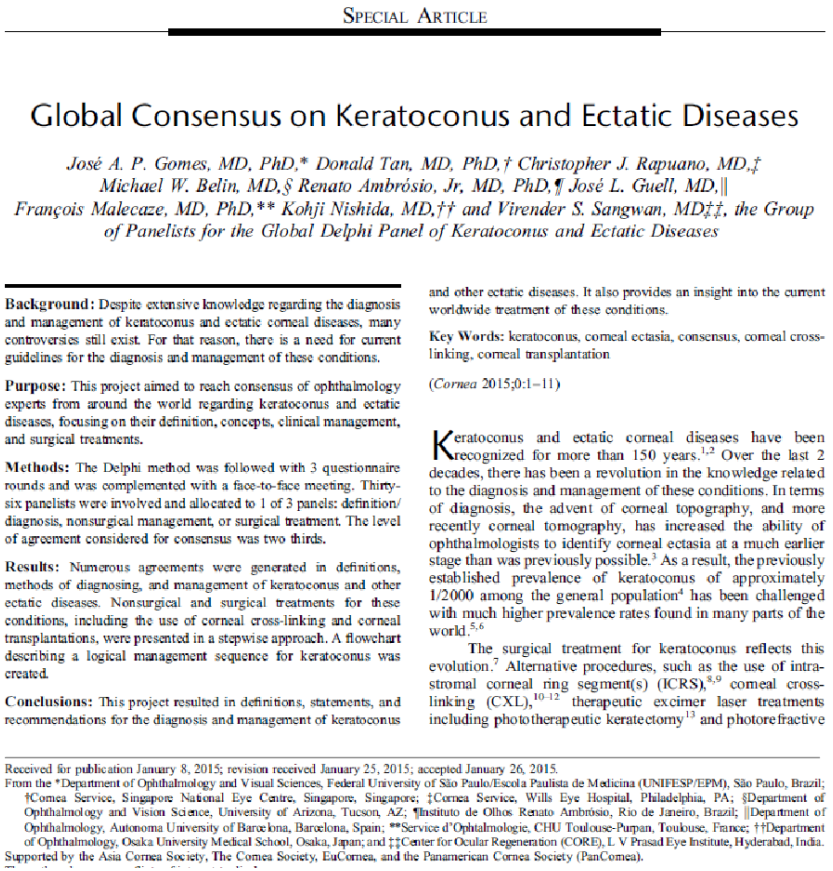





Sjögren's FOUNDATION

# KC DEFINITION

- Abnormal posterior ectasia
- Abnormal corneal thickness distribution
- Clinically non-inflammatory corneal thinning



SPECIAL ARTICLE

## Global Consensus on Keratoconus and Ectatic Diseases

*José A. P. Gomes, MD, PhD,* Donald Tan, MD, PhD,† Christopher J. Rapuano, MD,‡ Michael W. Belin, MD,§ Renato Ambrósio, Jr, MD, PhD,¶ José L. Guell, MD,‖ François Malecaze, MD, PhD,** Kohji Nishida, MD,†† and Virender S. Sangwan, MD‡‡, the Group of Panelists for the Global Delphi Panel of Keratoconus and Ectatic Diseases*

**Background:** Despite extensive knowledge regarding the diagnosis and management of keratoconus and ectatic corneal diseases, many controversies still exist. For that reason, there is a need for current guidelines for the diagnosis and management of these conditions.

**Purpose:** This project aimed to reach consensus of ophthalmology experts from around the world regarding keratoconus and ectatic diseases, focusing on their definition, concepts, clinical management, and surgical treatments.

**Methods:** The Delphi method was followed with 3 questionnaire rounds and was complemented with a face-to-face meeting. Thirty-six panelists were involved and allocated to 1 of 3 panels: definition/diagnosis, nonsurgical management, or surgical treatment. The level of agreement considered for consensus was two thirds.

**Results:** Numerous agreements were generated in definitions, methods of diagnosing, and management of keratoconus and other ectatic diseases. Nonsurgical and surgical treatments for these conditions, including the use of corneal cross-linking and corneal transplantations, were presented in a stepwise approach. A flowchart describing a logical management sequence for keratoconus was created.

**Conclusions:** This project resulted in definitions, statements, and recommendations for the diagnosis and management of keratoconus and other ectatic diseases. It also provides an insight into the current worldwide treatment of these conditions.

**Key Words:** keratoconus, corneal ectasia, consensus, corneal cross-linking, corneal transplantation

(*Cornea* 2015;0:1–11)

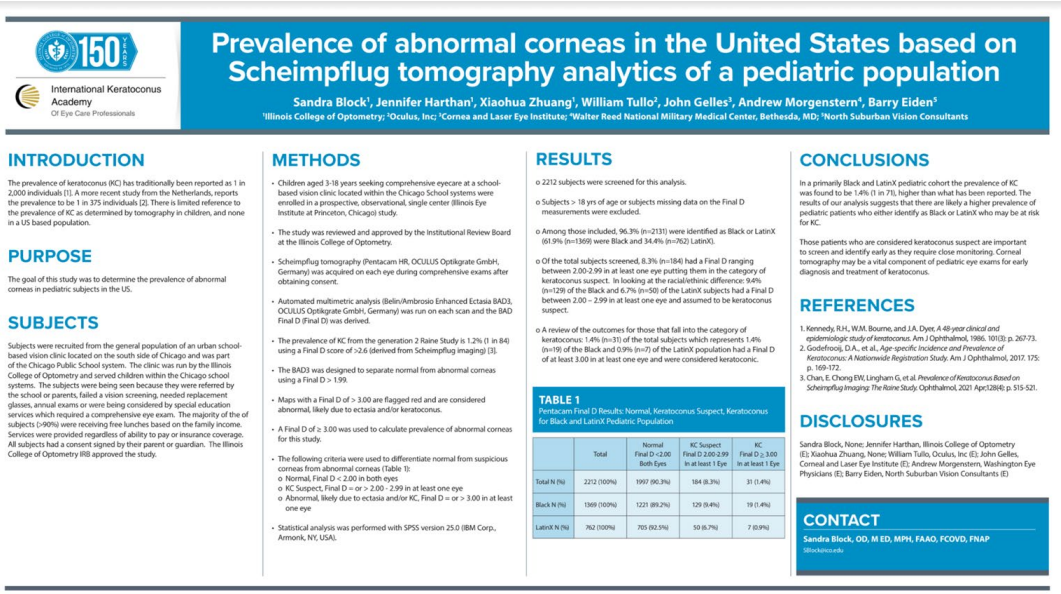
Keratoconus and ectatic corneal diseases have been recognized for more than 150 years.[1,2] Over the last 2 decades, there has been a revolution in the knowledge related to the diagnosis and management of these conditions. In terms of diagnosis, the advent of corneal topography, and more recently corneal tomography, has increased the ability of ophthalmologists to identify corneal ectasia at a much earlier stage than was previously possible.[3] As a result, the previously established prevalence of keratoconus of approximately 1/2000 among the general population[4] has been challenged with much higher prevalence rates found in many parts of the world.[5,6]

The surgical treatment for keratoconus reflects this evolution.[7] Alternative procedures, such as the use of intrastromal corneal ring segment(s) (ICRS),[8,9] corneal cross-linking (CXL),[10–12] therapeutic excimer laser treatments including phototherapeutic keratectomy[13] and photorefractive

Received for publication January 8, 2015; revision received January 25, 2015; accepted January 26, 2015.
From the *Department of Ophthalmology and Visual Sciences, Federal University of São Paulo/Escola Paulista de Medicina (UNIFESP/EPM), São Paulo, Brazil; †Cornea Service, Singapore National Eye Centre, Singapore, Singapore; ‡Cornea Service, Wills Eye Hospital, Philadelphia, PA; §Department of Ophthalmology and Vision Science, University of Arizona, Tucson, AZ; ¶Instituto de Olhos Renato Ambrósio, Rio de Janeiro, Brazil; ‖Department of Ophthalmology, Autonoma University of Barcelona, Barcelona, Spain; **Service d'Ophtalmologie, CHU Toulouse-Purpan, Toulouse, France; ††Department of Ophthalmology, Osaka University Medical School, Osaka, Japan; and ‡‡Center for Ocular Regeneration (CORE), L V Prasad Eye Institute, Hyderabad, India.
Supported by the Asia Cornea Society, The Cornea Society, EuCornea, and the Panamerican Cornea Society (PanCornea).

# New US Based Prevalence Study

- IKA & ICO United States Pediatric Data
  - Prevalence of 1:352
- Why? ADVANCED SCREENING DEVICES!!!



International Keratoconus Academy
Of Eye Care Professionals

## Prevalence of abnormal corneas in the United States based on Scheimpflug tomography analytics of a pediatric population

Sandra Block[1], Jennifer Harthan[1], Xiaohua Zhuang[1], William Tullo[2], John Gelles[3], Andrew Morgenstern[4], Barry Eiden[5]
[1]Illinois College of Optometry; [2]Oculus, Inc; [3]Cornea and Laser Eye Institute; [4]Walter Reed National Military Medical Center, Bethesda, MD; [5]North Suburban Vision Consultants

### INTRODUCTION

The prevalence of keratoconus (KC) has traditionally been reported as 1 in 2,000 individuals [1]. A more recent study from the Netherlands, reports the prevalence to be 1 in 375 individuals [2]. There is limited reference to the prevalence of KC as determined by tomography in children, and none in a US based population.

### PURPOSE

The goal of this study was to determine the prevalence of abnormal corneas in pediatric subjects in the US.

### SUBJECTS

Subjects were recruited from the general population of an urban school-based vision clinic located on the south side of Chicago and was part of the Chicago Public School system. The clinic was run by the Illinois College of Optometry and served children within the Chicago school systems. The subjects were being seen because they were referred by the school or parents, failed a vision screening, needed replacement glasses, annual exams or were being considered by special education services which required a comprehensive eye exam. The majority of the of subjects (>90%) were receiving free lunches based on the family income. Services were provided regardless of ability to pay or insurance coverage. All subjects had a consent signed by their parent or guardian. The Illinois College of Optometry IRB approved the study.

### METHODS

- Children aged 3-18 years seeking comprehensive eyecare at a school-based vision clinic located within the Chicago School systems were enrolled in a prospective, observational, single center (Illinois Eye Institute at Princeton, Chicago) study.
- The study was reviewed and approved by the Institutional Review Board at the Illinois College of Optometry.
- Scheimpflug tomography (Pentacam HR, OCULUS Optikgrate GmbH, Germany) was acquired on each eye during comprehensive exams after obtaining consent.
- Automated multimetric analysis (Belin/Ambrosio Enhanced Ectasia BAD3, OCULUS Optikgrate GmbH, Germany) was run on each scan and the BAD Final D (Final D) was derived.
- The prevalence of KC from the generation 2 Raine Study is 1.2% (1 in 84) using a Final D score of >2.6 (derived from Scheimpflug imaging) [3].
- The BAD3 was designed to separate normal from abnormal corneas using a Final D > 1.99.
- Maps with a Final D of > 3.00 are flagged red and are considered abnormal, likely due to ectasia and/or keratoconus.
- A Final D of ≥ 3.00 was used to calculate prevalence of abnormal corneas for this study.
- The following criteria were used to differentiate normal from suspicious corneas from abnormal corneas (Table 1):
  - o Normal, Final D < 2.00 in both eyes
  - o KC Suspect, Final D = or > 2.00 - 2.99 in at least one eye
  - o Abnormal, likely due to ectasia and/or KC, Final D = or > 3.00 in at least one eye
- Statistical analysis was performed with SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

### RESULTS

- o 2212 subjects were screened for this analysis.
- o Subjects > 18 yrs of age or subjects missing data on the Final D measurements were excluded.
- o Among those included, 96.3% (n=2131) were identified as Black or LatinX (61.9% (n=1369) were Black and 34.4% (n=762) LatinX).
- o Of the total subjects screened, 8.3% (n=184) had a Final D ranging between 2.00-2.99 in at least one eye putting them in the category of keratoconus suspect. In looking at the racial/ethinic difference: 9.4% (n=129) of the Black and 6.7% (n=50) of the LatinX subjects had a Final D between 2.00 – 2.99 in at least one eye and assumed to be keratoconus suspect.
- o A review of the outcomes for those that fall into the category of keratoconus: 1.4% (n=33) of the total subjects which represents 1.4% (n=19) of the Black and 0.9% (n=7) of the LatinX population had a Final D of at least 3.00 in at least one eye and were considered keratoconic.

**TABLE 1**
Pentacam Final D Results: Normal, Keratoconus Suspect, Keratoconus for Black and LatinX Pediatric Population

| | Total | Normal Final D <2.00 Both Eyes | KC Suspect Final D 2.00-2.99 In at least 1 Eye | KC Final D ≥ 3.00 In at least 1 Eye |
|---|---|---|---|---|
| Total N (%) | 2212 (100%) | 1997 (90.3%) | 184 (8.3%) | 31 (1.4%) |
| Black N (%) | 1369 (100%) | 1221 (89.2%) | 129 (9.4%) | 19 (1.4%) |
| LatinX N (%) | 762 (100%) | 705 (92.5%) | 50 (6.7%) | 7 (0.9%) |

### CONCLUSIONS

In a primarily Black and LatinX pediatric cohort the prevalence of KC was found to be 1.4% (1 in 71), higher than what has been reported. The results of our analysis suggests that there are likely a higher prevalence of pediatric patients who either identify as Black or LatinX who may be at risk for KC.

Those patients who are considered keratoconus suspect are important to screen and identify early as they require close monitoring. Corneal tomography may be a vital component of pediatric eye exams for early diagnosis and treatment of keratoconus.

### REFERENCES

1. Kennedy, R.H., W.M. Bourne, and J.A. Dyer, *A 48-year clinical and epidemiologic study of keratoconus*. Am J Ophthalmol, 1986. 101(3): p. 267-73.
2. Godefrooij, D.A., et al., *Age-specific Incidence and Prevalence of Keratoconus: A Nationwide Registration Study*. Am J Ophthalmol, 2017. 175: p. 169-172.
3. Chan, E. Chong EW, Lingham G, et al. *Prevalence of Keratoconus Based on Scheimpflug Imaging: The Raine Study*. Ophthalmol, 2021 Apr;128(4): p. 515-521.

### DISCLOSURES

Sandra Block, None; Jennifer Harthan, Illinois College of Optometry (E); Xiaohua Zhuang, None; William Tullo, Oculus, Inc (E); John Gelles, Cornea and Laser Eye Institute (E); Andrew Morgenstern, Washington Eye Physicians (E); Barry Eiden, North Suburban Vision Consultants (E)

### CONTACT

Sandra Block, OD, M ED, MPH, FAAO, FCOVD, FNAP
SBlock@uic.edu

Contact Lens and Anterior Eye 45 (2022) 101717

Contents lists available at ScienceDirect

Contact Lens and Anterior Eye

journal homepage: www.elsevier.com/locate/clae

Check for updates

## Analysis of corneal tomography in select Black and LatinX children

Xiaohua Zhuang [a,1], Jennifer S. Harthan [a,1], Sandra S. Block [a,*], William Tullo [b], S. Barry Eiden [c]

[a] *Illinois College of Optometry, Chicago, IL, USA*
[b] *OCULUS Inc, Arlington, Washington*
[c] *North Suburban Vision Consultants and International Keratoconus Academy, Deerfield IL, USA*

ARTICLE INFO

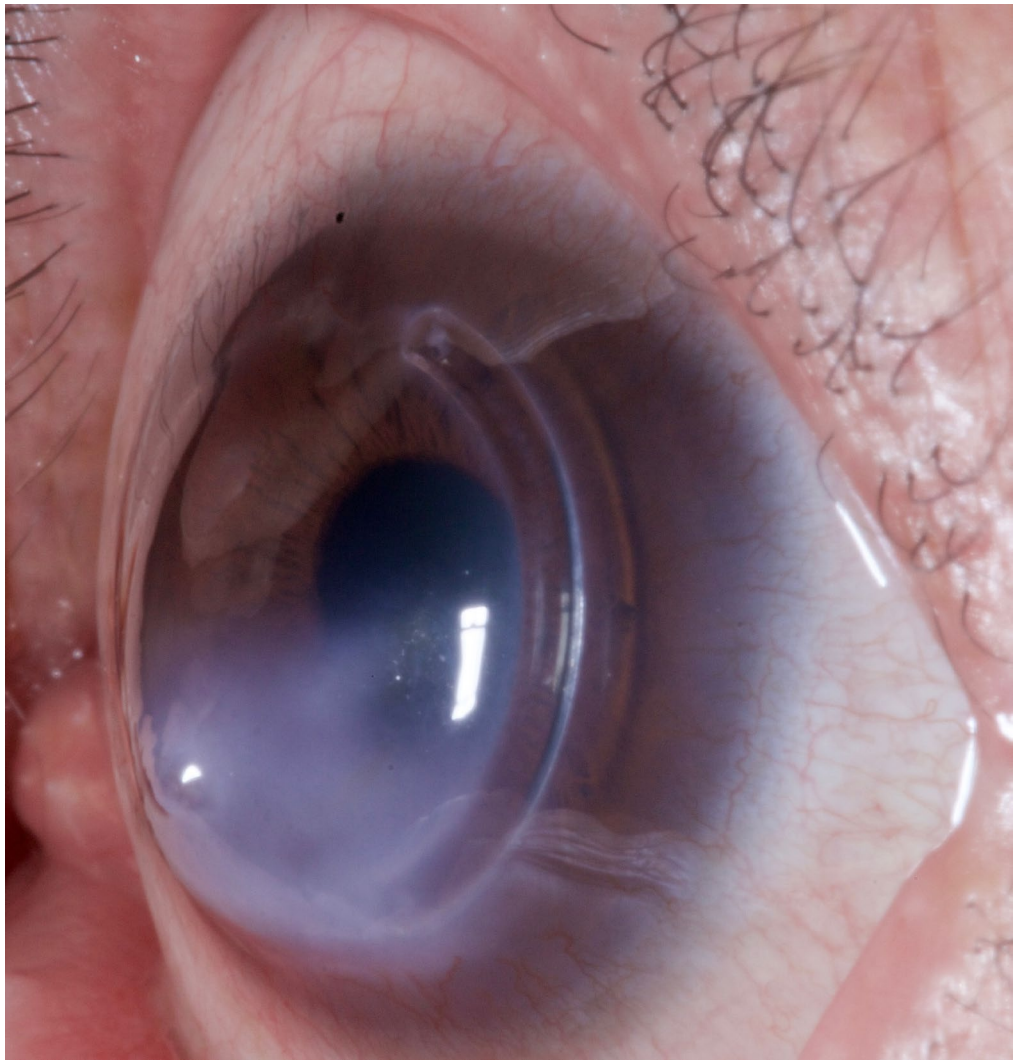
*Keywords:*
Keratoconus
Tomography
Corneal crosslinking
Pediatric population

ABSTRACT

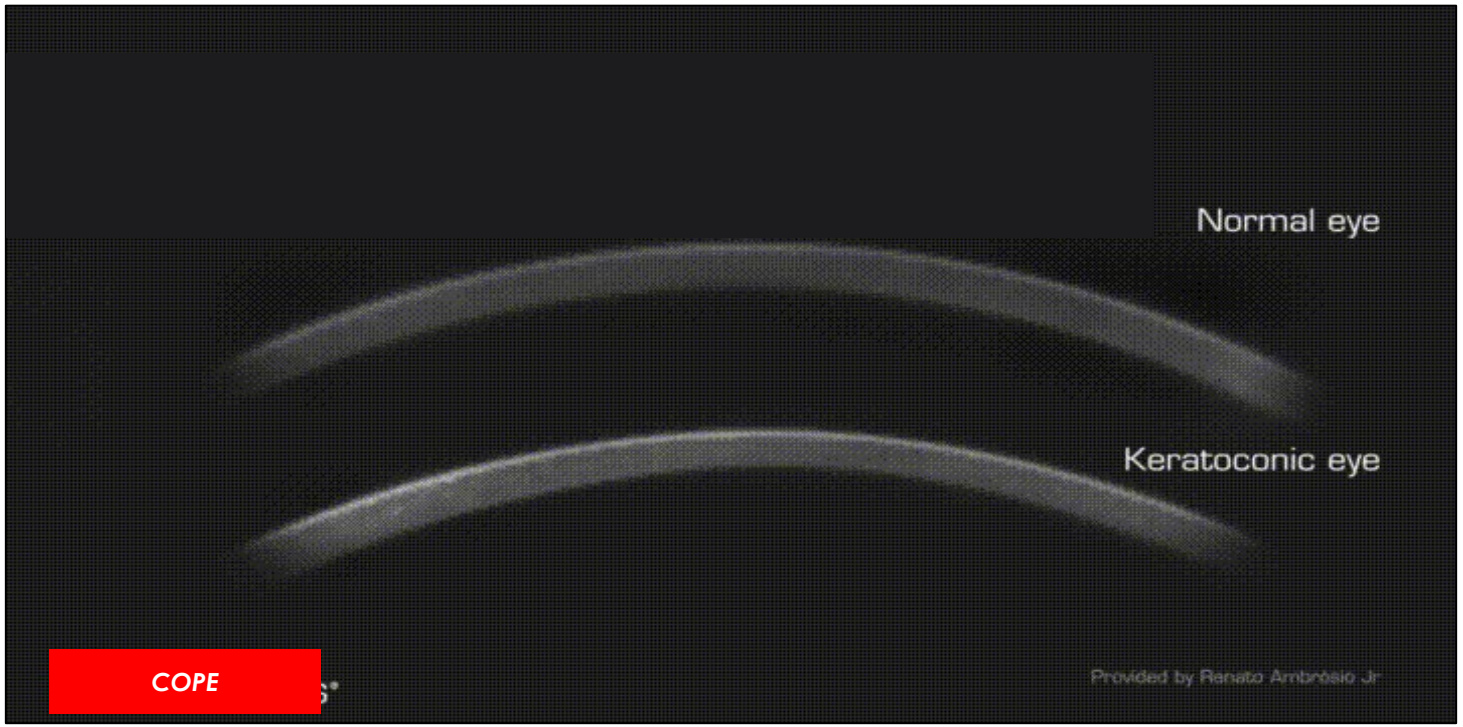
*Purpose:* Keratoconus (KC) is a bilateral and often asymmetric disease which can progress to corneal thinning and protrusion. Keratoconus in children appears to be more aggressive than in adults. Research on pediatric keratoconus is limited, and treatments rely on research and experience in adult populations. The current study aimed to provide an analysis on the distribution of the corneal tomography measurements in an underserved, Black and LatinX, primarily low-income pediatric population.
*Methods:* This was a prospective study approved by the Illinois College of Optometry's IRB. A total of 2133 children, presented to a school-based vision clinic within the Chicago Public Schools, were included in the analysis and were classified into three age groups: 3–6 years, 7–12 years, and 13–18 years. Four specific tomography measurements were obtained from the Pentacam (BAD Final D, ART-Max, I-S Ratio, and Thinnest Point Asymmetry).
*Results:* The mean front corneal astigmatism of the study cohort was −1.39D ± 1.45. Tomography indices means were 0.95 ± 0.74 for BAD Final D, 457.34 ± 94.83 for ART-Max, 0.01 ± 0.68 for I-S ratio, and 9.60 ± 25.55 for Thinnest Point Asymmetry. A statistically significant difference was observed among age groups for BAD Final D ($p < 0.001$), ART-Max ($p < 0.001$) and Thinnest Point Asymmetry ($p = 0.006$).
*Conclusion:* This study provided the first set of normative data for a pediatric population on the four tomography measurements, offering a reference for potential diagnosis of keratoconus for Black and LatinX children. Further study could include evaluation of additional races along with a comparison with the adult data, which will provide guidance on evaluating the current keratoconus diagnosis criteria to aid early diagnosis of keratoconus in the pediatric population.

# *Pregnancy and KC*

- Change due to rise in pregnancy-related hormones (estrogen and relaxin)
- Alter the biomechanical properties of the cornea and increase its refractive power



# *Visualization of Keratoconus vs Normal*




- High Speed Scheimpflug Video Comparison



Slide credit John Gelles, OD

# PREGNANCY AND KC

- Case-controlled report
- 22 patients with bilateral KC
- 11 intended to become pregnant
- 11 did not intend to become pregnant

- Compared refractive and topographic data
  - Before pregnancy
  - During the third trimester
  - 6 months postpartum

## Topographic, tomographic and biomechanical corneal changes during pregnancy in patients with keratoconus: a cohort study

Mohammad Naderan[1] and Ali Jahanrad[2]

[1]School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[2]AJA University of Medical Sciences, Tehran, Iran

**Table 4.** Severity of the disease in patients with keratoconus before, during and after pregnancy.

| Feature | Stage 1 | Stage 2 | Stage 3 | Stage 4 | p Value* |
|---|---|---|---|---|---|
| Pregnant patients | | | | | |
| Before Pregnancy | 10 (45.5%) | 8 (36.4%) | 1 (4.5%) | 3 (13.6%) | **0.038** |
| During Pregnancy | 8 (36.4%) | 9 (40.9%) | 2 (9.1%) | 3 (13.6%) | |
| After Pregnancy | 5 (22.7%) | 4 (18.2%) | 9 (40.9%) | 4 (18.2%) | |
| Non-pregnant Patients | | | | | |
| Before Pregnancy | 10 (45.5%) | 9 (40.9%) | 2 (9.1%) | 1 (4.5%) | 1.000 |
| During Pregnancy | 10 (45.5%) | 9 (40.9%) | 2 (9.1%) | 1 (4.5%) | |
| After Pregnancy | 10 (45.5%) | 9 (40.9%) | 2 (9.1%) | 1 (4.5%) | |

*Chi-square test. Bold value is statistically significant.

# PREGNANCY AND KC

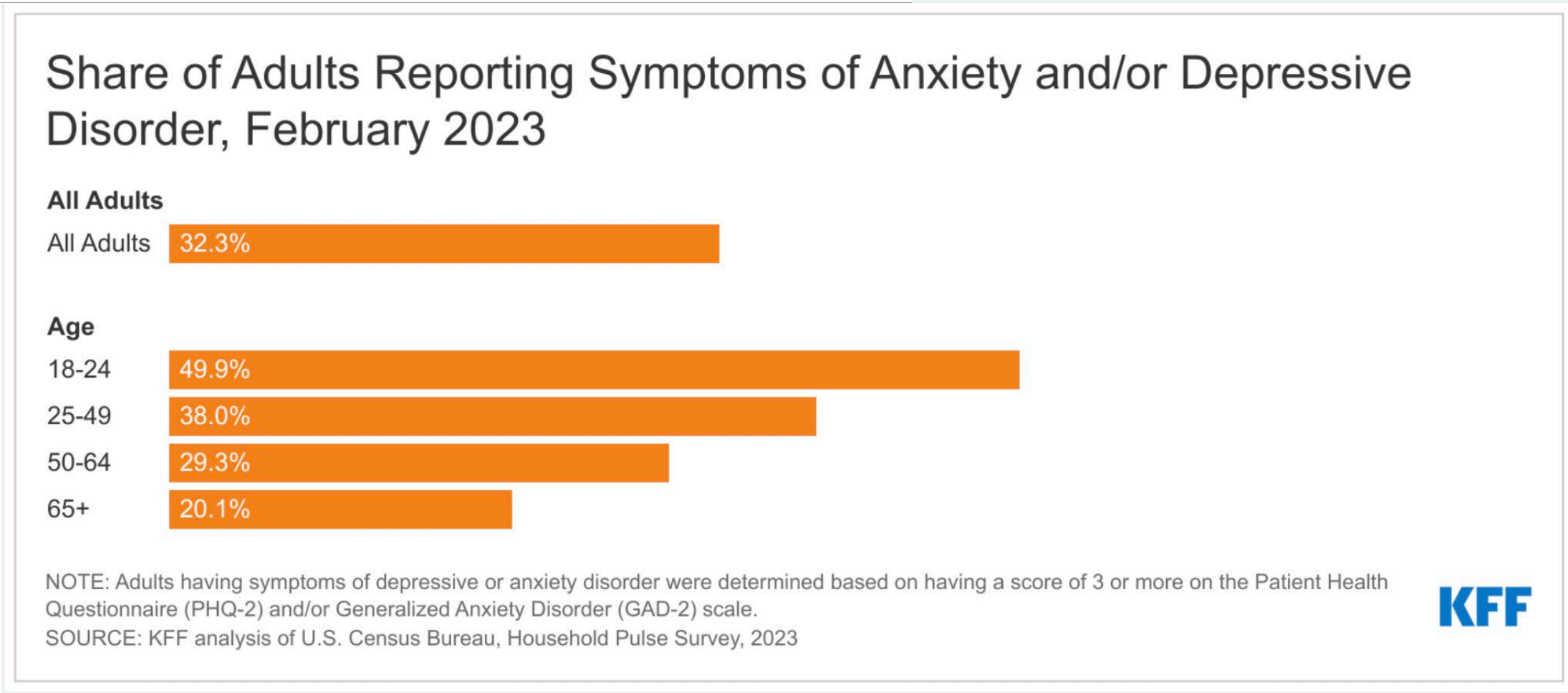
- 100% of eyes in the pregnancy group had significant KC progression
- None of the eyes in the control group had progression
- No evidence of reversal after pregnancy
- No long-term follow up data

News Release

# Latest Federal Data Show That Young People Are More Likely Than Older Adults to Be Experiencing Symptoms of Anxiety or Depression

Americans' Mental Health Continues to Be A Concern as Many People Try to Move Beyond the Pandemic

Mar 20, 2023




https://www.kff.org/mental-health/press-release/latest-federal-data-show-that-young-people-are-more-likely-than-older-adults-to-be-experiencing-symptoms-of-anxiety-or-depression/

Clinical Optometry

Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

# A Review of Ocular Complications Associated with Medications Used for Anxiety, Depression, and Stress

Paul A Constable, Dalia Al-Dasooqi, Rhiannon Bruce, Mallika Prem-Senthil

Caring Futures Institute, College of Nursing and Health Sciences, Flinders University, Adelaide, Australia

- "The increased use of antidepressants within the community may result in more patients presenting with ocular complications of their therapeutics."

- Higher levels of systemic side effects such as dry mouth and drowsiness with those using tricyclic antidepressants than in those using SSRIs

Clinical Optometry

Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

# A Review of Ocular Complications Associated with Medications Used for Anxiety, Depression, and Stress

Paul A Constable, Dalia Al-Dasooqi, Rhiannon Bruce, Mallika Prem-Senthil

Caring Futures Institute, College of Nursing and Health Sciences, Flinders University, Adelaide, Australia

- Main ocular side effects of SSRIs
  - Dry eye
  - Possible development of cataracts
- The presumed pathophysiology is the upregulation of serotonin in tear film and aqueous that induces inflammatory and apoptotic pathways in the corneal epithelium and lens fibers
- Rare complications
- Elevated intraocular pressure
- Angle closure glaucoma (patients with narrow angles or being followed as a glaucoma suspect may require more frequent monitoring)

**Table 2** Common Ocular Side Effects Associated with Therapeutics Used for the Treatment and Management of Depression, Anxiety, and Stress

| Drug Class | Name | Ocular Side Effect |
|---|---|---|
| Tricyclic antidepressants | Chlorpromazine | Decreased lacrimation and dry eye, mydriasis, cataracts, blurred vision, corneal oedema, corneal epithelial keratopathy, abnormal pigmentation of the eyelids/conjunctiva/cornea/peripheral retina[2] |
| | Amitriptyline (Endep, Entrip) | Decreased lacrimation and dry eye, mydriasis, blurred vision, cataracts, acute angle closure due to pupil block (amitriptyline, imipramine) |
| | Clomipramine (Anafranil, Placil) | |
| | Doxepin (Deptran, Sinequan) | |
| | Nortriptyline (Allegron, NortriTABS) | |
| | Imipramine (Tofranil, Tolerade) | |
| | Dosulepin/dothiepin (Dothep) | |
| Monoamine oxidase inhibitors | Tranylcypromine (Parnate) | Blurred vision<br>Rare: occipital headache, ping-pong gaze (phenelzine) |
| | Moclobemide (Reversible inhibitor of Monoamine oxidase) | |
| | Phenelzine (Nardil) | |
| SSRIs | Citalopram (Celapram, Celica, Cipramil, Talam) | Dry eye, mydriasis, intraocular pressure elevation, acute angle closure crisis<br>Rare: ocular dystonia, oculogyric crisis, diplopia, optic neuropathy, maculopathy (sertraline), eyelash loss (escitalopram) |
| | Escitalopram (Lexapro) | |
| | Fluoxetine (Fluotex, Lovan, Prozac, Prozet, Zactin) | |
| | Fluvoxamine (Facerin, Luvox, Movox, Voxam) | |
| | Sertraline (Eleva, Sertra, Sertracor, Setrona, Xydep, Zoloft) | |
| | Paroxetine (Aropax, Extine, Paxtine, Roxet, Roxtine) | |
| SNRIs | Venlafaxine (Altven, Efexor-XR, Elaxine, Enlafax-XR) | Dry eye, blurred vision, mydriasis, shallow anterior chamber depth, cataracts, intraocular pressure depression, acute angle-closure crisis (venlafaxine, duloxetine)<br>Rare: retrobulbar optic neuritis (duloxetine), pendular nystagmus (venlafaxine) |
| | Desvenlafaxine (Desfax, Desven, Pristiq) | |
| | Duloxetine (Andepra, Coperin, Cymbalta, Depreta, Dytrex, Tixol) | |

(*Continued*)

Clinical Optometry Dovepress
open access to scientific and medical research
Open Access Full Text Article REVIEW

# A Review of Ocular Complications Associated with Medications Used for Anxiety, Depression, and Stress

Paul A Constable, Dalia Al-Dasooqi, Rhiannon Bruce, Mallika Prem-Senthil

Caring Futures Institute, College of Nursing and Health Sciences, Flinders University, Adelaide, Australia

**Table 2** (Continued).

| Drug Class | Name | Ocular Side Effect |
|---|---|---|
| Benzodiazepines | Lorazepam (Ativan) | Blurred vision, increased risk of bilateral acute angle closure<br>Rare: impaired tracking (alprazolam), diplopia (lorazepam) |
| | Temazepam (Euhypnos, Normison) | |
| | Nitrazepam (Alodorm, Mogadon) | |
| | Diazepam (Valium, Ducene) | |
| | Oxazepam (Alepam, Murelax, Serepax) | |
| | Alprazolam (Xanax) | |
| Atypical antipsychotics | Risperidone (Risperdal, Rispa, Rixadone) | Blurred vision, mydriasis, decreased lacrimation (clozapine), cataracts (quetiapine)<br>Rare: floppy iris syndrome, oculogyric crisis |
| | Aripiprazole (Abilify, Abyraz) | |
| | Clozapine (Clozaril) | |
| | Olanzapine (Zyprexa, Pryzex) | |
| | Quetiapine (Seroquel, Syquet, Quetia XR, Tevatiapine XR) | |
| | Ziprasidone (Zeldox, Ziprox) | |
| Gamma-aminobutyric acid analogues | Pregabalin (Lyrica) | Blurry vision, diplopia<br>Rare: bilateral macular detachment, visual hallucinations |
| | Gabapentin (Aspen) | Nystagmus, increased risk of angle closure glaucoma |