DRY EYE: A MULTIFACTORIAL DISEASE
DEFINITION OF DRY EYE DISEASE

Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.


THE IMPACT OF DRY EYE
PREVALENCE OF DRY EYE DISEASE

- Up to 33 million Americans are estimated to be suffering from Dry Eye symptoms\(^1,3\)
- Results from the 2015 Gallup Poll (n = 776) project the number of adults who report experiencing Dry Eye on a regular basis\(^2\)

Results from the 2015 Gallup poll project the number of adults who report experiencing Dry Eye on a regular basis. Projections of frequent Dry Eye sufferers are calculated by applying incidence by age to US Census population estimates in each age group in 2015 and 2025. Projections assume no change in incidence levels over the next decade.\(^2\)

DRY EYE AND OTHER CONDITIONS

Prevalence of Dry Eye in Patients With Various Conditions

Percentage of Patients With Dry Eye

- Allergy¹: 25% (n = 2319)
- Contact Lenses²: 50% (n = 3285)
- Diabetes³: 54% (n = 199)
- Glaucoma/Ocular Hypertension⁴: 59% (n = 101)

A PERSISTENT, CHRONIC PROBLEM FOR MANY PATIENTS

• In combined analysis of Dry Eye data from the Women’s Health Study (n = 386) and Physicians’ Health Study (n = 398)

• Over a mean of 10.5 years, the most common report was no improvement
  – Ocular surface symptoms: 32%
  – Vision-related symptoms: 52%

• In general, a higher rate of worsening in women
  – Ocular surface symptoms: 28% of women, 20% of men
  – Vision-related symptoms: 31% of women, 27% of men

POTENTIAL TO AFFECT DAILY ACTIVITIES$^{1,2}$

- Reading
- Watching television
- Working on the computer
- Driving at night
- Wearing contact lenses (CL)
- Effects greater in women than in men$^3$

THE HEALTHY EYE
HEALTHY TEAR PRODUCTION, THE TEAR FILM, AND OCULAR SURFACE

IMPORTANCE OF HEALTHY TEAR FILM

Serves 4 important functions:

1. Provides a smooth optical surface for normal vision.
2. Maintains ocular surface comfort.
3. Protects from environmental and infectious insults.
4. Maintains ocular surface epithelial cell health.

The tear film is composed of 3 layers:

Lipid layer
Aqueous layer
Mucin layer

GOBLET CELLS CONTRIBUTE TO A HEALTHY OCULAR SURFACE AND TEAR FILM

- Secrete mucins and immunoregulatory factors that function to:
  - Increase tear film viscosity and help resist tear thinning
  - Normalize composition of the tear film
  - Maintain ocular surface health

DRY EYE – REDUCED TEAR PRODUCTION, COMPROMISED TEAR FILM AND OCULAR SURFACE
deferred to reference 1.

IMPACT OF AN ALTERED TEAR FILM

May lead to:

1. Tear film instability
2. Loss of factors needed to support ocular surface
3. Irritation, visual disturbance
4. Abnormal sloughing of ocular surface epithelium
5. Poorly lubricated ocular surface
6. Apoptosis of epithelial cells
7. Disruption of corneal epithelial barrier function

Relative to healthy tears, Dry Eye tears are hyperosmotic, have decreased levels of mucins, proteins, and other factors that support ocular surface health, as well as increased levels of pro-inflammatory cytokines.

LOW GOBLET CELL DENSITY AND THE CYCLE OF DRY EYE¹

- Decreased levels of goblet cell-secreted mucin seen in people with Dry Eye²
- Evidence suggests that inflammatory cytokines can alter human goblet cell numbers¹
- Diminished goblet cell numbers and reduced secretion of the remaining cells, leads to mucin deficiency¹
- Inflammatory cytokines decrease goblet cell proliferation and increase apoptosis¹

MULTIPLE MECHANISMS IN DRY EYE DISEASE

OCULAR SURFACE HEALTH

INFLAMMATION

IMMUNOMODULATION

T-cell activation and release of inflammatory cytokines 1-3
T-cell migration and homing 4,6-8
Conjunctival and lacrimal gland apoptosis 9,10
Epithelial barrier disruption 3-6
• NF-κB 1-3
• CD147 6,8
• ICAM-1 4,7
• MMP-9 3-6
• MPTP 9

INFLAMMATION

IMMUNOMODULATION

OCULAR SURFACE HEALTH

DEFINITION AND CLASSIFICATION

PISELLA, ET AL. OPHTHALMOL. 2000;
A PERSISTENT, CHRONIC PROBLEM FOR MANY PATIENTS

VISION QUALITY

POTENTIAL TO AFFECT DAILY ACTIVITIES

VISIONAL & OCULAR SURFACE SYMPTOMS

Dry Eye

CONCLUSIONS

• Up to 33 million Americans are estimated to be suffering from Dry Eye symptoms\textsuperscript{14,15}

• A persistent, chronic problem\textsuperscript{1} that has potential to affect daily activities\textsuperscript{2,3}

• Goblet cells contribute to a healthy ocular surface and tear film\textsuperscript{4}

• Multiple mechanisms are involved in Dry Eye
  – Inflammatory factors (eg, NF-κβ,\textsuperscript{5-7} MMP-9\textsuperscript{7-9})
  – Factors that damage the ocular surface (eg, MPTP\textsuperscript{10})
  – Immunomodulatory factors (eg, ICAM-1,\textsuperscript{11} and CD147\textsuperscript{12-13})

• Multiple mechanisms of disease offer multiple targets for therapeutic intervention
  – Appropriate therapy may require addressing multiple targets

THANK YOU