The Eye and the ED

- Why people go to the ED with eye problems
  - Most common ICD Diagnosis
    - Conjunctivitis 33%
    - Corneal injury 13%
    - Corneal F.B. 8%
    - Hordeolum 4%
- Mean ED charge $989.30 for eye visit
- Eye visits: 1.5% of all visits
- 32,000 eye-related visits per year

Perspective on Betadine

- "The instillation of 5% povidone iodine solution in the conjunctival sac to prevent endophthalmitis has been shown to be effective and has been widely used for decades."
- "One in three ASC’s prepares the 5% solution by diluting commercially available 10% povidone-iodine with saline solution. This practice has been shown to be safe and effective despite the labeling ‘do not use in the eye’ present on the 10% Betadine solution."

Adenoviral Infections

- Common cause of "red eyes"
- Assume adenovirus until proven otherwise
- Often have pre-auricular node
- Non-purulent watery discharge
- Usually starts in one eye and spreads to fellow eye in a few days
- Always evert lids to survey tarsal conjunctiva
- With EKC, spotty sub-epithelial infiltration in 50 to 75% of untreated cases

Financial Disclosure

Drs Ron Melton and Randall Thomas are consultants to, on the speakers bureau of, on the advisory committee of, or involved in research for the following companies: ICARE and Valeant.

Povidone - Iodine 5% ophthalmic solution

- Broad spectrum microbicide
- Indicated for "irrigation of the ocular surface" and "off label" use: Tx adenoviral keratoconjunctivitis
- Anesthetize with proparacaine
- Instill 1 or 2 drops of NSAID
- Instill several drops Betadine 5% in eye(s), close eye(s)
- Swab or rub excess over eyelid margin
- After 1 minute, irrigate with sterile saline
- Instill 1 or 2 drops of NSAID
- Rx steroid qid x 4 days
- No reports in clinical trials of adverse reactions.
- Avoid use if patient is allergic to iodine
- Marketed as Betadine 5% ophthalmic prep solution (30 ml opaque bottle) by Alcon surgical
- CPT 99070 supply code

Povidone-Iodine 5% solution

- Broad spectrum microbicide
- Indicated for "irrigation of the ocular surface" and "off label" use: Tx adenoviral keratoconjunctivitis
- Anesthetize with proparacaine
- Instill 1 or 2 drops of NSAID
- Instill several drops Betadine 5% in eye(s), close eye(s)
- Swab or rub excess over eyelid margin
- After 1 minute, irrigate with sterile saline
- Instill 1 or 2 drops of NSAID
- Rx steroid qid x 4 days
- No reports in clinical trials of adverse reactions.
- Avoid use if patient is allergic to iodine
- Marketed as Betadine 5% ophthalmic prep solution (30 ml opaque bottle) by Alcon surgical
- CPT 99070 supply code
Literature on Adenoviral Keratoconjunctivitis

- Pseudo-membranes are a frequent complication of EKC
- In untreated cases, 50% of corneas develop subepithelial infiltrates – a cellular immune reaction against viral antigens
- AdenoPlus® is highly sensitive, specific, simple and inexpensive
- Bacterial superinfection is rare
- “Topical steroids relieve symptoms, and 5% betadine kills the virus in tears, thus reducing the risk of disease spread.”
- Restasis does not affect the natural course of the disease.


Treatment Options - Ocular Allergy

- Artificial Tears
- Mild Vasoconstrictors
- Decongestant / Astringents
- Vasoconstrictor / Antihistamines
- Antihistamines
- Antihistamine / Mast Cell Stabilizers
- Mast Cell Stabilizers
- Non-steroidal Anti-inflammatories
- Mild Corticosteroids
- Systemic Antihistamines
- Potent Corticosteroids
- Homeopathic Formulations

Cetirizine 0.24% ophthalmic solution

- Now Indicated for ocular itching associated with allergic conjunctivitis
- Instill 1 drop in each affected eye BID (8 hr apart)
- Adverse Effects:
  - Hyperemia (1-7%)
  - Instillation site pain (1-7%)
  - Reduced visual acuity (1-7%)
- Marketed by Nicox as Zerviate ophthalmic solution

A Fresh Look at Ocular Allergy

Avoidance:

- Bathe after being outdoors
- Dust mite covers for pillows and mattresses
- HEPA filters

Treatments:

- Chilled artificial tears
- Cold compresses (frozen bag of peas or corn)
- Alrex with glycerin moisturizer
- Topical antihistamines selectively blocking the H1 receptor to avoid exacerbating dry eye such as Bepreve or Lastacaft


Intranasal Steroids for Ocular Symptoms in Allergic Rhinitis

- In a randomized trial, intranasal steroids relieved both nasal and ocular symptoms.
  - Because intranasal steroids are the most effective medications for allergic rhinitis symptoms (especially congestion), guidelines recommend them as first-line agents for moderate-to-severe disease
  - As many as 85% of patients with seasonal allergic rhinitis also have ocular symptoms
  - For these patients, many clinicians prescribe oral antihistamines or ocular products rather than (or in addition to) intranasal steroids

Antihistamine/Mast Cell Stabilizer

- Highly selective H1 receptor blockers with prolonged receptor binding
- Good mast cell stabilization
- All bid dosing, except Pataday and Lastacaft qd

<table>
<thead>
<tr>
<th>Drug</th>
<th>Concentration</th>
<th>Container Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olopatadine</td>
<td>0.1%</td>
<td>(Patanol) (5 ml)</td>
</tr>
<tr>
<td></td>
<td>0.2%</td>
<td>(Pataday) qd (2.5 ml)</td>
</tr>
<tr>
<td></td>
<td>0.7%</td>
<td>(Pazeo) qd (2.5 ml)</td>
</tr>
<tr>
<td>Bepotastine</td>
<td>1.5%</td>
<td>(Bepreve) (5, 10 ml)</td>
</tr>
<tr>
<td>Epinastine</td>
<td>0.05%</td>
<td>(Elestat and generic) 5 ml</td>
</tr>
<tr>
<td>Alcaftadine</td>
<td>0.25%</td>
<td>(Lastacaft) qd (3 ml)</td>
</tr>
<tr>
<td>Azelastine</td>
<td>0.05%</td>
<td>(Optivar and generic) (6 ml)</td>
</tr>
<tr>
<td>Ketotifen</td>
<td>0.025%</td>
<td>(generic and OTC)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Claritin Eye) (5 ml)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Zyrtec Itchy Eye) (5 ml)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Zaditor) (5 ml)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Alaway) (10 ml)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Refresh) (5ml)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(TheraTears) (5 ml)</td>
</tr>
</tbody>
</table>
Anti-Viral Medicines

<table>
<thead>
<tr>
<th>Topical</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trifluridine</td>
<td>Acyclovir</td>
</tr>
<tr>
<td>Viroptic</td>
<td>Zovirax</td>
</tr>
<tr>
<td>Ganciclovir</td>
<td>Valacyclovir</td>
</tr>
<tr>
<td>Zirgan</td>
<td>Valtrex</td>
</tr>
</tbody>
</table>

- These are anti-herpetic drugs and are ineffective against the various adenoviral serotypes -

Finer Points to Antiviral Prescribing

- For lactose intolerant patients: valacyclovir
- For children, use the oral suspension: acyclovir
- For patients over 65, famciclovir is recommended


Herpes Simplex Keratitis

- Epithelium is primarily infected
- Also acute unilateral follicular conjunctivitis
- Affected cornea has decreased sensitivity
- Factors predisposing to prolonged healing:
  - delay in seeking care
  - pre-treatment with steroids
  - infectious foci near limbus
  - stromal inflammation
- Tx: topical or systemic antivirals

Zostavax

- Vaccine for prevention of shingles in adults age 50 and older
- Marketed by Merck as Zostavax and is given as a single dose by injection
- Anyone who has been infected by chicken pox (more than 90% of adults in US) is at risk for developing shingles
- Contraindicated if Hx of allergy to gelatin, neomycin; Hx of acquired immunodeficiency states; pregnancy
- In landmark Shingles Prevention Study, Zostavax reduced risk of developing shingles by 51% (4 yrs of follow-up)

References: www.cdc.gov/vaccine/vpd-vac/shingles; FDA News Release, March 24, 2011 “FDA approves Zostavax vaccine to prevent shingles in individuals 50 to 59 years of age.”

Zostavax Efficacy: How Long?

- “After 10 years, vaccination lost most of its power”
- “Efficacy against HZ incidence fell from 46% in year 7 to 14% in year 10 and was negligible among 1470 participants who were followed for the 11th year.”
- “Vaccination at age 60 is unlikely to confer protection for the duration of a person’s life.”
- We foresee new public health recommendations advising re-vaccination after about 8 years. This certainly sounds prudent to us.

Reference: Clinical Infectious Disease. March 13, 2015

Shingrix Replaces Zostavax

- Shingrix is the 2nd vaccine to be FDA approved to help prevent shingles.
- Approved for people aged 50 and older
- A non-live vaccine (Zostavax is live, attenuated)
- Administered in 2 - I.M. doses (initially then 2-6 months later)
- About 90% effective and maintained over four years
- If the last Zostavax vaccine was at least 5 years ago, can have Shingrix
- Marketed by GlaxoSmithKline
**Herpes Zoster Ophthalmicus**

- Acute vesicular eruption of ophthalmic division of 5th cranial nerve
- Etiology: varicella-zoster virus; more common after 50 or in the immuno-compromised
- Symptoms: skin pain most common
- Ocular involvement in 50%
  - more common - zoster epithelial lesions, anterior uveitis, stromal keratitis, episcleritis
  - Tx: valacyclovir 1000mg tid for 1 wk; famciclovir 500 mg tid for 1 wk; acyclovir 800mg 5x d for 1 wk
  - ocular - if ocular involvement, treat with potent steroids

**Antibiotic Therapy for Infectious Sinusitis**

- Clinical guidelines recommend only 5-7 days, not the usual 10.
- "Use of azithromycin generally discouraged because of known risk for developing antibiotic resistance."
- In this study, 25% of prescriptions were for azithromycin; more than half were for penicillins.
- Success rates were identical for 5-7 day course vs. 10 days
- "Following both recommendations would advance the battle against antibiotic resistance."

   **JAMA Intern Med, March 2018**

**Antibiotic Resistance Monitoring in Ocular micRorganisms (ARMOR) Study**

- Prospective, multicenter, longitudinal survey of antibiotic susceptibility trends
- Participating sites in the US include community hospitals, university hospitals, and ocular centers
- ARMOR isolates:
  - *Staphylococcus aureus*
  - *Coagulase-negative staphylococci* (CoNS)
  - *Streptococcus pneumoniae*
  - *Haemophilus influenzae*
  - *Pseudomonas aeruginosa*

   **Asbell PA et al. JAMA Ophthalmol. 2015:1-10**

**MIC<sub>90</sub> Comparisons for ARMOR Surveillance Study Isolates**

<table>
<thead>
<tr>
<th></th>
<th>S. aureus</th>
<th>MRSA</th>
<th>CoNS</th>
<th>MRCoNS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=1163)</td>
<td>(n=83)</td>
<td>(n=502)</td>
<td>(n=83)</td>
</tr>
<tr>
<td>Besifloxacin</td>
<td>0.25</td>
<td>2</td>
<td>0.25</td>
<td>4</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>0.12</td>
<td>&gt;2</td>
<td>0.12</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Oxolin</td>
<td>&gt;2</td>
<td>&gt;2</td>
<td>&gt;2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>1</td>
<td>16</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>2</td>
<td>16</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>6</td>
<td>16</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>16</td>
<td>16</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>8</td>
<td>&gt;8</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>128</td>
<td>128</td>
<td>64</td>
<td>64</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>&gt;256</td>
<td>&gt;256</td>
<td>&gt;128</td>
<td>&gt;128</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>&gt;512</td>
<td>&gt;512</td>
<td>&gt;512</td>
<td>&gt;512</td>
</tr>
</tbody>
</table>

**Background**

- *Staphylococcus aureus*, CoNS, *S. pneumoniae*, *P. aeruginosa*, *H. influenzae* are significant causes of ocular bacterial infections

**Fluoroquinolone therapy has been associated with possible tendinitis of the EOM’s, resulting in diplopia.**


**IMPORTANT DRUG WARNING**

- Fluoroquinolones, including AVELOX® / CIPRO®, are associated with an increased risk of tendinitis and tendon rupture in all ages. This risk is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants.

   **Reference: HCNN (electronic health alerts) 10-22-08**

   **Fluoroquinolone therapy has been associated with possible tendinitis of the EOM’s, resulting in diplopia.**


**MIC<sub>90</sub> Comparisons for ARMOR Surveillance Study Isolates**

<table>
<thead>
<tr>
<th></th>
<th>S. aureus</th>
<th>MRSA</th>
<th>CoNS</th>
<th>MRCoNS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=1163)</td>
<td>(n=83)</td>
<td>(n=502)</td>
<td>(n=83)</td>
</tr>
<tr>
<td>Besifloxacin</td>
<td>0.25</td>
<td>2</td>
<td>0.25</td>
<td>4</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>0.12</td>
<td>&gt;2</td>
<td>0.12</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Oxolin</td>
<td>&gt;2</td>
<td>&gt;2</td>
<td>&gt;2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>1</td>
<td>16</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>2</td>
<td>16</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>6</td>
<td>16</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>16</td>
<td>16</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>8</td>
<td>&gt;8</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>128</td>
<td>128</td>
<td>64</td>
<td>64</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>&gt;256</td>
<td>&gt;256</td>
<td>&gt;128</td>
<td>&gt;128</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>&gt;512</td>
<td>&gt;512</td>
<td>&gt;512</td>
<td>&gt;512</td>
</tr>
</tbody>
</table>
Fluoroquinolone Non-susceptibility to Staphylococcal Epidermidis

- This Bascom Palmer study was done between 1995 and 2016
- Over half of Staphylococcus epidermidis pathogens were resistant, in vitro, to fluoroquinolones in 2016
- Conclusion: Prescribe based on science, not habit


Differential Diagnosis of Corneal Ulcers vs. Infiltrates

<table>
<thead>
<tr>
<th>Ulcer (UK)</th>
<th>Infiltrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Usually painful</td>
<td>Mild pain</td>
</tr>
<tr>
<td>Tend to be central</td>
<td>Tend to be peripheral</td>
</tr>
<tr>
<td>1 to 1 staining defect to lesion ratio</td>
<td>Staining defect size relatively small</td>
</tr>
<tr>
<td>Cells in anterior chamber</td>
<td>Rare cells in anterior chamber</td>
</tr>
<tr>
<td>Generalized conjunctival injection</td>
<td>Sector skewed injection pattern</td>
</tr>
<tr>
<td>Usually solitary lesion</td>
<td>Can be multiple lesions</td>
</tr>
<tr>
<td>Possible tear lake debris</td>
<td>Clear tear lake</td>
</tr>
</tbody>
</table>

Expert Perspective on Infiltrates

“Left untreated, marginal infiltrates generally disappear within a week or two. Ocular steroids have been shown to be the best and only recognized drug therapy for sterile marginal infiltrates, and their application will shorten the course of inflammation, regardless of causative origin. For many patients, a quicker recovery from symptoms such as redness, tearing, and discomfort is important for improving their quality of life. Steroids are often prescribed in conjunction with an antibiotic in order to decrease the chance of developing a secondary infection or corneal ulcer and to protect against misdiagnosis.”


Dry Eye Disease

- “Dry eye disease is a heterogeneous disorder of the ocular surface in which the common denominator is inflammation.”
- “Topical corticosteroids also play an important role in breaking the inflammatory cycle.” “Repeated short-term pulse therapy has produced a disease-free state for more than 1 year in a study of patients with Sjögren’s syndrome.”
- “When meibomian glands function correctly, the lipids secreted reduce ocular surface water evaporation and prevent dry eye. When these glands are reduced, absent or dysfunctional, the impact on the ocular surface can be immense.”
- “Treatment of DED is based on minimizing inflammation and optimizing various components of the tear film.”
Dry Eye Disease

- "Inflammation is one of the major targets in treating DED, and breaking the cycle of inflammation is crucial in improving symptoms. All patients DED deserve a trial of anti-inflammatory therapy at some point during their treatment." "Corticosteroids are one of the most effective and rapid therapies available for suppressing inflammation on the ocular surface."
- "Omega-3 supplementation is a well-tolerated therapy to improve ocular surface health in nearly all forms of DED and is generally recommended to be used for all patients with no other medical contraindications."

Discordance Between Symptoms and Signs

- Patients with chronic pain syndromes (CPSs) had 30% greater symptoms than signs.
- Important CPSs are irritable bowel syndrome, fibromyalgia, chronic pelvic pain and osteoarthritis.
- There is "growing evidence that part of the dry eye population may show signs of dysfunctional somatosensory pathways, indicating neuropathic ocular pain."
- It is thought that "patients with atopy or allergy have a sensitized ocular surface because of inflammatory processes influencing corneal nerves, which can lead to symptoms of dry eye even when the homeostasis of the ocular surface is minimally compromised."

Expert Perspective on DE Inflammation

"It is now well understood that inflammation is one of the most important aspects of DED pathogenesis, and no matter the trigger, untreated or undertreated, established disease can lead to severe refractory disease. At this time, there are three topical prescription therapies available to treat inflammation in DED: corticosteroids, topical cyclosporine A and lifitegrast. Oral essential fatty acid supplementation and tetracycline-class antibiotics are also commonly prescribed for inflammatory ocular conditions, including DED."

Sheppard J. Advanced Ocular Care, April 2017

Steroids and Dry Eye Disease (DED)

- "Because chronic inflammation at the ocular surface plays an essential role in the pathogenesis of DED, topical steroids have been commonly used in these patients."
- "Although the pathogenesis of DED is multifactorial and not fully understood, inflammation has been recognized as a key mechanism in its development and propagation."

Sheppard J. Advanced Ocular Care, April 2017

Melton-Thomas Recommendations for Dry Eye Treatment

- **Artificial Tears**
  - We recommend Soothe XP artificial tears. These tears contain mineral oil, which makes them more soothing for your eyes. Another good option is Systane Balance tears.
  - Use these artificial tears 2-4 times a day (morning and evening are critical).

- **Warm Compresses**
  - Wet a washcloth with warm water and place it over your closed eyelids. Leave it there for 5-10 minutes; do this once per day.
  - This will help stimulate the glands in your eyelids to produce more oil, helping to make better quality tears.

- **Blinking Exercises**
  - Close your eyes, squeeze them using your eyelid muscles, and release. Repeat these motions every 5 seconds for 1 minute. Do this one-minute exercise 4 times a day (breakfast, lunch, dinner, and bed times).
  - These exercises will help your oil glands work better and will keep your eyes from drying out as much.

- **Fish Oil Supplements**
  - Take 2000 mg fish oil supplements every day.
### Topical Therapies for Ocular Surface Dryness

- Aqueous-based PF artificial tears did little or nothing to alleviate symptoms.
- Adding a topical steroid, signs and symptoms were improved.
- The majority of dry eye sufferers use AT’s, yet many still experience exacerbations of irritation and ocular surface disease in low-humidity environments.


### How important is “Preservative Free”?

- “Published studies have not demonstrated any clear benefits of the BAK-Free formulations.”
- “There is a lack of evidence of clinically significant harm from a small number of BAK preserved drops in patients without OSD. This means that generally more expensive PF glaucoma medications should only be recommended for those on poly-pharmacy or those with OSD but are not necessarily required for all patients.”

*Br J Ophthalmol, July, 2018*

### Cyclosporine 0.05% Ophthalmic Emulsion

- Topical immunomodulator with anti-inflammatory effects – exact mechanisms unknown
- Indication: “to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation”
- Available in 0.4 ml unit dose vials by Allergan. Supplied in 30-vial tray.
- Dosage: one drop to affected eye(s) b.i.d. Usually takes 4-6 months to reach full therapeutic effect
- Concurrent treatment with ester-based steroid for the first 1-2 months may hasten results
- Available in multi-dose bottle and unit-dose PF vials
- Generically available in 0.09% amd 0.1% bottles

### Xiidra (lifitegrast 5%)

- Only FDA-approved drug to treat both signs and symptoms of DED
- A lymphocyte function-associated antigen antagonist
- 5%, unit-dose (0.2ml), PF, foil-pouched solution
- Dosage is approximately every 12 hours for many months or years
- Takes 2-4 weeks to achieve clinical results
- Stored at room temperature – protect from light
- Side effects seen in 5-25% of patients include instillation site irritation, taste perversion (dysgeusia), and transient blurred vision
- Marketed as Xiidra by Shire (1 carton contains 12 foil packs holding 5 unit-dose containers)

### Alternative Supplementation

- Orally administered omega-3 essential fatty acids
- May take 4-6 months to obtain a significant clinical effect
- Liquid formulations are available for those patients who have difficulty swallowing large capsules.

### Role of Omega 3 EFA’s in DED

- 30% reduction in the risk of DED for each gram consumed per day
- Recommend: about 1000mg of EPA and about 500mg of DHA per day
- Tear film BUT highly sensitive and specific
- Onset of benefits, including hyperemia; 30-60 days
- Loteprednol .5% QID x 2 weeks reduces ocular surface inflammation
- Krill oil appears to be slightly more effective than fish oil.

*Reference: Oph, January 2017*
Disturbing News on DED and Fish Oil

- Fish oil supplementation provides no benefit in treating DED!
- Conclusions: “Among patients with DED, those who were randomly assigned to receive supplements containing 3000mg of fish oil for 12 months did not have significantly better outcomes than those who were assigned to receive placebo.”

Reference: NEJM, April, 2018

Friction-Related DED Sub-types

- There are three of these sub-type diseases
  - Superior Limbic Keratoconjunctivitis
  - Conjunctivochalasis
  - Lid Wiper Epitheliopathy
- These cause “mechanical trauma and consequent inflammation during blinking.”
- “A shortened TBUT was the most prominent finding among all ocular signs in DED.”
- “Given the contributions of MGD and these friction-related diseases to DED severity, identifying and treating these conditions deserve greater attention”.

Reference: Ophthalmology, Aug. 2018

Neurostimulation and the Goblet Cell

- It is recognized that neural stimulation of the nasal mucosa plays a crucial role in stimulating homeostable aqueous tear production.
- Questions remaining:
  - How long the increased aqueous or mucus tear volume lasts after a single application?
  - How many treatment sessions per day are optimal?
- Numerous studies have found evidence of ocular surface inflammation.
- Such nasal neurostimulation might stimulate conjunctival goblet cell degranulation.
- Such an approach may be a unique feature of this therapy compared to other currently available treatments.


Intranasal Neurostimulation

- FDA approved in April 2017
- Novel approach in dry eye treatment
- MOA: intranasal stimulation of tear production
- Triggers goblet cell degranulation
- Unknown: length, frequency of Tx sessions, efficacy, and duration of effect
- Marketed as TrueTear by Allergan

Summary

1. Global consensus – MGD is the leading cause of Dry Eye
   - Chronic and progressive
   - The sequelae can be catastrophic
2. Function and structure
   - A turning point for understanding MGD and dry eye and to practice both restorative treatment and prevention
3. Consider MGD first – the root cause of 86% (?) of all dry eye
   - DE is complex due to the infinite sequelae of MGD
   - Understanding and treating MGD is now straightforward
**Progressive MGD**

- **Function**
  - Normal Function
  - Nonobvious MGD
  - Obvious MGD
  - Obvious MGD

- **Structure**
  - Normal Structure
  - Gland Duct Dilatation & Drop Out
  - Gland Transection & Drop Out
  - Gland Duct Dilatation, Transection & Drop Out

**Thermal Pulsation**

1. Apply controlled heat to the inner surfaces of both upper & lower lids
2. Simultaneously maintains pulsating pressure for 12 minutes

**Thermal Pulsation Treatment Increases CL Wearing Time**

- “Conclusion: In SCL wearers with MGD, a single VTP treatment significantly improved mean meibomian gland function and significantly reduced dry eye signs and symptoms compared to an untreated control. The treatment increased mean comfortable lens wearing time by 4 hours (approximately doubling the pretreatment findings). This was sustained for up to 3 months post-treatment on average.”
  
  *Clinical Ophthalmology*, Jan, 2018

**Lid Margin Debridement - Scaling**

- “Hypothetically, early and frequent debridement-scaling of the Line of Marx (i.e., the muco-cutaneous junction) and lid margin could prevent or delay the cascade of increased osmolarity, tissue desiccation, and ultimately inflammation and tissue damage simply because of mechanical barriers to oil entering the tear film.”
- “The single debridement-scaling procedure improved comfort and improved MG function.”
- “There are significant benefits to a single D-S of the LOM and keratinized lid margin.”

*Cornea, December, 2013*

**MG Scraping in Treating DES**

- “In the future, the health and maintenance of the MCJ and keratinized lid margin may be considered integral to routine eye care. This shift in our culture will involve improvements in our observation skills and also the willingness to incorporate novel techniques such as debridement-scaling of the MCJ and keratinized lid margin in our clinical practice.”

*Korb/Blackie. Cornea. December 2013*

**Pediatric DED and Risk Factors: Things to Ponder**

- “Multi-screen” lifestyle – major risk factor
- Vegetarian and vegan lifestyle – insufficient consumption of Omega 3 EFA’s
- Meibography revealed that about 10% of grade school children had compromised Meibomian glands.
- This compromise was directly correlated to the amount of time looking at screens
- “Evaporative DED associated with smartphone use is a lifestyle disease.”

*Reference: OSN, January 25, 2016*
Lid and Lash Hygiene

- Eye care products containing hypochlorous acid .01%/ .02%
- Fast-acting cleanser for lids, lashes, periorbital skin with low toxicity
- Used for blepharitis and other conditions of eyelids or eyelashes which often cause inflammation and discomfort
- Effective against broad range of pathogens usually found on the lids and lashes
- Available in variety of formulations (solution, gel, spray)

Eyelid Cleansing Treatments for Blepharitis

- Study compared “dedicated eyelid cleanser to diluted baby shampoo”
- Cleaning was done bid for four weeks
- Conclusion: improvements occurred with both treatments. “However only the dedicated eyelid cleanser proved effective in reducing inflammation and was the preferred therapy.”

The Ocular Surface, October, 2017