53 year old female
cc: her left eye started bothering her a little last night; is a lot more red this morning. Some discharge and the eye is feeling more irritated
VA – OS 20/20
IOP – OS 16 mm Hg at 10:00 am

Viral Conjunctivitis

• 20-70% of infectious conjunctivitis is thought to be of viral etiology
• Viral infections are less common in children under 12 years old and more common in those over 12 years old
• Between 65-90% are thought to be caused by adenovirus

Viral vs. Bacterial

• Bacterial
  - More common in children less than 12 years old - redness, mucoid discharge, purulent discharge, eyelid matting
• Viral
  - More common in those greater than 12 years old - itching, burning, watery discharge, mucoid discharge, foreign body sensation, lymphadenopathy, hemorrhages

Clinical Accuracy1-4

- Leibowitz et al.2
  - 31% of presumed bacterial conjunctivitis were culture positive
  - 52% with presumed viral conjunctivitis were culture positive for pathogenic bacteria
- Cheung et al.3
  - 67% of Adenoviral cases presented unilaterally and the misdiagnosis rate was 42% in these patients
- During a clinical trial to evaluate cidofovir treatment at 16 academic centers, experts showed a clinical accuracy of about 48%

Viral Conjunctivitis

- Nonspecific Follicular Conjunctivitis
  - Occurs more often in children, can be associated with a URI, unilateral or bilateral presentation, usually resolves in 14 days
- Pharyngeal Conjunctival Fever
  - More common in children and is usually associated with a pharyngitis and low grade fever
  - More commonly seen as a unilateral presentation
  - Typically 2 week resolution

Viral Conjunctivitis

- Acute Hemorrhagic Conjunctivitis
  - Most common in developing countries
  - Large subconjunctival hemorrhages
  - Preauricular lymphadenopathy, keratitis
- Epidemic Keratoconjunctivitis
  - Highly contagious
  - Most commonly seen in those 20-40 years
  - Keratitis, foreign body sensation, blurred vision
  - Signs and symptoms may last for up to 4 weeks

How to Use AdenoPlus

1. Use a “dab and drag” motion in 6-8 locations on the palpebral conjunctiva (lower eyelid) to collect a tear sample.
2. Snap the sample collector into the test cassette and press firmly where indicated.
3. Dip the test cassette into the provided buffer vial for 20 seconds. Replace the cap.
4. Read the results: 2 lines (1 red, 1 blue) = positive, 1 line (blue) = negative

AdenoPlus Result

If anything shows up, you have adenovirus.

Viral Conjunctivitis

- Treatment:
  - Artificial tears
  - Cool compresses
  - Topical Antihistamines
  - Topical povidone iodine
  - Gancyclovir gel
  - Steroids – when there is significant light sensitivity or reduced visual acuity

Off-Label Adenoviral Treatments

Ganciclovir .15% Gel vs Preservative Free Tears (N=18)

<table>
<thead>
<tr>
<th></th>
<th>Ganciclovir .15% gel N=9</th>
<th>Preservative free tears N=9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovery time [mean (range)]</td>
<td>7.7 (7-12) days</td>
<td>18.5 (7-30) days</td>
</tr>
<tr>
<td>SEIs</td>
<td>2 patients</td>
<td>7 patients</td>
</tr>
</tbody>
</table>

**Off-Label Adenoviral Treatments**

Open-label, uncontrolled study with ganciclovir 0.15% gel in 36 patients with epidemic keratoconjunctivitis (EKC)
- GCV given QID at each EKC episode
- Ocular discomfort alleviated in 1 week and no patients developed keratitis

Sig: 1-2 gttts to affected eye qid for 1 week

Plan: return in 3-5 days for a follow up

**Treatment technique with Betadine 5% wash**

- Instill 3 drops of tetracaine
- Instill 5 drops of Betadine 5%
- Instruct patient to close eye(s) and move side to side, up and down for 60 seconds; use gloved finger to spread Betadine over lid margin and lashes to eradicate any virus on external adnexa.
- After 60 seconds, thoroughly rinse eye
- Follow up: 2-3 days, 4-5 days, and 7-14 days

**Differential of Corneal Opacities**

- EKC
- Thygeson’s SPK
- Contact lens infiltrative events
Adenoplus Result

Negative result

Thygeson’s SPK

- A viral etiology has been suggested
- Not responsive to anti-viral therapy
- Non-specific immune response has been suggested
- May last from 4-6 weeks
- Can recur for several years

Entering Presentation

- Superficial stellate lesions
- Will stain with fluorescein
- Tiny grey – white dots that are slightly elevated
- May have mild conjunctival injection

Entering Presentation

- Variable discomfort – typically burning or irritation
- Foreign body sensation
- Tearing
- Photophobia
- Decreased visual acuity

Treatment

- No treatment necessary if little to no symptoms
- Ocular lubricants (tears, gels and ointments)
- Low dose steroids with a slow taper
  - 0.5% Loteprednol qid until signs/symptoms resolve then a slow taper over several weeks
- Consider cyclosporine 0.05% for recurrent cases
- Therapeutic contact lens

sig: 1 gtt qid in the affected eye
Bacteria leach toxins and by-products

Toxins Flushed/Eliminated from Eye

Bacteria Laden Lens

Build up of Toxins

Irritation of Surface
Cornea, Conj, Limbus

Red Eye
Infiltration of corneal peripheral/mid-periphery with inflammatory cells from limbus

No Flush Mechanism
Increased Bacterial Load
Pro-inflammatory status (increase cytokines, IgA, Ect)

Flush/Eliminated Toxins

Build up of Toxins

Irritation of Surface
Cornea, Conj, Limbus

Red Eye
Infiltration of corneal peripheral/mid-periphery with inflammatory cells from limbus

The TFOS International Workshop on Contact Lens Discomfort: Introduction

Jason J. Nichols, Tyler Jones, J. Daniel Nelson, P. Rena Skapinsek, David A. Sullivan, Mark D. Wilcox, and the members of the TFOS International Workshop on Contact Lens Discomfort

The Ocular Surface Institute, University of Rochester Medical Center, Rochester, New York

Purpose

For many years, the contact lens field has focused on safety

Compliments of Dave Kading, OD, FAAO

TABLE OF CONTENTS APRIL 2007, VOLUME 5, NUMBER 2

SPECIAL ISSUE

2007 Report of the International Dry Eye WorkShop (DEWS)

Sponsored by the Tear Film & Ocular Surface Society

http://www.tearfilm.org/dewsreport/
http://www.tearfilm.org/mgdworkshop/
http://www.iovs.org/content/54/11/TFOS1.full.pdf+html

sig: 1 gtt qid in the affected eye

http://www.tearfilm.org/dewsreport/
http://www.tearfilm.org/mgdworkshop/
http://www.iovs.org/content/54/11/TFOS1.full.pdf+html
**TBUT**

1) If the TBUT pattern is dynamic and changes with every blink, consider an aqueous or lipid issue.

2) If the TBUT pattern is stagnant and is in the same spot after every blink, consider the mucin layer or the ocular surface as being effected.

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80% of symptomatic CL wearers
13% of asymptomatic CL wearers

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<table>
<thead>
<tr>
<th>Horizontal length of staining</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 mm</td>
<td>0</td>
</tr>
<tr>
<td>2-4 mm</td>
<td>1</td>
</tr>
<tr>
<td>5-9 mm</td>
<td>2</td>
</tr>
<tr>
<td>&gt;10 mm</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sagittal width of staining</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25% of the width of wiper</td>
<td>0</td>
</tr>
<tr>
<td>25%-&lt;50% of the width of wiper</td>
<td>1</td>
</tr>
<tr>
<td>50%-&lt;75% of the width of wiper</td>
<td>2</td>
</tr>
<tr>
<td>≥75% of the width of wiper</td>
<td>3</td>
</tr>
</tbody>
</table>
Anterior Blepharitis
- Eyelid cleaning in exam room with cotton tip applicator
- Eyelid hygiene at home
- Topical antibiotic (if little to no inflammation)
- Topical antibiotic / steroid combination (if inflammation is present)
Meibomian Gland Dysfunction

Types of MGD

- Obvious – plugged glands, gland dropout, lid inflammation
- Non-Obvious - Requires gland expression to evaluate quality and quantity of meibum


Overall Therapeutic Goal of the LipiFlow®

- Alleviate meibomian gland obstruction in both upper and lower eyelids simultaneously, using a short in-office procedure (12 mins per eye)

Lipid Based Products
Meibomian Gland Dysfunction Treatment

- Oral Antibiotics
- Doxycycline
  – 20 to 100 mg bid po x 3 months, then taper

The effect of low-dose doxycycline therapy in chronic meibomian gland dysfunction
Yoo SE1, Lee DC Chang MH.

- Patients with meibomian gland dysfunction unresponsive to eyelid hygiene
- 150 patients randomized to 20 mg bid p.o. or 200 mg bid p.o.
- Identical effectiveness
- 39% of high dose experienced side effects vs. 17% of low dose

Meibomian Gland Dysfunction Treatment

- Oral Antibiotics
- Side Effects
  – Gastrointestinal upset
  – Yeast infections
  – Photosensitivity
  – Do not prescribe to children and pregnant women
  – Shouldn’t be taken with milk or dairy products

Doxycycline hyclate
100mg bid p.o. vs. topical Azithromycin 1% bid for 2 days then qd for 2 months

Why Do Omega 3’s Work?

Eicosapentaenoic acid / Docosahexaenoic acid (EPA/DHA)

Cyclooxygenase

Prostaglandin - 3 (Anti-inflammatory)
**The Effect of Decreasing the Dosage of Cyclosporine A 0.05% on Dry Eye Disease After 1 Year of Twice-Daily Therapy**

**Cyclosporine A 0.05% qd ou**

- 100 Dry Eye patients using tCSA bid ou, with symptom relief for at least 1 year
- Observer masked study
- Patients were randomized to continue with tCSA bid ou or reduce to qd ou

**Measures Tested at Baseline, 3 Months, and 6 Months**

- TBUT
- Flourescein Staining
- Lissamine Green Staining
- Schirmer Tear Test (anesthetized)
- Ocular Surface Disease Index (OSDI)

**Results**

- After 3 months: study group (qd) had better TBUT, OSDI values, and less corneal staining
- After 6 months: No statistically significant differences between the two groups, except OSDI scores
- Study group patients with “severe” dry eyes reported superior OSDI scores compared to those in the control group

*Su MY, et al. The Effect of Decreasing the Dosage of Cyclosporine A 0.05% on Dry Eye Disease After 1 Year of Twice-Daily Therapy. Cornea 2011 Oct;30(10):1098-1104*
Clinical Significance

- Enhanced patient compliance
- Improved therapeutic outcome
- Financial savings for the patient
- Non-FDA approved therapeutic regimen, but research supported
- Educate your patients, and monitor at 1-3 months to ensure stability

When do I Use steroids?

- What are the signs?
- What are the symptoms?

Visual function changes after punctal occlusion with the treatment of short BUT type of dry eye

Kaido M1, Ishida R, Dogru M, Tsubota K.

- Upper vs. Lower punctal occlusion
- Improvement with TBUT and vital staining in both groups
- Visual angle improved with upper punctal occlusion

The Dirty Dish Water Analogy

What is MMP-9?

- Matrix metalloproteinases (MMP) are proteolytic enzymes that are produced by stressed epithelial cells on the ocular surface
- Non-specific inflammatory marker
- Normal range between 3-41 ng/ml
- More sensitive diagnostic marker than clinical signs
- Correlates with clinical exam findings
- Ocular surface disease (i.e. dry eye) demonstrates elevated levels of MMP-9 in tears

**MMP-9 and Dry Eye Severity**

<table>
<thead>
<tr>
<th>Patient’s Dysfunctional Tear Syndrome Level</th>
<th>Average MMP-9 Level</th>
<th>Statistical Significance vs Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (n=18)</td>
<td>8.39ng/ml</td>
<td>NO</td>
</tr>
<tr>
<td>Severity Level 1 (n=15)</td>
<td>35.57 ng/ml</td>
<td>NO</td>
</tr>
<tr>
<td>Severity Level 2 (n=11)</td>
<td>66.17 ng/ml</td>
<td>YES</td>
</tr>
<tr>
<td>Severity Level 3 (n=9)</td>
<td>101.42 ng/ml</td>
<td>YES</td>
</tr>
<tr>
<td>Severity Level 4 (n=11)</td>
<td>381.24 ng/ml</td>
<td>YES</td>
</tr>
</tbody>
</table>

Positive Result = Chronic Dry Eye ≥ 40 ng/ml

**How to Use InflammaDry: Four-step Process**

1. Gently dab the Sample Collector in 6-8 locations on the palpebral conjunctiva (lower eyelid) to collect a tear sample. Do not use a dragging motion.
2. Snap the sample collector into the test cassette and press firmly where indicated.
3. Dip the test cassette into the provided buffer vial for 20 seconds. Replace the cap.
4. Read the results: 2 lines (1 red, 1 blue) = positive, 1 line (blue) = negative

**InflammaDry Clinical Trial**

<table>
<thead>
<tr>
<th>N = 206</th>
<th>Clinical Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+</td>
</tr>
<tr>
<td>InflammaDry</td>
<td>121</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>85% (121/143)</td>
</tr>
<tr>
<td>Specificity</td>
<td>94% (59/63)</td>
</tr>
<tr>
<td>Overall Agreement</td>
<td>87% (180/206)</td>
</tr>
</tbody>
</table>

**Sjogren’s Syndrome**

- Having a better understanding of Sjogren’s Syndrome will help guide who appropriate candidates for the test may be
- Sjogren’s syndrome is an autoimmune condition
- Autoimmune disease – “An illness that occurs when the body tissues are attacked by its own immune system”
- Chronic inflammation causes significant damage
- Increased incidence of Non-Hodgkin’s lymphoma


**Why does it have systemic effects?**

- Autoimmunity
  - There is cross reactivity with auto-antibodies
  - In other clinical manifestations the pathogenesis seems to be completely different as it may involve vasculitis and/or immune complex deposition and complement activation
- This sets the stage for a condition that has multiple ramifications

Lymphoma

- Patients with Sjogren’s Syndrome have a 10 to 50 times higher risk of lymphoma compared to healthy individual
- 2 to 9% of patients with Sjogren’s Syndrome develop lymphoma
- Majority of lymphoma in Sjogren’s Syndrome patient is non-Hodgkin’s lymphoma

Traditional Serological Disease Markers for Sjögren’s

- The classical serological markers for Sjögren’s are anti-Ro/SS-A and anti-La/SS-B antibodies
- Other antinuclear antibodies (ANA) and rheumatoid factors (RF) are also included as the more common serological markers detected
- The combined serology sensitivity and specificity of the classical markers is around 40-60%
- None of the currently recommended serology tests diagnose Sjögren’s early in the disease progression
- In approximately 20-30% of cases no classic Sjögren’s antibodies are found

Recent Clinical Findings for Sjögren's - Diagnostics

- Recent identification of additional serological markers beyond the classical autoantibodies Ro/SSA and La/SSB may allow for improvement in the speed and consistency of diagnosis by ECP’s and other clinicians
  - SP-1 – Salivary Protein 1: high expression in lacrimal and submandibular glands
  - CA6 – Carbonic Anhydrase 6: high expression in acinar cells of the submandibular and parotid glands
  - PSP – Parotid Secretory Protein: expressed in the acinar cells of the salivary glands
- The above markers improve the sensitivity and specificity of detection of Sjögren’s, particularly patients at an early stage of the disease.

Sjö – Early Detection of Sjögren’s Syndrome

1) Significant ocular surface staining (by itself)

2) Moderate dry eye with any two of the following

- Dry mouth - Xerostomia
- Respiratory issues – nasal crusting, recurrent sinusitis, dry cough, difficulty breathing
- Cutaneous manifestations – excessively dry skin
- Arthritic symptoms
- Gastrointestinal manifestations – nausea, dysphagia, epigastric pains (due to dryness of the pharynx and esophagus)
- Thyroid abnormalities – known diagnosis of Grave’s disease or Hashimoto’s or excessive fatigue
- Kidney problems
- Liver problems
- Peripheral neuropathy
Advancing Wave Like Epitheliopathy

The Abrasion that didn’t heal

* 34 year old female
* 1 ½ weeks ago was moving a shelf and her right eye started to itch
* The next day the right eye started bothering her more and was red
* She went to her primary care physician who started her on Ciloxan
* The drops didn’t help

Herpetic Keratitis Disease

- Herpetic keratitis infection is one of the leading causes of corneal transplants in the U.S.
- Herpes Simplex Virus (HSV-type 1 and HSV-type 2) and Herpes Zoster cause herpetic keratitis.
- A 2002 report estimated that 400,000 Americans had experienced ocular HSV infection
  * Estimated 20,000 primary infections per year in the U.S.
  * Estimated 28,000 relapses in the U.S. per year
Herpes Simplex Keratitis

Pathophysiology
- Initial recurrences present as epithelial disease
- Recurrent infection caused predominantly by HSV-1
- Subsequent recurrences may progress toward deeper layers resulting in stromal keratitis and/or anterior uveitis
- Repeated outbreaks involving the corneal stroma can ultimately lead to alteration of the corneal transparency
- Patients may develop corneal scarring and blindness which can lead to loss of vision or blindness
- Prompt treatment of ulcers is imperative to limit scarring and other more serious complications

Trifluridine (Viroptic)
- Approved in 1980, TFT was the last topical ocular antiviral therapy approved in the US
- Activated by cell and viral thymidine kinase
- Incorporated into both virus & host DNA
- Non-selective - incorporates into the DNA of healthy, as well as infected cells and therefore, can increase the potential for epithelial toxicity
- Instilled 9 times per day and use not recommended for more than 21 days due to potential ocular toxicity

TFT Toxicity
- TFT toxicity contributes to superficial punctate keratitis or filamentous keratitis, blepharitis, and canicular punctal occlusion
- Prolonged use beyond 21 days can lead to corneal epithelial dysplasia, conjunctival scarring, anterior ocular ischemia, and contact dermatitis

ZIRGAN Mechanism of Action
- GCV is a nucleoside analog of deoxyguanosine
- Penetrates cell infected with the virus
- Phosphorylated within the cell to ganciclovir monophosphate by a viral thymidine kinase
- Affinity for viral thymidine kinase allows for specificity in its action
- Further activation by several cell kinases leads to the formation of ganciclovir triphosphate which:
  - Inhibits viral DNA polymerase
  - Incorporates into viral DNA resulting in DNA chain termination and prevention of replication

Ganciclovir Mechanism of Action
- Activated GCV inhibits the synthesis of viral DNA in 2 ways:
  1. Competitive inhibition
     - Activated GCV directly inhibits viral DNA polymerase, preventing viral replication
  2. Chain termination
     - Activated GCV incorporates into viral DNA, preventing DNA synthesis

<table>
<thead>
<tr>
<th>Dosage Frequency</th>
<th>Zirgan</th>
<th>Viroptic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instill 1 drop in the affected eye 5 times per day until corneal ulcer heals and then 1 drop 3 times per day for 7 days</td>
<td>Instill 1 drop Viroptic Ophthalmic Solution, 1% onto the cornea of the affected eye every 2 hours while awake for a maximum daily dosage of 9 drops until the cornea ulcer has completely re-epithelialized. Following re-epithelialization, treatment for an additional 7 days of 1 drop every 4 hours while awake for minimum daily dosage of 5 drops is recommended.</td>
<td></td>
</tr>
</tbody>
</table>
Recommended dosage of administration should not be exceeded. Continuous administration of trifluridine for periods exceeding 21 days should be avoided because of potential ocular toxicity. For topical use only. Patients should not wear contact lenses if they have signs or symptoms of herpetic keratitis or during the course of therapy with Zirgan.

### HSV Prophylaxis

- **Acyclovir 400mg bid**
- **Valacyclovir 500mg qd**
- **History of severe stromal keratitis**
- **Those who experience more than one episode epithelial keratitis per year**
- **Those receiving corneal transplant for vision loss related to herpetic scarring**
- **1 week prior to cataract or glaucoma surgery and 1 to 6 months postoperatively**

### Recurrent HSV Keratitis

- Topical or oral antivirals typically given as prophylaxis for recurrence of HSV keratitis
- **GCV 0.15% gel** studied in nonrandomized interventional case series
  - GCV prophylaxis given BID for a mean period of 12 months in 6 patients with recurrent geographic herpetic keratitis
  - None of the patients developed recurrence of HSV keratitis during follow-up
  - No ocular side effects noted

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**Thank You**

mile@optometricinsights.com