Current Trends in Medical Management

Ron Melton, OD, FAAO
Randall Thomas, OD, MPH, FAAO

www.eyeupdate.com

Academy 2013
Seattle, WA

Tafluprost Ophthalmic Solution

- FDA approved February 2012
- First “preservative-free” prostaglandin
- Reduces IOP similarly to the other prostaglandins
- Dosage: once daily, preferably in the evening
- Most common side-effect – conjunctival hyperemia
- Available in unit dose containers
- Marketed as Zioptan 0.0015% ophthalmic solution by Merck

Simbrinza – (brinzolamide 1.0% and brimonidine 0.2% combination)

- Combination drug without a beta blocker where both ingredient drugs are dosed the same (b.i.d.)
- Combines 1% brinzolamide (Azopt ophthalmic suspension) with 0.2% brimonidine
- Offers a wide range of treatment possibilities due to its strong efficacy and ability to decrease elevated IOP by 21-35%
- Marketed by Alcon under the brand name Simbrinza suspension

RESCULA (unoprostone isopropyl) ophthalmic solution 0.15%

- Docosanoid class
- Reduces elevated IOP by increasing outflow through the trabecular meshwork
- Reduced mean IOP by 3-4mm Hg in clinical trials
- FDA approved for bid use; flat 12-hour diurnal curve
- Burning/stinging upon instillation more frequent compared to timolol
- RESCULA may be used as a first-line agent or concomitantly with other topical ophthalmic drug products to lower intraocular pressure.
- Rescula is supplied 5 ml in a 7.5 mL bottle
- Marketed by Sucampo Pharma Americas, LLC

Topiramate (Topamax) and Vision

- Uses: anticonvulsant, migraine prevention, bipolar disorder, obesity, OCD, IHH, neuropathic pain, essential tremor, post-herpetic neuralgia, and other esoteric uses.
- Topiramate is a sulfa derivative (like CAI’s)
- Idiosyncratic ciliochoroidal effusion is the most common ocular side effect, and most always results in a myopic shift with or without increased IOP
- This rare event usually occurs within 2 weeks of initiation (or doubling) of dosing
- First described in 2001 – 70% are female
- Tx: D/C the medicine; use (PRN) beta-blocker, brimonidine, or, in refractory case, oral prednisone or IV methylprednisolone. Also, instill cycloplegic agent, and do not use pilocarpine. Clinical Ophthalmology. January 2012

Qsymia: Potential for Decreased Weight and Increased Risk of Angle Closure

- New drug for weight loss patients who are overweight or obese and also have at least one weight-related condition such as high blood pressure, diabetes or high cholesterol.
- Combination of two older drugs
  - Phentermine (appetite suppressant)
  - Topiramate (feeling of satiation)
- Lesser dosages of each component drug tend to act synergistically
- On average, patients lose about 10% of their body weight over one year
- Marketed by Vivus Inc (Mountain View, California)
- FDA approval July 17, 2012
Are Generics OK?

“The more recent (since 1992) ophthalmic generics are approved according to strict criteria for sameness and are expected to behave in the same manner as the innovator.”

Reference: Ophthalmology, June 2012. Editorial by W. Chambers, MD of the FDA

Trimethoprim with Polymyxin B

- Polymyxin B has been discussed earlier
- Trimethoprim, a non-antibiotic antibacterial
  - Bacteriostatic and broad spectrum
  - Inhibits bacterial dihydrofolate reductase
  - Effective against most common ocular pathogens, except pseudomonas species
  - Excellent for bacterial infections in children
  - Haemophilus influenzae and streptococcus pneumoniae
- Available in solution only (Polytrim and generic)

Aminoglycosides

- Bactericidal
- Inhibits protein synthesis
- Effective against most commonly encountered gram positive and gram negative bacteria
- Available in both solution and ointment form
  - Gentamicin - toxic/allergic reactions do occasionally occur (visit www.ferapharma.com for free samples)
  - Tobramycin - resistance, toxic and allergic reactions rare (Category B)

Moxifloxacin 0.5% / Corneal Ulcers

- 0.5% Vigamox was found “to be as effective as a combination therapy of fortified cefazolin and tobramycin” in this study.
- However, dosing was impractically intense: hourly – round the clock – for 3 days, then Q 2 hrs for the next 7 days.
- Small sample size, predictive power of only 32%
- Tobra, Moxi, Cipro, and Gati all had at least 98% in vitro sensitivities to staph. Epi.


Evolving Fluoroquinolone Resistance

“Fourth-generation fluoroquinolones are significantly more expensive than generic traditional antibiotic eyedrops such as gentamicin sulfate and polymyxin B sulfate/trimethoprim, which have been shown to cover endophthalmitis isolates at least as well . . . “Given the frequent and increasing resistance, subtherapeutic penetration, and higher cost compared with other antibiotic eyedrops, the widespread perioperative and periprocedural use of fourth-generation fluoroquinolone antibiotic eyedrops should be reevaluated.

Reference: Archives of Ophthalmology, December 2012
Drugs and Antibiotic Resistance

• Study: 200 patients - 90% Gm+, 10% Gm–
• Least susceptible: penicillins (17%) and erythromycin (48%)
• Highest susceptible: gentamicin (94%), tobramycin (90%), tetracycline (91%)
• Intermediate susceptible: moxifloxacin and gatifloxacin (75%)
• About half of Gm+ were methicillin resistant

“The fluoroquinolones are failing to cover 20% or more potential pathogens; additionally, we found that fluoroquinolones may cover 1 but not all CNS strains present in a patient. One should therefore entertain alternatives to fluoroquinolones. Indeed, given the overall 90-plus percent susceptibility rate, one should perhaps consider instead the aminoglycosides.”

Reference: AJO, January 2013

Antimicrobial Resistance

• Staph. Epi. was the most common pathogen in this study
• 97% of all isolates were sensitive to gentamicin
• Fluoroquinolone resistance ranged from 32% to 40%
• “The high prevalence of fluoroquinolone-resistant organisms among ocular and nasal flora in our patient population raises concern with regards to the usefulness of topical fluoroquinolones as the best first-line agent in the setting of ophthalmic prophylaxis and for empiric use in acute ophthalmic infectious processes.”

Reference: AJO, December 2011

Further Corroboration . . .

“Short-term and repeated exposure of ocular flora to topical antibiotics selects for antibiotic resistance strains of coagulase-negative staphylococci. More alarming was the fact that these resistant coagulase-negative staphylococci also demonstrated co-resistance to other commonly used classes of antibiotic.”

JAMA-Oph. May 2013

Preventing Eye Infections (Intravitreal Injections)

• Kill time for Betadine (povidone iodine) 15-120 seconds…at any concentration!
• Anaphylaxis to iodine does not exist!
• “Topical moxifloxacin .5% had no additional effect on reducing conjunctival bacterial counts beyond the effect of 5% povidone iodine alone.”
• “Preinjection antibiotics either before the day of injection or immediately prior to injection are not generally recommended.”
• Gentamicin was vastly more effective than fluoroquinolones


Antibiotics and Intravitreal Injections

• Preoperative and postoperative antibiotics might have a negative impact on the safety of the procedure because, with repeated injections, patients develop ocular surface bacteria that are antibiotic-resistant.
• Topical antibiotics before the day of injection did not reduce conjunctival bacterial counts more than the immediate pre-injection use of povidone-iodine
• In spite of this knowledge, 27% of surveyed retina specialists continue to use pre-injection antibiotics and 63% use post-injection antibiotics.


Implications of Azithromycin and Fluoroquinolone Use

• “The repeated use of azithromycin or fluoroquinolone antibiotics significantly alters the composition of conjunctival flora by increasing the percentage of S. epidermidis.”
• “Resistant strains of S. epidermidis emerge rapidly after antibiotic exposure and possess co-resistance to other classes of antibiotics.”
• “The high percentage (75%) of baseline resistance to azithromycin may have allowed resistant S. epidermidis strains to readily out-compete other flora.”
• “The practice of long-term or repeated use of azithromycin for blepharitis may therefore select for not only azithromycin-resistant but also doxycycline-resistant strains of S. epidermidis.”

Oph. May 2013
A Novel Fluoroquinolone - Besifloxacin

- New chemical entity: An 8-chloro fluoroquinolone
- NOT used systemically – only available in U.S.
- Relative resistance-proof: No oral counterpart
- FDA-approved medication: Bacterial conjunctivitis
- FDA-approved treatment protocol: tid for 7 days
- Pediatric approval: ages 1 and older
- Preserved with 0.01% BAK (Durasite vehicle)
- Marketed as Besivance 0.6%) ophthalmic suspension by B&L Pharmaceuticals – 5 ml

2009 ARMOR Surveillance
All S. aureus (n= 200)

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</table>

39% of ocular S. aureus isolates were MRSA
38% of ocular S. aureus isolates were FQ-resistant

Haas et al. Presented at ARVO, Fort Lauderdale, FL, May 2-6, 2010. Abstract #D965, % resistance based on oxacillin and ciprofloxacin breakpoints.

Antibiotics - Systemic

- Penicillins
- Cephalosporins
- Tetracyclines
- Macrolides
- Fluoroquinolones

Consult Drug Facts & Comparisons (www.drugfacts.com)

Amoxicillin/Clavulanic Acid (Augmentin)

- Clavulanic acid enables amoxicillin to be bactericidal against common gram positive pathogens
- Useful in treating soft tissue infections
- Cannot use if patient is allergic to penicillin
- Tx: 250, 500 & 875 (generic) or 1000 mg (branded only) tablet q 12 hrs x 7-10 days
- Can be taken with meals

Cephalexin (Keflex)

- Cephalexin - 1st generation cephalosporin
- Effective against most gram positive pathogens
- All cephalosporins share a 1-2 % cross-sensitivity to PCN (true allergy to PCN)
- Usual dosage: 500 mg bid x 1 week
- Useful in soft tissue staph infections, such as internal hordeola, preseptal cellulitis, etc.

Options for True Penicillin Allergy Patients

- 2<sup>nd</sup> or 3<sup>rd</sup> generation cephalosporin
- Sulfamethoxazole/trimethoprim (Bactrim or Septra)
- A fluoroquinolone (Levofloxacin)
- Doxycycline
- Erythromycin
### The Tetracyclines
- Tetracycline, doxycycline, minocycline
- Doxycycline most commonly used
- Advantages over tetracycline
  - Maintenance dose 20 - 100 mg daily
  - Can be taken without regard to meals
- Contraindicated in pregnancy, nursing mothers, under age 8; photosensitivity warning
- Indication in primary eye care
  - Meibomianitis (chronic inspissated glands)
  - Adult inclusion conjunctivitis (chlamydia)
  - Recurrent corneal erosion

### Oral Doxycycline and Pterygial Angiogenesis
- UV light is a known trigger for pterygogenesis and progression
- Doxycycline (and corticosteroids) can inhibit neovascularization
- Perhaps pterygium management can be augmented with 50 mg P.O. doxycycline daily for many weeks or many months after (or concurrent with) topical loteprednol q.i.d. for 1 month, the b.i.d. for 2 months


### Oracea
- Doxycycline 30 mg immediate release and 10 mg delayed release beads (once daily 40 mg capsule)
- First and only oral therapy approved by FDA to treat rosacea
- Works by controlling inflammation
- Recommended to take in morning with a full glass of water
- Contraindications and side effects similar to tetracyclines (photosensitivity and yeast infections not observed in clinical trials).
- Marketed by Galderma

### Minocycline, MGD, and Dry Eye
- “Lid hygiene plus minocycline showed significant improvements in clinical signs and remarkable changes in fatty acid composition.”
- “There is no agreement on the ideal dosage of minocycline.”
- “Our study showed remarkable benefit with 50 mg oral minocycline twice daily for two months without any fatal complications.”
- “To obtain meaningful patient satisfaction and favorable clinical results we should consider minocycline as a first-line therapy for the treatment of moderate and severe MGD.”

AJO, December 2012

### Physician Care of Dry Eye Patients
- “Surprisingly, the cornea specialists did not show better conformance (to established Preferred Practice Patterns) than other ophthalmologist subtypes because they received special training in the diagnosis and management of dry eye syndrome.”
- It is our opinion that an attentive, compassionate doctor of optometry should be the best at caring for patients with dry eye disease!

Reference: J. Daniel Nelson, MD.
Supplement to Ophthalmology, October 2012
Off label

- “An estimated 50 percent of medications used routinely in ophthalmic practice are used off-label.”
- “Clinical practice should be guided by the best interest of the patient.”
- “In many instances, off-label treatments may be the best, or the only, available treatment, and withholding treatment would be unethical.”


Azithromycin - (Zithromax)

- Used for soft tissue infection; heavy prescribing has resulted in much resistance
- Drug of choice for chlamydial infections
- Dosage for chlamydial eye infection - four 250 mg capsules or two 500 mg capsules for one day or a single dose of a 1,000 mg suspension
- Zmax is a 2,000 mg oral suspension
- 1.0% AzaSite ophthalmic solution by InSite Vision

THERMODYNAMIC TX TO EXPRESS AND EVACUATE MGs

A new thermodynamic treatment to express & evacuate the MGs

The device applies controlled heat to the inner upper and lower palpebral conjunctival surfaces and lid margins, while simultaneously applying pulsating pressure over the upper and lower (outer) eyelids.

The LIPIFLOW
(TearScience Inc., Morrisville, NC)

FDA approved LipiFlow July 2011

SUMMARY – NEW PARADIGM

“It is important to note that MGD, a condition of MG obstruction, may be the leading cause of dry eye syndrome throughout the world.”

TFOS 2008, Report to Professions, 2011

- Lipid deficiency & not aqueous deficiency is usually the catalyst for DRY EYE & inflammatory cascade
- In contrast to conventional models and treatment
- MGD and MG OBSTRUCTION may be obvious or non-obvious, most frequently non-obvious
- Dx of MG functionality requires expression – new metrics
- Treatment of MGD with new technology can treat obstruction improving meibomian gland function to effectively treat dry eye disease & CL intolerance
Medical Approach to RCE

- Small study – limited follow-up
- 100 mg doxycycline per day for 1 month and Lotemax q.i.d. for 1 month
- Results: Curative in almost all cases
- An alternative (or adjunctive) to ASP or conventional therapies

Bactrim or Septra

- Drug of choice for MRSA infections
- Combination of 160 mg of trimethoprim and 800 mg of sulfamethoxazole
- Rule out true sulfa allergy
- Sig: Take 1 or 2 DS tabs p.o. bid x 7-10 days
- Note that the standard strength of these drugs is “double strength” (DS)
- If sulfa-allergic, then doxycycline 100 mg used bid for 7-10 days
- Both are old, generic, and highly-effective

Ester vs Ketone Corticosteroids

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<tr>
<th>Ester</th>
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<tr>
<td>Loteprednol</td>
<td>Prednisolone</td>
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<td>Fluorometholone</td>
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<td>Dexamethasone</td>
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<td>Rimexolone</td>
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<td></td>
<td>Difluoroprednisolone</td>
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Difluprednate 0.05% (Durezol)

- “There is increased bioavailability and dose uniformity resulting from the formulation of difluprednate as an emulsion, rather than a suspension.”
- Steroid-induced hypertension seen in 8% of the normal population, and is more common in patients with glaucoma.
- Steroid-induced hypertension is “generally not seen until 3 to 6 weeks of corticosteroid use.”
- “Difluprednate was shown to provide better results compared with prednisolone acetate…”
- “We believe the effects seen are the result of the greater anti-inflamatory potency of difluprednate.”
- AJO, October, 2011

Lotemax Gel

- A new and improved gel drop formulation of ester-based loteprednol corticosteroid
- This eye drop possesses “adaptive viscosity”
- Provides clear vision in a gel drop delivery system
- No shaking required!
- pH of 6.0-6.5 vs 5.3-5.6 in the suspension
- 70% less BAK than Lotemax suspension
- No increased IOP vs vehicle in phase III study
- FDA approval: post-operative pain and inflammation
- Marketed by B&L as Lotemax Gel in a 5 gm bottle

Loteprednol Ophthalmic Ointment

- The only ester-based steroid ointment available
- It is a 0.5% concentration and preservative-free
- FDA-approved: Post-operative inflammation and pain
- Numerous “off-label” clinical uses: dry eye, allergy, corneal transplant protection, blepharitis, GPC, chronic uveitis, stromal immune herpetic keratitis, Thygeson’s SPK, RCE, augmentation of steroid eyepad therapy in acute, advanced uveitis or episcleritis, following Betadine EKC Tx, contact dermatitis, and other inflammatory conditions as indicated
- Available in a 3.5 gm ophthalmic tube as Lotemax 0.5% ophthalmic ointment by B&L
Remissions and exacerbations (of ocular surface inflammatory disease) are common, and occasionally these require another short course of topical steroids. I believe ophthalmologists as a whole are relatively ‘steroid shy’ because of potentially serious complications including steroid-induced glaucoma and secondary cataract, but newer steroids such as loteprednol, which is now also available in an ointment form along with two strengths of suspension, reduce these risks significantly. For the patient who requires a generic alternative for economic reasons, I find fluorometholone is an effective drop with a similar safety profile.


Long-Term FML Use After PKP

“In summary, we found that the prolonged use of 0.1% fluorometholone was beneficial for the prevention of rejection after PKP. Because no adverse consequences associated with the use of the eye drops were noted, we recommend continuing the use of low-dose corticosteroids, even in non-high-risk cases.” Reference: Oph, April 2012

M & T: If such prolonged use of a ketone-based steroid is safe and effective, it would stand to reason that long-term use of loteprednol would be even safer. This has clear implications for long-term use in dry eye-related ocular surface inflammation.

Children and Steroids

“A tapering regimen of FML for ocular surface disease in children constitutes a safe anti-inflammatory treatment option to avoid steroid-induced glaucoma.”

“These patients may need prolonged treatment with FML to control the inflammation, a tapering regimen may help avoid steroid-induced glaucoma.”

No study had an increased IOP above 19mmHg. (Reference: BJO; 2011, 95 (11), Pp 1531-1533)

M&T Commentary: We would be much more comfortable using an ester-based corticosteroid such as loteprednol with these patients.

Non-ophthalmic steroid: ointment/cream/lotion

Triamcinolone - moderate potency steroid
Available in cream, ointment and lotion (0.5%, 0.1%, 0.025%)
Our favorite: the 0.1% cream

Reference: Drug Facts and Comparisons

Systemic Prednisone

Most common Rx’d systemic corticosteroid
Common initial dosage 40-60 mg
Available generically in both tablets and DosePaks (5 or 10 mg at 6 or 12 day course)
Questions to ask before prescribing?
• Diabetic?
• Peptic Ulcer Disease?
• Tuberculosis?
• Pregnant?

Lipid-Based Artificial Tears (For Evaporative Dry Eye)

Vast majority of dry eye patients have MGD
Meta-stable emulsions are optimum Tx
Rapidly provides a protective lipid barrier
Reduces harmful evaporation to prevent tear loss
Replenishes the complete tear film
• Systane Balance emulsion (10 ml) – Alcon
• Refresh Optive Advanced (10 ml) – Allergan
• FreshKote (15 ml Rx) – Focus Labs
• Retaine MGD - OCU SOFT
Aqueous-Based Artificial Tears (For Aqueous Deficient Eye)

• Relatively uncommon cause of dry eyes
• Aqueous-based solutions are optimum Tx
• Rapidly provides ocular surface hydration
• Main ingredients commonly include
  • Cellulose
  • Glycerin
  • Polyethylene Glycol
  • Propylene Glycol
  • Soothe Xtra Hydration (15 ml) – B&L
  • Systane Ultra (15 ml) – Alcon
  • Optive (15 ml) - Allergan
  • Blink (15 ml) - AMO

Perspective on Therapeutic Approaches

• “... it is clear that many patients with DED do not show a consistent therapeutic response to topical cyclosporin A, and . . . some patients experience bothersome adverse effects (e.g., burning or irritation) that impair medication tolerability.”
• “Clinical trials have demonstrated the efficacy of topical corticosteroid treatment at diminishing symptom severity and minimizing ocular surface staining.”
• “Repetitive short-term pulsatile administration of topical corticosteroids is a promising method of harnessing their beneficial effects, while minimizing the risk of adverse events.”

Archives of Ophthalmology, January 2012

Tear Dysfunction Perspectives

• “Over the past decade there has been a trend towards increased use of anti-inflammatory therapies to improve comfort, corneal smoothness, and barrier function.”
• Corticosteroids, doxycycline, and EFA’s have been found to decrease production of a variety of inflammatory mediators and improve corneal epithelial disease.

AJO, December 2011

Supplemental Therapeutic Approaches in Dry Eye Disease (DED)

• “Most of the available evidence suggests that administration of omega 3 EFAs can lessen DED severity.”
• Regarding omega 3 EFAs, “... more evidence is needed to identify the most efficacious forms and doses.”
• “The evidence implicating inflammation in pathogenesis of DED has opened new avenues for the treatment of this complex disorder. The successful application of anti-inflammatory medications in the treatment of DED provides hope for the millions of individuals who daily experience this deleterious condition.”

Archives of Ophthalmology, January 2012

FDA Draft Guidance on Generic Eye Drug

“... the U.S. Food and Drug Administration proposed allowing companies to apply for marketing approval of generic versions of Restasis based on laboratory tests, not on human clinical trials.

The FDA said in its proposed guidance that conducting a study in humans to test whether the drugs are essentially equivalent would not be feasible or reliable due to the ‘modest efficacy’ of Restasis.”

(Reuters) by Toni Clarke on June 24, 2013
“Alternative Supplementation”

- Orally administered omega-3 essential fatty acids
- Like cyclosporine and doxycycline, may take 3-4 months to obtain a significant clinical effect

Vascepa (icosapent ethyl)

- FDA-approved prescription product containing only the Omega-3 fatty acid EPA.
- Used along with low-fat, low-cholesterol diet to help reduce triglyceride levels in adults with severe (≥500 mg/dL) hypertriglyceridemia without raising LDL (bad) cholesterol
- Most commonly reported side effect is arthralgias. The effect of VASCEPA on patients at risk for pancreatitis, cardiovascular mortality and morbidity has not been determined.
- Pregnancy category C
- www.vascepa.com

Nepafenac Ophthalmic Suspensions

- Nevanac 0.1% AND Ilevro 0.3%
- Indication: Treatment of pain and inflammation associated with cataract surgery
- Nevanac is dosed tid; Ilevro, once daily
- Ilevro is to be prescribed the day before surgery, the day of surgery and then 14 more days
- BAK 0.005%, pH 6.8, pregnancy category C, pediatric use down to age 10
- Marketed by Alcon as Ilevro 0.3% ophthalmic suspension 1.7 ml in a 4 ml bottle

Bromfenac Ophthalmic Solutions

- Bromday 0.09% and Prolensa 0.07% (22% less concentration)
- Indication: Treatment of pain and inflammation associated with cataract surgery
- Both are dosed once daily
- Both are prescribed the day before surgery, the day of surgery and then 14 more days
- BAK 0.005% BAK pH 7.8, pregnancy category C, pediatric use down to age 18
- Marketed by B&L at Prolensa 0.07% ophthalmic solution 1.6 ml and 3 ml in a 7.5 ml bottle

Neomycin, Polymyxin B, and 0.1% Dexamethasone

- Excellent coverage against most bacteria
- Effective suppressor of inflammation
- Has been a time honored work horse in medical eye care
- Guard against aminoglycoside reactions and IOP increase by limiting use to <1 week
- Now a relatively obsolete combination
- Marketed as Maxitrol and generically

Treatment of Blepharitis-Related Dry Eye

- “Antibiotic/steroid combination agents can play an important role in a rational, stepwise dry eye treatment plan.”
- “These drugs do not appear to alter meibomian gland secretions. However, they can effectively reduce both bacterial proliferation and inflammation of the lid margins.”
- Treat with “...combination antibiotic/steroids as needed on a pulsed basis as part of a long-term treatment plan for recalcitrant or recurrent blepharitis.”

Reference: Refractive Eyecare, December 2011

Obviously, in chronic conditions, an aminoglycoside combined with loteprednol would be the wisest choice
### Tobramycin 0.3% and Loteprednol etabonate 0.5%

- Excellent coverage against most ocular pathogens with minimal concern of aminoglycoside toxicity
- Safe, effective suppressor of inflammation
- Marketed as Zylet Ophthalmic Suspension by B&L Pharmaceuticals
- Available in 2.5, 5, and 10 ml bottles
- Lotemax and Zylet ointments are in development

**Reference:** M. McDonald. Refractive Eyecare, September 2011

### Cliradex for Demodex

- A derivative of Tea Tree Oil ingredients
- Terpinen-4-ol (T4o) is the most demodexicodal
- For cleansing the face and eyelid skin
- Has a transient slight stinging, menthol-like sensation
- If ocular contact, rinse with saline or artificial tear
- Must keep eyes closed, and allow to air dry for 1 min
- Try this once daily for 6-8 weeks (bid if severe)
- Available from BioTissue, Doral, Fl
- See www.cliradex.com for more information

### Resistance and Unnecessary Antibiotic Use

- “Now that we know that unnecessary treatment fosters resistance, and resistance has become a significant threat to our patients, we cannot simply prescribe for any conjunctivitis on the grounds that it may be bacterial. Fortunately, there is now a test available that will detect adenovirus, the most common cause of viral conjunctivitis.”
- Dr. McDonald is referring to the RPS Adenodetector (www.RPSdetectors.com)

**Reference:** M. McDonald. Refractive Eyecare, September 2011

### AdenoPlus™

- Convenient in-office, 10 minute immunoassay
- Detects all known serotypes of adenovirus
- Clinical Laboratory Improvement Amendment (CLIA) waived
- Has sensitivity of 90% and specificity of 96%
- Adenoviral infection is commonly a clinical diagnosis
- Helpful for challenging cases, and for primary care physicians
- CPT code 87809QW
- [www.nicox.com](http://www.nicox.com)

**Reference:** JAMA-Oph, January 2013

### Clinical Perspective on AdenoPlus Immunoassay

- Adenovirus can cause: nonspecific follicular conjunctivitis, PCF, acute hemorrhagic conjunctivitis, and EKC
- Clinical diagnostic accuracy ranges from 40-70%
- AdenoPlus is a rapid in-office assay having 90-95% sensitivity and specificity
- AdenoPlus results correlates with disease infectivity (i.e. the intensity of the positive result line is directly proportional to the amount of antigen present)
- “In addition to the typical management strategy for adenovirus conjunctivitis, 2 novel treatments, topical povidone iodine and ganciclovir gel, have become more widely used.”
- www.nicox.com

**Reference:** JAMA-Oph, January 2013

### 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

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<td>0.2%</td>
<td>(Pataday) qd (2.5 ml)</td>
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<td>(Alaway) (10 ml)</td>
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<td>(Refresh) (5 ml)</td>
</tr>
</tbody>
</table>

**Reference:** JAMA-Oph, January 2013
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>
<tr>
<td>Famciclovir</td>
<td>Famvir</td>
</tr>
</tbody>
</table>

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

Topical Ganciclovir

- Used systemically to treat CMV retinitis
- A new topical “pro-drug” for treating epithelial HSV
- Only acts on virally infected cells
- Used 5 x D for 4 to 6 days, then tid for 3 to 4 more days
- Is a 0.15% ophthalmic gel-drop with BAK
- Marketed as Zirgan ophthalmic gel
- Comes in a 5 gram tube
- Marketed by B+L Pharmaceuticals

Topical Antiviral Options

**Trifluridine**
- Old drug
- Indiscriminate expression
- Potentially toxic
- More frequent dosing
- Refrigerate until opened
- Thimerisol preserved
- Solution (7.5 ml bottle)
- Viroptic and generic

**Ganciclovir**
- New drug
- Infected cell-specific
- Minimally toxic
- Less frequent dosing
- No refrigeration needed
- BAK preserved
- Gel (5 gram tube)
- Zirgan by B+L

Valacyclovir vs. Acyclovir for Recurrent HSV

“One-year suppression therapy with oral valacyclovir (500-mg tablet daily) was shown to be as effective and as well-tolerated as acyclovir (400-mg tablet twice daily) in reducing the rate of recurrent ocular HSV disease.”


Study on Stromal HSK

- OD response rate, 6% - MD response rate 15%
- ALL: 95% treated epithelial keratitis correctly
- For stromal immune keratitis
  - 54% OD correct
  - 74% MD correct
  - 82% corneal subspecialist correct
- Correct = topical steroids with antiviral cover
- Correct use of oral antiviral prophylaxis for recurrences
  - 51% - OD, 60% - MD, 62% corneal subspecialist
- “Training” was most significant determining factor

Preventing HSV Disease Recurrences

- Patients being treated with oral antiviral therapy were 9 times less likely than untreated patients to develop recurrent keratitis
- Recurrence rates: 27% at 1 year
  - 50% by 5 years
  - 57% by 10 years
  - 63% by 20 years
- Stromal disease is more likely to recur than epithelial disease
- Length of prophylaxis: Generally 5 disease-free years

**Pediatric Herpes Simplex Disease**

- Herpes simplex virus (HSV) and herpes blepharoconjunctivitis (HSB) frequently misdiagnosed
- Recurrence of HSV more common in children (50%) than adults
- 30% of patients with HSK initially misdiagnosed
- Suspect HSV keratitis in recurrent unilateral keratoconjunctivitis with corneal neovascularization and decreased corneal sensation
- Peds patient HSV shows severe inflammation and stromal keratitis; in adults, most common manifestation is dendritic keratitis
- Tx: Oral ACV

*Reference: Ophthalmology, October 2012 (Lin, Pavan-Langston, Colby)*

**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)
- Duration of protection after vaccination unknown

*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.***

**Zoster Disease: Young (<60) vs Old (>60)**

- Overall peak incidence of HZO: 50-59 years of age
- Because of childhood chickenpox immunization, there will be an increased incidence of younger people developing HZ for a few decades
- Younger: secondary inflammation “flares” (pseudodendrites, keratouveitis) more common
- Older: neurotrophic keratitis in about 25%, therefore need to enhance tear film function
- Long-term oral antiviral and corticosteroid therapy may be indicated in many HZO patients

*Reference: Ophthalmology, November, 2011*

**Antiviral Treatment for VZD**

- Unlike stromal keratitis and uveitis, the dendriform lesions do harbor active virus, and respond to oral and topical antiviral therapy
- Such “late dendriform keratopathy” occurs in 2-10% of patients after HZO
- While corticosteroids are commonly used to treat the sequela of HZO, if the tissues do not respond as expected, perhaps trying a seven day course of oral antiviral could be tried.

*Reference: Arch. Oph. January 2012*