Current Therapy in Ocular Disease
-The Vision Institute of Canada-

- Melton-Thomas Treatment Guidelines
- Current Trends in Medical Management
- Eye to Eye: A Clinical Overview
Anterior Segment Update

• Medication Overview
• Clinical Guidelines and Pearls
• Case Presentations
Ophthalmic Journal References

- American Journal of Ophthalmology (ajo.com)
- Archives of Ophthalmology (archopht.ama-assn.org)
- Survey of Ophthalmology (www.elsevier.com)
- Audio-Digest Ophthalmology (audiodigest.org)
- Review of Ophthalmology (revophth.com)
- OphSource (ophsource.org) convenient online access to ophthalmology publications including:
  - Ophthalmology
  - American Journal of Ophthalmology
  - Survey of Ophthalmology
- Advanced Ocular Care (www.advancedocularcare.com)
Antibacterial Medications

• Sulfa Preparations
• Azithromycin
• Erythromycin
• Bacitracin
• Bacitracin / Polymyxin B
• Bacitracin / Polymyxin B / Neomycin
• Chloramphenicol
• Gentamicin
• Tobramycin
• Trimethoprim / Polymyxin B
• Fluoroquinolones
• Oral antibiotics
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
Sodium Sulfacetamide

- Bacteriostatic - competes with PABA
- Broad spectrum antibacterial
  - poorly active against staph species
  - good activity against strep species
- Allergy to sulfa preparations is common
- Stings upon instillation
- Commonly available in 10% solution and ointment
Azithromycin 1% Ophthalmic Solution

• Topical eyedrop solution of azithromycin
• Only macrolide ophthalmic formulation
• Broad spectrum coverage, especially against gram positive pathogens
• Good tissue penetration; viscous vehicle
• Package insert dosage: BID for 2 days then QD for 5 days
• Avoid use if patient is allergic to erythromycin
• Pregnancy category B; approved down to age 1
• Marketed as AzaSite 1% ophthalmic solution in a 2.5 ml opaque bottle by Merck
Clinical Cure of Bacterial Conjunctivitis with Azithromycin 1%: Vehicle-Controlled, Double-Masked Clinical Trial

“Conclusions: Azithromycin 1% ophthalmic solution in DuraSite showed statically significant differences in clinical resolution and bacterial eradication rates when compared with vehicle. Because it was well tolerated in this population, it may be a viable treatment option for children and adults with bacterial conjunctivitis.”

Unsubstantiated Claims

The Journal Ad includes the claim, "AzaSite® Can Restore a Healthy Ocular Surface By Delivering Significant Anti-Inflammatory and Antimicrobial Effects Directly to the site of the Problem." (bolded emphasis in original; underlined emphasis added) This claim is misleading because it implies that AzaSite delivers anti-inflammatory effects, when this has not been demonstrated by substantial evidence or substantial clinical experience.
Perspective on Topical Azithromycin

“Dr. Donnenfeld highlighted the (MGD Workshop) recommendation for initiating topical AzaSite for all patients with symptomatic disease.”

“Topical azithromycin penetrates the lid tissue and provides antimicrobial and anti-inflammatory effects that have been proven to improve MGD dramatically, Dr. Donnenfeld said.”

“Ophthalmologists must be aware of potential conflicts of interest with the use of off-label medications, including financial gain, notoriety or recognition, advancement of a personal research program or promotion of a third party interest, and carefully assessing whether those interests are affecting treatment recommendations.

Bacitracin

- Bactericidal - destroys cell walls
- Highly efficacious against gram positive bacteria
- Bacterial resistance is very rare
- Toxicity and allergic responses are very rare
- Available only in ointment form
Bacitracin and Polymyxin B

- Polymyxin B
  - Bactericidal - destroys cell membranes
  - Highly efficacious against gram negative bacteria
  - Resistance, toxicity, and allergic responses are very rare
  - Available only in ointment form
  - Pregnancy category B
Bacitracin, Polymyxin B, and Neomycin

• Neomycin
  • Bactericidal - inhibits protein synthesis
  • Effective against most gram positives and gram negatives (except pseudomonas species)
  • Bacterial resistance is very rare
  • Toxic/allergic reactions seen in 5-10% of patients
  • Available in both solution and ointment

• Neosporin (polymyxin B, neomycin and gramicidin)
  • “The combination of polymyxin B, neomycin and gramicidin is an effective and safe treatment of suspected corneal ulceration.”

Chloramphenicol

• Bacteriostatic - inhibits protein synthesis
• Broad spectrum of antibacterial activity
  • Not very effective against staph species
  • Not effective against pseudomonas species
• Exhibits excellent intraocular penetration
• Extremely easy on corneal/conjunctival tissues
• May cause non-dose-related fatal aplastic anemia
• Available in both solution and ointment form
Update on Chloramphenicol

• “One of the most widely prescribed topical antibiotics in the world.”

• Heavily prescribed in Ireland, England, Australia, Far East

• 1982 report on possible aplastic anemia killed drug in US

• HPLC could not detect chloramphenicol in the blood

• No proof of casualty, however an association “is probable”.

• Do not use if Hx of family Hx or blood dyscrasia

• “Efficacious, affordable, broad-spectrum, and very rarely causes blood dyscrasias”.

Reference: AJO, January 2007
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 as a 10ml solution (Polytrim and generic)
Sometimes Older is Better

“Antibiotic use should be appropriately limited, employing narrower spectrum or older agents whenever possible – particularly for mild or self-limiting infections. It should be recognized, further, that newer antimicrobials are not necessarily better than older ones: trimethoprim, polymyxin B, for example, maintains excellent activity against MRSA (>95% of strains susceptible) and most methicillin-resistant coagulase-negative staphylococci (>90% of strains susceptible).”

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 (Category C)
  • Tobramycin - resistance, toxic and allergic reactions rare (Category B)
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
Fluoroquinolones

- Potent, broad-spectrum bacterial antibiotics
- Inhibit bacterial DNA Gyrase and topoisomerase IV
- Cross-resistance between other antibiotics is rare
- Development of bacterial resistance is increasing with older fluoroquinolones
  - Ciloxan* (ciprofloxacin) and Ocuflox* (ofloxacin)
  - Ciprofloxacin and ofloxacin generically available
  - Quixin (levofloxacin 0.5%)
  - IQUIX* (levofloxacin 1.5%)
  - Zymar (gatifloxacin 0.3%)
  - Zymaxid (gatifloxacin 0.5%)
  - Vigamox (moxifloxacin 0.5%)
  - Moxeza (moxifloxacin 0.5%)
  - Besivance (besifloxacin 0.6%)

- All are approved for pediatric use
- All are FDA category “C”

*Approved to treat microbial keratitis
Gatifloxacin

- Inhibits topoisomerase types 2 and 4
- Highly effective against Gram+ and Gram− bacteria
- FDA-approved for bacterial conjunctivitis
- Pregnancy category C; pediatric to age 1
- BAK preserved
- Available from Allergan as 0.5% Zymaxid
- Systemically: Tequin (removed from market)
Moxifloxacin 0.5%

- **Actions:** Inhibits topoisomerase type 2 (DNA gyrase) and topoisomerase type 4
- **Highly effective against G+ and G– bacteria**
- **Pregnancy category C**
- **Pediatric indication:**
  - Vigamox - age 1
  - Moxeza - age 4 months
- **Xanthan gum prolongs ocular surface contact time, thus a decreased dosing frequency**
- **Dosing:**
  - Vigamox 0.5% tid x 7 days (pH 6.8)
  - Moxeza 0.5% bid x 7 days (pH 7.4)
- Vigamox and Moxeza 3ml – available by Alcon
- Systemically available as Avelox
Antibiotic Use Causes Multidrug Resistance

• “Conjunctival S. epidermidis repeatedly exposed to fluoroquinolone or azithromycin antibiotics rapidly develop resistance.”
• Gentamicin, Polytrim, doxycycline, and vancomycin remain very highly effective medicines in eradicating S. epidermidis.
• The fluoroquinolones and macrolide antibiotics exhibit high levels of resistance
• “These findings indicate the need for greater thought and more rational use of ophthalmic antibiotics to reduce the epidemic of antimicrobial resistance.”

Oph. October 2011
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

AJO, November 2011
Levofloxacin 1.5% Ophthalmic Solution

• First high concentration ophthalmic fluoroquinolone
• Ophthalmic version of oral Levaquin, the most highly prescribed oral fluoroquinolone
• FDA Indication:  Bacterial keratitis
• Lower concentration Quixin approved for bacterial conjunctivitis
• Clinical usefulness:  Any ocular bacterial infection
• Self-preserved in a 5 ml opaque bottle
• Marketed as IQUIX by Vistakon Pharmaceuticals

“Our study suggests a disturbingly high % of resistance to All fluoroquinolones tested.”

“The antibiotics most effective in eliminating multiresistance CNS are vancomycin and the aminoglycocides.”

Furthermore, and collaborating this 2003 article: “MRSA organisms may be resistant in vitro to all generations of fluoroquinolone antibiotics, but do seem to be sensitive to gentamicin and vancomycin.” AJO, March 2008 (p 413)
Topical Antibiotics in Perspective

• “In an era where products are heavily advertised by pharmaceutical companies, it is sometimes difficult to separate peer-reviewed scientific studies from promotional literature printed by the drug manufacturer.”

• “The fourth-generation fluoroquinolones demonstrated an in vitro efficacy of less than 80%.”

• “Many organisms, especially coagulase-negative staphylococci, are commonly resistant to the fourth-generation fluoroquinolones, which are the most popular topical antibiotics used in ophthalmology today.”

Ocular Trust: Nationwide Antimicrobial Susceptibility Patterns in Ocular Isolates

Reference: P Asbell et al. AJO. June 2008
Besifloxacin (A New Class: Chloro-fluoroquinolone)

- 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)

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC Range</th>
<th>MIC₅₀</th>
<th>MIC₉₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>0.25 – 2</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>Besifloxacin</td>
<td>≤0.008 – 4</td>
<td>0.03</td>
<td>1</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>≤0.008 – 64</td>
<td>0.06</td>
<td>8</td>
</tr>
</tbody>
</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.
ARMOR Study Methodology

• “Two things – the strength of ARMOR’s methodology and the number of isolates tested – make it an extremely trustworthy study.”

• “Among the fluoroquinolones tested, besifloxacin proved to be the most potent against staphylococci, particularly ciprofloxacin-resistant staphylococci; it was followed by moxifloxacin and gatifloxacin.”

Reference: M. McDonald, Refractive Eyecare, September 2011
“Preoperative treatment with povidone-iodine is now more important than ever. I still think that topical fluoroquinolones are our best option for surgical prophylaxis and also for treating post-surgical infections. But now I rely almost exclusively on besifloxacin, because ARMOR has demonstrated that it is the most effective of the fluoroquinolones against resistant organisms, particularly MRSA.”

Reference: M. McDonald, Refractive Eyecare, September 2011
Besivance in Children

“Treatment with besifloxacin ophthalmic suspension 0.6% administered twice daily for 3 days was effective and safe in adults and children with bacterial conjunctivitis.”

Antibiotics

Solutions:  
- Tobramycin*
- Fluoroquinolone**
- Polytrim* or AzaSite (Peds)

Ointments:  
- Polysporin*

*available in generic form

**Ofloxacin and ciprofloxacin available generically
## Pediatric Use of Ocular Medication

<table>
<thead>
<tr>
<th>Medication</th>
<th>Approved for use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibiotics</strong></td>
<td></td>
</tr>
<tr>
<td>Polytrim</td>
<td>≥ 2 mo</td>
</tr>
<tr>
<td>10% Sulfacetamide</td>
<td>≥ 2 mos</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>≥ 2 mos</td>
</tr>
<tr>
<td>Tobrex</td>
<td>≥ 2 mos</td>
</tr>
<tr>
<td>Ciloxan solu</td>
<td>≥ 1 yr</td>
</tr>
<tr>
<td>Ciloxan oint</td>
<td>≥ 2 yrs</td>
</tr>
<tr>
<td>Ocuflox</td>
<td>≥ 1 yr</td>
</tr>
<tr>
<td>Zymar</td>
<td>≥ 1 yr</td>
</tr>
<tr>
<td>Vigamox</td>
<td>≥ 1 yr</td>
</tr>
<tr>
<td>Quixin</td>
<td>≥ 1 yr</td>
</tr>
<tr>
<td><strong>Anti-inflammatory</strong></td>
<td></td>
</tr>
<tr>
<td>Fluorometholone</td>
<td>≥ 2 yrs</td>
</tr>
<tr>
<td><strong>Combination</strong></td>
<td></td>
</tr>
<tr>
<td>Tobradex</td>
<td>≥ 2 yrs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medication</th>
<th>Approved for use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Allergy Medications</strong></td>
<td></td>
</tr>
<tr>
<td>Acular</td>
<td>≥ 3 yrs</td>
</tr>
<tr>
<td>Alamast</td>
<td>≥ 3 yrs</td>
</tr>
<tr>
<td>Alocril</td>
<td>≥ 3 yrs</td>
</tr>
<tr>
<td>Emadine</td>
<td>≥ 3 yrs</td>
</tr>
<tr>
<td>Optivar</td>
<td>≥ 3 yrs</td>
</tr>
<tr>
<td>Zaditor</td>
<td>≥ 3 yrs</td>
</tr>
<tr>
<td>Patanol</td>
<td>≥ 3 yrs</td>
</tr>
<tr>
<td>Opticrom</td>
<td>≥ 4 yrs</td>
</tr>
<tr>
<td>Alomide</td>
<td>≥ 2 yrs</td>
</tr>
<tr>
<td>Crolom</td>
<td>≥ 4 yrs</td>
</tr>
<tr>
<td><strong>Antiviral</strong></td>
<td></td>
</tr>
<tr>
<td>Viroptic</td>
<td>≥ 6 yrs</td>
</tr>
</tbody>
</table>

FDA Pregnancy Categories

• **A-** Controlled studies show no risk
• **B-** No evidence of risk in humans
  • Either animal studies show risk, human studies do not; or if no human studies, animal studies negative
• **C-** Risk cannot be ruled out.
  • Human studies lacking, and animal studies positive for fetal risk or lacking. Potential benefits may justify potential risks
• **D-** Positive evidence of risk post-marketing data show risk to fetus. If needed in life-threatening
  • Investigational or situation or serious disease, drug may be acceptable if safer drugs cannot be used
• **X-** Contraindicated in pregnancy
  • Fetal risk clearly outweighs any benefit to patient
Drugs and Pregnancy - Antibiotics

• “No known congenital defects have been reported with the use of erythromycin and polymyxin B.”

• “Systemic tetracycline can cause the discoloration of primary teeth in the offspring of mothers who receive the antibiotic after the third month of pregnancy.”

• “Regarding the use of fluoroquinolones, no teratogenic effects have been noted in animal studies.”

• “The AAP has classified erythromycin, gentamicin, tetracycline, and ciprofloxacin as maternal medications usually compatible with breast-feeding.”

Reference: AAO Focal Points, September 2007
Antibiotics - Systemic

- Penicillins
- Cephalosporins
- Tetracyclines
- Macrolides
- Trimethoprim/sulfamethoxazole
- Fluoroquinolones

For expert, comprehensive information consult

*Drug Facts and Comparisons*

[www.drugfacts.com](http://www.drugfacts.com)
Perspective on the PDR

“Habits are hard to break. Reliance on the PDR is one. Discarding the previous year’s volume is another. Know the PDR for what it is: a limited resource for FDA – approved drug inserts written, chosen, and paid for by the drug manufacturers.”

“JAMA calls ePocrates™ software ‘indispensable,’ ‘state of the art’ and ‘the one to have and keep.’”
Dicloxacillin (Tegopen)

- Penicillinase-resistant PCN (since most all staph species produce penicillinase, wise choice for most lid infections)
- Useful in soft tissue staph infections, such as internal hordeola, preseptal cellulitis, etc.
- Usual dosage 250 mg qid x 1 wk
- If true allergy to PCN, then use oral fluoroquinolone as alternative
- Best taken on an empty stomach
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: 500, 875, (generic) or 1000 mg tablet q12 hrs x 7-10 days
- Can be taken with meals
Methicillin Resistant Staphylococcus Aureus (MRSA)

- Infection caused by Staphylococcus aureus ("Staph")
- Staph commonly carried on skin or in nose
- Skin infections (abscesses, boils) most common (25-30% colonized)
- MRSA is almost always spread by direct physical contact
- MRSA common in hospitals and healthcare facilities
- To prevent MRSA:
  - Keep infections clean and dry
  - Frequent hand washing
  - Avoid sharing personal items
MRSA Update

- 94,360 serious MRSA (invasive) in 2005
- 85% of invasive MRSA associated with healthcare
- Incidence highest in older persons (>65), blacks, and males
- www.cdc.gov/ncidod/dhqp/ar_mrsa_prevention.html
- In 1974, MRSA 2% of total staph infections; in 1995, MRSA 22%; in 2004 was 63%

Reference: Journal of the American Medical Association, October 2007
“CONCLUSIONS: Although all MSSA and MRSA isolates were sensitive to vancomycin, fewer than half of MRSA isolates were sensitive to the fourth-generation fluoroquinolones. Visual acuity outcomes between MRSA and MSSA eyes were not significantly different.”

Reference: J Major et al. AJO. February 2010
MRSA Endophthalmitis

• “MRSA ocular infections, both in total numbers and percentage of overall S. aureus infections, are becoming increasingly more prevalent.”

• “The increasing frequency of MRSA endophthalmitis cases mirror the increasing incidence and changing epidemiologic factors of MRSA infections in general.”

• “Fewer than half of MRSA isolates were sensitive to the fourth generation fluoroquinolones.”

Reference: AJO, February, 2010
North Carolina Guideline for Empiric Oral Antimicrobial Treatment of Outpatients with Suspected CA-MRSA Skin and Soft Tissue Infections (SSTI)

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Adult Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trimethoprim-sulfamethoxazole (TMP-SMX) DS</td>
<td>1 to 2 DS tablets (160 mg TMP/800 mg SMX) PO bid; use lower dose with impaired renal function.</td>
</tr>
<tr>
<td>Minocycline or doxycycline</td>
<td>100 mg PO bid</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>300-450 mg PO qid</td>
</tr>
</tbody>
</table>

Revised 03/2007
<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
<th>Dose/Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purulent cellulitis</strong></td>
<td>Clindamycin</td>
<td>300–450 mg PO TID</td>
</tr>
<tr>
<td>(defined as cellulitis associated with purulent drainage or exudate in the absence of a drainable abscess)</td>
<td><strong>TMP-SMX</strong></td>
<td>1–2 DS tab PO BID</td>
</tr>
<tr>
<td></td>
<td><strong>Doxycycline</strong></td>
<td>100 mg PO BID</td>
</tr>
<tr>
<td></td>
<td><strong>Minocycline</strong></td>
<td>200 mg × 1, then 100 mg PO BID</td>
</tr>
<tr>
<td></td>
<td><strong>Linezolid</strong></td>
<td>600 mg PO BID</td>
</tr>
<tr>
<td><strong>Nonpurulent cellulitis</strong></td>
<td><strong>β-lactam</strong> (eg, cephalexin and dicloxacillin)</td>
<td>500 mg PO QID</td>
</tr>
<tr>
<td>(defined as cellulitis with no purulent drainage or exudate and no associated abscess)</td>
<td><strong>Clindamycin</strong></td>
<td>300–450 mg PO TID</td>
</tr>
<tr>
<td></td>
<td><strong>β-lactam (eg, amoxicillin) and/or TMP-SMX or a tetracycline</strong></td>
<td>Amoxicillin: 500 PO mg TID See above for TMP-SMX and tetracycline dosing</td>
</tr>
<tr>
<td></td>
<td><strong>Linezolid</strong></td>
<td>600 mg PO BID</td>
</tr>
</tbody>
</table>
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, highly-effective
Cephalexin (Keflex)

• Cephalexin - 1st generation cephalosporin
• Effective against most gram positive pathogens
• All cephalosporins share a 5-10% cross-sensitivity to PCN (true allergy to PCN, oral fluoroquinolone or SMX-TMP alternative)
• Usual dosage: 500 mg (generic) bid x 1 week
• Useful in soft tissue staph infections, such as internal hordeola, preseptal cellulitis, etc.
Penicillin Allergy and Cephalosporins

“This retrospective study of outpatients found a low absolute risk (1.1%), but a high relative risk (10-fold increase), of reacting to a cephalosporin after having reacted to a penicillin. However, the relative risk of reacting to a sulfonamide was similar, suggesting that a specific cross-reaction between penicillins and cephalosporins might not exist. The current approach of avoiding cephalosporins only in patients with severe allergic reactions to penicillins seems appropriate.”

Source: Journal Watch, June 1, 2006

Penicillin and Cephalosporin Cross-Sensitivity

• Both possess a beta-lactam ring

• “Cephalosporins are first-line treatment for many infections and are widely in ophthalmology.”

• “More than 90% of patients who report a history of penicillin allergy lack penicillin-specific IgE and can tolerate the antibiotic safely.”

• Penicillin allergy “should not prevent the use of second- and third-generation cephalosporins with distinct side-chains.” These are: cefuroxime, cefprozil, ceftazidime, and cefpodoxime.

Reference: AJO, January 2011
Options for True Penicillin Allergy Patients

• 2nd or 3rd generation cephalosporin
• Sulfamethoxazole/trimethoprim (Bactrim or Septra)
• A fluoroquinolone (Levofloxacin)
• Doxycycline
• Erythromycin
Tetracycline (Oral)

- Bacteriostatic - inhibits protein synthesis
- Broad spectrum - not staph. or pseudomonas
- Dosage: 250 mg qid (1-2h before meals)
- Warnings: may create skin photosensitivity
  - should be avoided during pregnancy, nursing mothers, in children under age 8, and renal function impairment
- Side effects: GI upset possible
- Systemic TCN useful for meibomian gland dysfunction, acne rosacea, chlamydia, and possibly RCE

Doxycycline

- Vibramycin original brand name
- Effective member of tetracycline family
- Advantages over tetracycline
  - Dosage 50 mg bid
  - Can be taken without regard to meals
- Contraindicated in pregnancy, nursing mothers, under age 8; may cause photosensitivity
- Indication in primary eye care
  - Meibomianitis (chronic inspissated glands)
  - Adult inclusion conjunctivitis (chlamydia)
  - Recurrent corneal erosion (Inhibits matrix metalloproteinases)
Food and Doxycycline

• “Food decreases absorption of tetracyclines, except doxycycline and minocycline; these two agents may be taken without regard to food.”

• “Doxycycline has a low affinity for calcium binding. Gastrointestinal absorption of minocycline and doxycycline is not significantly affected by food or dairy products.”

Reference: Drug Facts and Comparisons - 2012
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
Glucocorticosteroids and Doxycycline in RCE

• The concentration and activity of metalloproteinase-9 are increased in patients with recurrent corneal erosion and ocular rosacea.

• Glucocorticosteroids have potent immunomodulatory effects, including downregulation of production of inflammatory cytokines such as interleukin 1 and tumor necrosis factor alpha, that stimulate metalloproteinase production.

• The rapid clinical response to doxycycline and corticosteroids in our patient group could be the direct result of direct inhibition of inflammation or inflammation-induced metalloproteinase activity.
Oral Doxycycline and Pterygial Angiogenesis

- UV light is a known trigger for pterygenesis 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

The Tetracyclines in PTC

• All tetracyclines can cause increased CSF pressure
• Minocycline: most lipophilic, longest-acting of the class
• Elimination half-life is about 24 hours
• However, increased ICP persists about a month after stopping the tetracycline drug.
• Therefore, acetazolamide may be needed 4-6 weeks
• ICP can return to normal before resolution of papilledema.

Reference: Archives of Ophthalmology, August 2007
Macrolide Antibiotics

• Erythromycin
• Azithromycin
• Clarithromycin
Erythromycin (Oral)

• Bacteriostatic
  • inhibits protein synthesis
• Broad Spectrum
  • mainly against gram positives
  • Staph. species often become resistant
• Dosage: 250 mg q6h or 500 mg q 12h x 7-10d (taken 1-2h before meals)
• Side effects: GI upset most common
• Use during pregnancy: Category B
• Alternative drug for styes, hordeola, lid infection
• To treat chlamydia infections in pregnancy
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
CDC Changes Gonorrhea Treatment, Asks for More Vigilance on Resistance

"With the percentage of N. gonorrhoeae isolates with elevated minimum inhibitory concentrations (MICs) to cephalosporins on the rise, the CDC is changing gonorrhea treatment recommendations and asking that clinicians report treatment failures to local or state health departments within 24 hours."

“Consequently, the CDC is recommending ceftriaxone (250 mg intramuscularly) and azithromycin (1g orally) ‘as the most effective treatment for uncomplicated gonorrhea’.

Reference: Journal Watch 7/8/11
Fluoroquinolones (Oral)

- Broad spectrum; especially effective for G–organisms (not effective against chlamydia)
- Resistant bacteria continue to emerge
- Side effects: mild GI, mild HA, dizziness
- Use conservatively in pregnancy and children when benefits outweigh risks; photosensitivity warning
- Avoid Ofloxacin and Levofloxacin with theophylline
- Avoid fluoroquinolones with Coumadin
- Cipro also available once daily; available generically
- Levofloxacin (Levaquin) has replaced Cipro as “gold standard” in oral fluoroquinolone therapy
### Fluoroquinolones (Oral)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand</th>
<th>Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>Cipro XR</td>
<td>500 mg qd</td>
<td>10 days</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>Floxin</td>
<td>400 mg q12h</td>
<td>10 days</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>Levaquin</td>
<td>500 mg qd</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>Avelox</td>
<td>400 mg qd</td>
<td>7 days</td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>Tequin ?</td>
<td>400 mg qd</td>
<td>7-10 days</td>
</tr>
</tbody>
</table>
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.

Diplopia and Fluoroquinolones

“Conclusions: According to World Health Organization criteria, the relationship between fluoroquinolone therapy and diplopia is “possible.” This causality assessment is based on the time relationship of drug administration and ADR development, the multiple positive dechallenge and rechallenge reports, and the plausible mechanism by which diplopia could occur: possible tendinitis of the extraocular muscles.”

Oral Fluoroquinolones and the Risk of Retinal Detachment

Objective: To examine the association between use of oral fluoroquinolones and the risk of developing a retinal detachment.

Main Outcome Measure: The association between retinal detachment and current, recent, or past use of an oral fluoroquinolone.

Conclusion: Patients taking oral fluoroquinolones were at a higher risk of developing a retinal detachment compared with nonusers, although the absolute risk for this condition was small.

Steroid Medications

- Hydrocortisone
- Fluorometholone(s)
- Prednisolone
- Dexamethasone
- Rimexolone
- Loteprednol
- Difluprednate
- Systemic prednisone
## Ester vs Ketone Corticosteroids

<table>
<thead>
<tr>
<th>Ester</th>
<th>Ketone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loteprednol</td>
<td>Prednisolone</td>
</tr>
<tr>
<td></td>
<td>Fluorometholone</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone</td>
</tr>
<tr>
<td></td>
<td>Medrysone</td>
</tr>
<tr>
<td></td>
<td>Rimexolone</td>
</tr>
<tr>
<td></td>
<td>Difluoroprednisolone</td>
</tr>
</tbody>
</table>
# Relative Clinical Efficacy of Steroids

Here, based on our clinical experience and the comparative information we have available, we rate the relative efficacy of the topical steroids:

<table>
<thead>
<tr>
<th>Steroid</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone 1%</td>
<td>1</td>
</tr>
<tr>
<td>Prednisone 1/8%</td>
<td>2</td>
</tr>
<tr>
<td>Loteprednol 0.2%</td>
<td>3</td>
</tr>
<tr>
<td>Fluorometholone alcohol 0.1%</td>
<td>3</td>
</tr>
<tr>
<td>Dexamethasone 0.1%</td>
<td>4</td>
</tr>
<tr>
<td>Fluorometholone acetate 0.1%</td>
<td>4</td>
</tr>
<tr>
<td>Rimexolone 1%</td>
<td>4.5</td>
</tr>
<tr>
<td>Loteprednol 0.5%</td>
<td>4.5</td>
</tr>
<tr>
<td>Difluprednate 0.05%</td>
<td>5</td>
</tr>
<tr>
<td>Prednisolone 1%</td>
<td>5</td>
</tr>
</tbody>
</table>
Steroids - General Principles

• Correct diagnosis is essential before prescribing
• Dose must be given on an individual basis
• Avoid prolonged use if possible
• Incidence of side-effects increases with time
• Steroids function by suppressing inflammation
• Aggressive short-term use is much wiser than under treatment
• Should be tapered off if used more than 5-7 days
A Clinical Guide to Corticosteroid Indications

- Iritis/iridocyclitis
- Episcleritis
- Inflammatory keratitis
- Post-operative care
- Ocular trauma
- Corneal infiltrates
- Ocular H2O2 inflammation
- Adenoviral infection
- Periocular contact dermatitis
- Eczematoid blepharitis
A Clinical Guide to Corticosteroid Indications

• Post-infectious inflammation
• x 1 month in inflammatory blepharitis
• Staph toxin tissue erosions
  • angular blepharitis
  • marginal corneal ulcers
  • limbal infiltration
  • microcystic corneal edema
• . . . and a host of other non-specific ocular inflammatory conditions
When NOT to use Steroids Alone

- Herpes Simplex Epithelial Keratitis
- Bacterial or fungal infection
- Large corneal epithelial defects
- Unsure of diagnosis, if not one of the above 3
- If what is seen at the slit lamp defies precise diagnosis yet does not include one of these first three findings it is generally fine to treat with a steroid. In such cases, wisdom would dictate use of a combination drug, such as Zylet or TobraDex. This does not mean that therapy in such cases should always include a steroid; however, a steroid (preferably as a combination drug) could be rationally prescribed.
Exceptions to Steroid Guidelines: Using Antibiotic/Steroid Combinations

- Herpes Simplex Epithelial Keratitis - None (note that some cases of stromal HSK may require the judicious use of steroids)
- Bacterial Infections - If much secondary inflammation
- Epithelial Defects - If associated inflammation makes steroid suppression desirable, then use a combination drug
- Unsure - If a steroid is not contraindicated, then use of a combination drug is very acceptable.
Therapeutic Effectiveness of the Corticosteroids

- **Potency** -
  the power of a drug to produce a desired effect as compared on a mg. for mg. basis

- **Bioavailability** –
  the ability of a drug to get to a target tissue.

- These two factors combined determine the therapeutic effectiveness of a drug.
Prednisolone

- Classic ketone-based corticosteroid
- Used for treating severe ocular conditions
- Percent concentration and frequency of administration allow therapy to match the clinical condition
- Available in suspension and solution
- Generic formulations are suboptimally effective
Prednisolone Suspensions

- Usually acetate or alcohol derivatives
- Confers lipid solubility to the drug
- Lipophilicity allows good intraocular penetration
- Most suspensions possess some biphasic properties
- Suspensions naturally settle out of concentration
- MUST shake well prior to each instillation
- Generic formulations are suboptimally effective
Prednisolone Solutions

- Usually the sodium phosphate derivative
- Solutions are usually water (aqueous) soluble
- Still penetrates cornea, but not as efficiently
- Excellent for treating moderate to severe ocular surface inflammatory conditions
- No need to shake bottle
Dexamethasone

- Classic ketone-based corticosteroid
- Concentration does not exceed .1% because of potency
- Has the greatest ocular hypertensive effect of the corticosteroids
- Therapeutic effectiveness less than prednisolone
- Rarely used as monotherapy
- Available in suspension and solution
Fluorometholone Alcohol

- A progesterone-based steroid
- Useful in treating mild to moderate ocular conditions
- Has a reduced potential to increase IOP
- Available as FML 0.1% suspension and ointment (Allergan) and generic suspensions
- Also available as FML-Forte, a 0.25% solution (no increase in efficacy beyond the 0.1% concentration)
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.
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
Hydrocortisone

• The prototypic "reference" corticosteroid
• Limited therapeutic effectiveness
• Commonly used by dermatologists
• Used for treating mild inflammatory conditions, e.g. contact or allergic dermatoblepharitis
• Available in ointment form for external use only; not for ophthalmic use
• Only used in antibiotic-steroid combination ophthalmic products (Cortisporin and generics)
# Relative Potency of Selected Topical Corticosteroid Products

<table>
<thead>
<tr>
<th>Potency</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Potency</td>
<td>0.1% dexamethasone cream</td>
</tr>
<tr>
<td></td>
<td>1% hydrocortisone cream</td>
</tr>
<tr>
<td>Medium Potency</td>
<td>0.1% triamcinolone cream</td>
</tr>
</tbody>
</table>

- These are dermatologic products and are excellent for treating contact blepharodermatitis.
- Our favorite is the 0.1% triamcinolone cream. These come in a 15 gram tube and are cheap.

Reference: Drug Facts and Comparisons
Fluorometholone Acetate

- A progesterone-based steroid
- Therapeutic profile not quite that of prednisolone acetate
- Has less tendency to increase IOP compared to prednisolone and, of course, dexamethasone
- Useful in treating moderate conditions
- Available as an ophthalmic suspension
- Known commonly as Flarex
Rimexolone (Vexol) 1%

• Similar to Prednisolone Acetate 1%
• Safety profile similar to fluorometholone alcohol (FML)
• First steroid approved for post-op inflammation; also for anterior uveitis
• Available as an ophthalmic suspension by Alcon
Loteprednol Etabonate

• Only ester-based, site-specific steroid
• Works at target tissues, and then is subsequently metabolized into inert compounds
• LE has high intrinsic activity when applied locally
• 0.5% loteprednol similar in therapeutic equivalence to 1% prednisolone acetate, yet causes little, if any, increase in IOP
• Available as 0.5% (Lotemax) and 0.2% (Alrex) ophthalmic suspensions and 0.5% (Lotemax) ointment by B & L
Loteprednol Etabonate: Design

• Unique topical steroid
  - Retro-metabolic drug design\(^1\)\(^-\)\(^3\)
    • Prednisolone derivative
    • Modified to reduce or eliminate unwanted adverse events
    • Position 20 ester group replaces the ketone group

Prednisolone

\[
\begin{align*}
\text{Position 20 Chloromethyl Ester} & : \quad OCH_2\text{Cl} \\
\text{Position 20 Hydroxymethyl Ketone} & : \quad CH_2OH \\
\end{align*}
\]
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 eyedrop 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
Lotemax Gel 0.5%

- 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

Difluprednate 0.05% Ophthalmic Emulsion

- FDA approved September 2008
- Potent, broad-spectrum topical corticosteroid
- Deacetylated in vivo to difluoroprednisolone
- “Structurally similar to other corticosteroids”
- Preserved with sorbic acid 0.1%
- Marketed as Durezol ophthalmic emulsion by Alcon in an opaque 5 ml bottle
**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-inflammatory potency of difluprednate.”

*AJO, October, 2011*
## Steroid Summary

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Product(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspensions:</td>
<td>Lotemax</td>
</tr>
<tr>
<td></td>
<td>Durezol or Pred Forte</td>
</tr>
<tr>
<td>Ointment:</td>
<td>Lotemax or FML</td>
</tr>
<tr>
<td>Cream:</td>
<td>Triamcinolone .1%</td>
</tr>
<tr>
<td></td>
<td>(for skin use only)</td>
</tr>
</tbody>
</table>
Drugs and Pregnancy - Corticosteroids

“The fetal effect of topically administered corticosteroids to the pregnant woman is unknown.”

“Topical steroids have not been noted to cause teratogenic effects.”

“Ophthalmic corticosteroids such as prednisolone have a pregnancy Category C rating.”

“It is unknown whether the topical ocular administration of corticosteroids could result in detectable levels in breast milk.”

Reference: AAO Focal Points, September 2007
Dry Eye Syndrome

- Common presenting problem
- Symptoms: burning, gritty-sandy feeling, foreign body sensation, and/or tearing or watering
- Diagnosis: Good History, decreased lacrimal lake, decreased BUT, Lissamine Green staining, InflammaDry
- Treatment: Frequent use of lipid-based artificial tears; anti-inflammatory medications, punctal plugs, oral doxycycline, oral omega-3 fatty acids
- Patient education is vitally important to maximize care.
RPS InflammaDry Detector

- Detects presence of MMP-9 (cytokine – a reliable marker for ocular surface inflammation)
- MMP-9 not found in normal eye
- May predict response to cyclosporin, doxycycline, and steroids
- Procedure is simple, taking 10 minutes
- Cost approximately $15

Dry Eye Screening: Tear Osmolarity

• “Elevated tear film osmolarity is both a sensitive and specific indicator of dry eye. The problem with using osmolarity as a screening tool is that a single reading may not be sufficient. One of the hallmarks of early dry eye disease is variability of tear film osmolarity, and it is not unusual to find normal osmolarity in an eye with developing dry eye on any single measurement.”

• “So although highly useful in confirming dry eye diagnosis and monitoring therapy, osmolarity testing is not ideal for screening with a single exam.”

“Osmolarity measurements with the TearLab System disclosed no ability to distinguish between healthy individuals and patients with dry eye.”

Dry Eye Treatment

• Lipid-based artificial tears
• Anti-inflammatory agents
• Meibomian gland treatments
• Nutritional supplements
• Doxycycline
• Punctal Plugs
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
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
  - Others
“Corticosteroids are an effective anti-inflammatory therapy in dry eye disease”
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 (eg, 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

- Encompasses changes in tear composition rather than tear volume
- MMP-9 is increased in dry eye, and regulates epithelial shedding
- “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
“Ocular surface disease, including dry eye, blepharitis/meibomian gland dysfunction and ocular allergy, comprises the most common diagnosis encountered on a daily basis by the comprehensive ophthalmologist.”

“The pathophysiology of each of the three ocular surface diseases includes inflammation. While classical teaching is to begin treatment with palliative therapy such as artificial tears for ocular surface disease, I favor treating these patients more aggressively when I initiate therapy.”

“I have suggested we use the term ‘ocular surface inflammatory disease’ to remind us that the core issue in these diseases is inflammation and to lead us to consider more aggressive initial therapy.”

Inflammation and Dry Eye Disease (DED)

• “Inflammation has a prominent role in the development and amplification of the signs and symptoms of DED.”

• “Regardless of the origin, a self-perpetuating cycle of inflammation develops that is central to the pathogenesis of DED.”

• “Doxycycline ameliorates DED by inhibiting the activity of MMPs, primary MMP-9, promoting ocular surface integrity.”

Archives of Ophthalmology, January 2012
Melton & Thomas Dry Eye Management Protocol

One Month
- Lipid-Based Artificial Tear
  Four to six times a day as needed
- Loteprednol 0.5%
  Four times a day

Two Months
- Lipid-Based Artificial Tear
  Three to four times a day as needed
- Loteprednol 0.5%
  Two times a day
  (Consider punctual plugs if needed)

Indefinitely
- Lipid-Based Artificial Tear
  Two to four times a day as needed
- Discontinue Loteprednol 0.5%
  If symptoms breakthrough or continue, then either pulse dose Lotemax or Alrex four times a day for two weeks, or consider Lotemax or Alrex once daily as needed.

The risk of increased IOP with Loteprednol is uncommon at high dosage and rare at low dosage. Our experience has been that if an increase in IOP is going to occur, it will do so at the initial one month follow-up, and not later.

Omega-3 essential fatty acids (derived from fish and/or flaxseed oil) can be initiated at any stage, based on clinical judgment.
“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.”

“Alternative Supplementation”

- Orally administered omega-3 essential fatty acids
- Like cyclosporine and doxycycline, may take 3-4 months to obtain a significant clinical effect
Lovaza
(Omega-3-acid ethyl esters)

• Dramatically reduces very high triglycerides in patients with TG > 500 mg/dl
• Available by prescription
• Contains Eicosapentaenoic acid (EPA) 465 mg and Docosahexaenoic acid (DHA) 375 mg
• Highly purified in patented process
• Monitor patients if on anticoagulants also
• Pregnancy category C
• Available in 1 gm capsules by GlaxoSmithKline
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
Punctal Plugs in the Management of Dry Eyes

“Generally, reversible punctal occlusion with nonabsorbable punctum plugs is underutilized and should be considered in the multimodal approach to the patient with dry eyes, particularly after any inflammatory cause of keratoconjunctivitis sicca has been adequately managed.”

Doxycycline

• Vibramycin original brand name
• Effective member of tetracycline family
• Advantages over tetracycline
  • Dosage 50 mg bid
  • Can be taken without regard to meals
• Contraindicated in pregnancy, nursing mothers, under age 8; may cause photosensitivity
• Indication in primary eye care
  • Meibomianitis (chronic inspissated glands)
  • Adult inclusion conjunctivitis (chlamydia)
  • Recurrent corneal erosion (Inhibits matrix metalloproteinases)
Cyclosporin 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
Cyclosporin vs. Loteprednol

“Most anti-inflammatory molecules - eg, cyclosporin - target one or two of the channels that contribute to the inflammatory process but leave the other arms unaffected. The exception is steroids, which are highly effective because they act on multiple arms of the inflammatory system simultaneously.”

Foulks, GN. Refractive Eyecare. March, 2012
“Topical corticosteroids have been mainstays of the eye care field more so than the newer agent Restasis, and less potent corticosteroid formulations with few side effects are now available. Pulse therapy of corticosteroids has been shown to stave off dry eye symptoms for several months, and patients are more likely to notice the beneficial effects of corticosteroids earlier than with Restasis. For these reasons, and because of the lower cost, corticosteroids are an attractive option for treating dry eye.”

Lacrisert

• A sterile, translucent, rod-shaped, water-soluble, ophthalmic insert (1.27 mm x 3.5 mm) made of hydroxypropyl cellulose 5 mg

• For moderate to severe dry eye sufferers

• Insert into inferior cul-de-sac of eye beneath base of tarsus

• Supplied by Valeant Pharmaceuticals in packages containing 60 unit doses, two reusable applicators and a plastic storage container for applicators after use.
The International Workshop on Meibomian Gland Dysfunction

“Meibomian gland dysfunction (MGD) is a chronic diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretions. This may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease.”

Table 1. Treatment Algorithm for Meibomian Gland Dysfunction

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical Description</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><strong>No symptoms</strong> of ocular discomfort, itching, or photophobia</td>
<td>Inform patient about MGD, the potential impact of diet, and the effect of work and home environments on tear evaporation, and the possible drying effect of certain systemic medications. Consider eyelid hygiene including warming/expression as described below (±).</td>
</tr>
<tr>
<td></td>
<td><strong>Clinical signs</strong> of MGD based on gland expression</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Minimally altered secretions: grade ≥2–4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Expressibility: 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>No ocular surface staining</strong></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Minimal to mild <strong>symptoms</strong> of ocular discomfort, itching, or photophobia</td>
<td>Advise patient on improving ambient humidity; optimizing workstations and increasing dietary omega-3 fatty acid intake (±).</td>
</tr>
<tr>
<td></td>
<td><strong>Minimal to mild MGD clinical signs</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Scattered lid margin features</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mildly altered secretions: grade ≥4–8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Expressibility: 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>None to limited ocular surface staining:</strong> DEWS grade 0–7; Oxford grade 0–3</td>
<td>Institute eyelid hygiene with eyelid warming (a minimum of 4 minutes, once or twice daily) followed by moderate to firm massage and expression of MG secretions (+).</td>
</tr>
<tr>
<td>3</td>
<td>Moderate <strong>symptoms</strong> of ocular discomfort, itching, or photophobia with limitations of activities</td>
<td>All the above, plus (±).</td>
</tr>
<tr>
<td></td>
<td><strong>Moderate MGD clinical signs</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↑ lid margin features: plugging, vascularity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderately altered secretions: grade ≥8–13</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Expressibility: 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Mild to moderate conjunctival and peripheral corneal staining, often inferior:</strong> DEWS grade 8–23; Oxford grade 4–10</td>
<td>Artificial lubricants (for frequent use, nonpreserved preferred). Topical azithromycin. Topical emollient lubricant or liposomal spray. Consider oral tetracycline derivatives.</td>
</tr>
<tr>
<td>4</td>
<td>Marked <strong>symptoms</strong> of ocular discomfort, itching or photophobia with definite limitation of activities</td>
<td>All the above, plus (±).</td>
</tr>
<tr>
<td></td>
<td><strong>Severe MGD clinical signs</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↑ lid margin features: dropout, displacement</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Severely altered secretions: grade ≥13</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Expressibility: 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Increased conjunctival and corneal staining, including central staining:</strong> DEWS grade 24–33; Oxford grade 11–15</td>
<td>Oral tetracycline derivatives (+). Lubricant ointment at bedtime (±). Anti-inflammatory therapy for dry eye as indicated (±).</td>
</tr>
<tr>
<td></td>
<td>↑ signs of inflammation: ≥moderate conjunctival hyperemia, pterygia</td>
<td></td>
</tr>
</tbody>
</table>

Note: DEWS, Dry Eye WorkShop grade; Oxford, Oxford Eye Institute grade.
“The comprehensive ophthalmologist should be comfortable in using and prescribing the treatments for stages 1 through 3. In stage 4, topical steroids are added. The same clinician may be uncomfortable with this treatment recommendation because of the possible complications of topical steroids and so may want to obtain a second opinion from a cornea or external disease specialist before starting the patient on topical steroids”

Reference: J. Daniel Nelson, MD.
Supplement to Ophthalmology, October 2012
Meibomian Gland Expression

- Source: Mastrota Meibomian Paddle / Cynacon-Ocusoft
A NEW INSTRUMENT & METRIC
STANDARDIZED DX EXPRESSION FOR MG FUNCTIONALITY

THREE DIAGNOSTIC QUALIFIERS

1. Standard force to mimic force of blink ≈ 1.0 gram/mm² ( .3 PSI )
2. Application = ≤ 15 seconds
3. Secretion must be liquid (MGYLS)

A new metric allowing standardized expression for diagnosis & quantification of MG functionality

Concept: an active – functional meibomian gland should yield liquid secretion = MGYLS

Korb & Blackie – Cornea 2008
Heat applied to both inner lid surfaces
Pulsatile pressure applied to outer lids

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.

**THERMODYNAMIC TX TO EXPRESS AND EVACUATE MGs**
A new thermodynamic treatment to express & evacuate the MGs

**THE LIPIFLOW**
(TearScience Inc., Morrisville, NC)

FDA approved LipiFlow July 2011
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!
Systemic Prednisone

- Most common systemic corticosteroid
- Common initial dosage 40-60 mg
- Available generically in both tablets and in 4 mg DosePak and 5 and 10 mg “dose packs”
- Questions to ask before prescribing?
  - Diabetic?
  - Peptic Ulcer Disease?
  - Tuberculosis?
  - Pregnant?
Patients with Bell’s palsy benefit significantly from corticosteroid therapy, and the addition of antiviral agents may confer even greater benefit, according to a JAMA meta-analysis.

Researchers examined 18 randomized controlled trials that compared antiviral or corticosteroid treatment with a control in nearly 2800 patients with Bell’s palsy. Among the findings:

- Corticosteroids alone reduced the risk for unsatisfactory facial recovery (number needed to treat, 11).
- Antiviral agents alone did not improve outcomes.
- Corticosteroids plus antivirals were somewhat more effective than corticosteroids alone.

Neither treatment caused an increase in major adverse events.

An editorialist concludes that the analysis "helps resolve lingering doubt about the benefits of corticosteroids, but raises questions about the adjunctive role of antiviral medications."
Bell’s Palsy Update

• “Early Treatment with Prednisolone or Acyclovir in Bell’s Palsy.” New England Journal of Medicine, Oct 18, 2007

• 496 patients with idiopathic facial paralysis randomized to Prednisolone, ACV, both, placebo

• Results: After 9 months, recovered facial function 95% Prednisolone, 81% No Prednisolone, 85% for ACV, 90% no ACV, 93% Both

• Conclusion: “In patients with Bell’s palsy, early treatment with prednisolone significantly improves the chances of complete recovery at 3 and 9 months. There is no evidence of a benefit of acyclovir given alone or an additional benefit of acyclovir in combination with prednisolone.”
“Pulse methylprednisolone is globally well tolerated in diabetic patients, but requires strict blood glucose and clinical monitoring.”

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.

Reference: journalwatch.com, June, 2010
• Based on this and previous studies, intranasal steroids are superior to oral antihistamines for alleviating nasal symptoms and are equal for relieving ocular symptoms.
• The mechanism is unclear but could involve a naso-ocular reflex pathway and appears to be a class effect.
• Adding an oral antihistamine to an intranasal steroid does not consistently confer greater benefits.
• For patients with moderate-to-severe seasonal allergic rhinitis with ocular symptoms, intranasal steroids are appropriate as monotherapy.
• If ocular symptoms are not controlled, addition of an ocular antihistamine or mast cell stabilizer is warranted.
• With respect to cataracts and glaucoma, safety data for intranasal steroids have been consistently reassuring.

Reference: journalwatch.com, June, 2010
Use of Inhaled and Oral Corticosteroids and the Long-term Risk of Cataract

“Conclusions: High long-term risks of PSC and nuclear cataract development were found for users of combined inhaled and oral corticosteroids.”

<table>
<thead>
<tr>
<th>Anti-infective/Anti-inflammatory Combinations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hydrocortisone</strong></td>
</tr>
<tr>
<td>Cortisporin</td>
</tr>
<tr>
<td><strong>Prednisolone</strong></td>
</tr>
<tr>
<td>Blephamide</td>
</tr>
<tr>
<td><strong>Betamethasone</strong></td>
</tr>
<tr>
<td>Garasone</td>
</tr>
<tr>
<td>Pentasone</td>
</tr>
<tr>
<td><strong>Dexamethasone</strong></td>
</tr>
<tr>
<td>Maxitrol</td>
</tr>
<tr>
<td>TobraDex</td>
</tr>
<tr>
<td>Opticort</td>
</tr>
<tr>
<td><strong>Loteprednol</strong></td>
</tr>
<tr>
<td>Zylet (U.S. only)</td>
</tr>
</tbody>
</table>
Fundamental Pearl

• Foundational to proper clinical use of the combination anti-bacterial corticosteroid ophthalmic medicines is:

\[\textit{ALWAYS} \text{ consider them to be primarily corticosteroids that happen to have an anti-bacterial agent along with them.}\]
Neomycin, Polymyxin B, Bacitracin, with Hydrocortisone 1%

• Broad spectrum of anti-infective activity
• Mild anti-inflammatory effectivity
• Minimally useful because of possible neomycin reactions, the relatively poor anti-inflammatory activity of hydrocortisone, and the availability of superior products
• Available as Cortisporin suspension (Monarch) and generic
Sodium Sulfacetamide 10% with Prednisolone .25-.5%

• Broad spectrum of anti-infective activity (many resistant bacteria, especially staphylococcal sp.)
• Mild to moderate range of anti-inflammatory activity
• Workhorse drugs in the routine office treatment of the gamut of mild to moderate inflammatory presentations
• Marketed in suspension, solution, and ointment formulations by numerous companies
• Blephamide (Allergan) is the prototype drug in this category
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
• Inexpensive combination drug
• Marketed as Maxitrol and generically
Tobramycin and Dexamethasone

- Excellent coverage against most ocular pathogens with minimal concern of aminoglycoside toxicity
- Effective suppressor of inflammation
- Guard against prolonged use with dexamethasone
- Marketed as TobraDex Suspension and Ointment (tobramycin 0.3% and dexamethasone 0.1%) by Alcon, (Suspension available generically)
- Also available as TobraDex ST (tobramycin 0.3% and dexamethasone 0.05%) by Alcon
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 5 and 10 ml bottles
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.
“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.”

“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
Other Combination Steroid/Antibiotics

• **Garasone** — betamethasone 0.1% (steroid) with gentamicin 0.3% (antibiotic) suspension and ointment

• **Pentasone** — betamethasone 0.1% (steroid) with gentamicin 0.3% (antibiotic) suspension and ointment

• **Opticort** — dexamethasone 0.5mg (steroid) with framycetin 5mg and gramicidin 50mcg (antibiotics) solution
Combination Steroid/Antibiotics

**Suspensions:**

Zylet / TobraDex / Maxitrol generic

**Ointments:**

TobraDex / Maxitrol generic
Treatment Options - Ocular Allergy

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

- Many patients have allergic symptoms only because they have primary dry eyes.
- Normal tear function washes away most environmental allergens before they can become absorbed into deeper conjunctival tissues.
- Always rule out tear film dysfunction in cases of mild to moderate "allergy".
Vasoconstrictor - Antihistamine Combinations

- Naphcon-A:
  
  .025% Naphazoline + .3% Pheniramine

- Opcon-A:
  
  .025% Naphazoline + .3% Pheniramine

- Vasocon-A:
  
  .05% Naphazoline + .5% Antazoline

- Visine-A*:
  
  .025% Naphazoline + .3% Pheniramine

* Very short acting, therefore must be used more frequently than prescription antihistamines
Acute and Chronic Conjunctivitis
Due to Over-the-counter Ophthalmic Decongestants

“Conclusion: Nonprescription Decongestant eyedrops can produce acute and chronic forms of conjunctivitis by pharmacological, toxic, and allergic mechanisms. Once recognized, conjunctival inflammation often takes several weeks to resolve.”

Topical Antihistamine

- Highly effective histamine (H1) receptor blockers
- Excellent against itch associated with allergy
- Provides unexplained vasoconstriction
- Use qid for a few days, then 1-3 x d prn
- Marketed as Emedastine – (Emadine) 0.05% solution - Alcon
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>Formulations</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>Bepotastine</td>
<td>1.5%</td>
<td>(Bepreve) (5, 10 ml)</td>
</tr>
<tr>
<td>Epinastine</td>
<td>0.05%</td>
<td>(Elestat) 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>
</tbody>
</table>
Non-Steroidal Anti-Inflammatory Drugs

- (NSAIDs)
- Ketorolac tromethamine 0.4%, 0.45%, and 0.5% is a prostaglandin synthesis inhibitor indicated for reduction of ocular pain and burning/stinging following corneal refractive surgery
- Usually prescribed qid prn for itch
- Contraindications: Allergy to NSAIDs
- Marketed as Acular (0.5%), Acular LS (0.4%) solution (Allergan)
- Preservative-free, unit dose 0.45%, marketed as Acuvail by Allergan
Mast Cell Stabilizers

- Prevent the degranulation of mast cells
- Mast cells contain many mediators of inflammation
- Prophylactic, not actively therapeutic, in nature
- Possesses no anti-inflammatory properties
- Most effective in mild to moderate conditions; adjunctive Tx of choice in vernal conjunctivitis; role in GPC not fully understood; safe and effective
  - 2% Nedocromil Sodium (Alocril) - Allergan
  - 0.1% Lodoxamide Tromethamine (Alomide) - Alcon
  - 4% Cromolyn Sodium (Crolom) - B+L; (Opticrom)-Allergan
Nedocromil sodium 2%

• Mast-cell stabilizer indicated for treatment of itching associated with allergic conjunctivitis
• Multicellular activity - relief in both early and late phases of allergic response
• Opened shelf life 4 wks; Age 3 and up; BAK
• Dosing is bid
• Medical solution has a light yellow color
• Side effects: headaches most common (approx. 40 % - comparable to placebo at 36%)
• Marketed as Alocril by Allergan
Loteprednol Etabonate

• Only ester-based, site-specific steroid
• Works at target tissues, and then is quickly metabolized into inert compounds
• LE has high intrinsic activity when applied locally
• 0.5% loteprednol similar in therapeutic equivalence to 1% prednisolone acetate, yet causes little, if any, increase in IOP
• Available as 0.5% (Lotemax) and 0.2% (Alrex) ophthalmic suspension as well as a 0.5% ointment
Study of the Long-Term Safety of Loteprednol 0.2% for Allergy Treatment

• 159 patients used Alrex continuously at least once per day for one year

• 84 patients had been using such for two years, and 22 patients for three years

• No cataract development, no increase in IOP more than 4mmHg

• Conclusion: Alrex is both safe and effective for long-term use.

Reference: Eye and Contact Lens. January 2004
Anti-Allergy

**Acute**
Mild/Moderate – Antihistamine/mast cell stabilizer
Moderate/Severe – Loteprednol (.2%)

**Chronic**
Antihistamine / mast cell stabilizer
Systemic Antihistamines

**OTC**
- Chlorpheniramine (Chlor-Trimeton)
- Diphenhydramine (Benadryl)
- Loratadine (Claritin) - 10 mg qd
- Fexofenadine (Allegra) - 60 mg bid; 180 mg qd
- Cetirizine (Zyrtec) - 5 or 10 mg qd

**Rx**
- Desloratadine (Clarinex) – 5 mg qd
- Levocetirizine (Xyzal) – 5 mg qd
  - Metabolized by the liver
  - Excreted in bile and urine (1/2 dose if renal disease)
## Topical vs. Systemic Antihistamines

- Systemics have more side effects (sedation, dizziness, tinnitus, nervousness, insomnia)
- Systemics may worsen the condition by causing dry eye
- Topicals appear to be more efficacious
- Topicals direct delivery to the desired site
- Topicals provide a higher concentration
- Topicals not prone to interact with alcohol or CNS depressants
Veramyst (fluticasone furoate)

- Treatment for seasonal and year-round allergy symptoms in patients 2 yrs and older
- Helps reduce the nasal symptoms of allergic rhinitis
- May also help red, itchy, and watery eyes in adults and teenagers with seasonal allergic rhinitis.
- Side effects: nose bleed or nasal sores, nasal fungal infection, glaucoma or cataracts may occur
- For best results use once daily
- Available in 10gm nasal spray (120 metered sprays, 27.5mcg per spray) by GlaxoSmithKline

Reference: www.veramyst.com
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.

Reference: journalwatch.com, June, 2010
Summary Comments

- Based on this and previous studies, intranasal steroids are superior to oral antihistamines for alleviating nasal symptoms and are equal for relieving ocular symptoms.
- The mechanism is unclear but could involve a naso-ocular reflex pathway and appears to be a class effect.
- Adding an oral antihistamine to an intranasal steroid does not consistently confer greater benefits.
- For patients with moderate-to-severe seasonal allergic rhinitis with ocular symptoms, intranasal steroids are appropriate as monotherapy.
- If ocular symptoms are not controlled, addition of an ocular antihistamine or mast cell stabilizer is warranted.
- With respect to cataracts and glaucoma, safety data for intranasal steroids have been consistently reassuring.

Reference: journalwatch.com, June, 2010
Anti-Viral Medicines

Topical
- Trifluridine Viroptic
- Ganciclovir Zirgan

Oral
- Acyclovir Zovirax
- Valacyclovir Valtrex
- Famciclovir Famvir
Trifluorothymidine (Trifluridine)

- A halogenated pyrimidine analog of thymidine
- Inhibits both virally-infected and non-infected cells
- Possesses good activity against both HSV-I and HSV-II
- Approved down to age 6
- Penetrates into epithelium, stroma, and aqueous
- Once dispensed by pharmacy, refrigeration not required
- Heals most herpetic ulcers in 5 to 8 days
- Use q 2h for first 4 to 5 days, then taper PRN
- Marketed as: Viroptic 1% (7.5 ml) by Monarch Pharmaceuticals and generic
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
• Marketed as Zirgan gel by B&L Pharmaceuticals
• Comes in a 5 gram tube
• Pregnancy category C
# Topical Antiviral Options

<table>
<thead>
<tr>
<th><strong>Trifluridine</strong></th>
<th><strong>Ganciclovir</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Old drug</td>
<td>- New drug</td>
</tr>
<tr>
<td>- Indiscriminate expression</td>
<td>- Infected cell-specific</td>
</tr>
<tr>
<td>- Potentially toxic</td>
<td>- Minimally toxic</td>
</tr>
<tr>
<td>- More frequent dosing</td>
<td>- Less frequent dosing</td>
</tr>
<tr>
<td>- Refrigerate until opened</td>
<td>- No refrigeration needed</td>
</tr>
<tr>
<td>- Thimerisol preserved</td>
<td>- BAK preserved</td>
</tr>
<tr>
<td>- Solution (7.5 ml bottle)</td>
<td>- Gel (5 gram tube)</td>
</tr>
<tr>
<td>- Viroptic and generic</td>
<td>- Zirgan by B+L</td>
</tr>
</tbody>
</table>
Update on Antiviral Treatment of Adenoviral Ocular Infections

“Since the initial description of epidemic adenoviral ocular infections in Austria in 1889 until the present day, no effective drug to treat such patients has been found.”


WRONG!
**Povidone - Iodine 5% ophthalmic solution**

- Broad spectrum microbicide
- Indicated for “irrigation of the ocular surface”
- “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 60-90 seconds, 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
Betadine: How it all began

• The 5% povidone iodine for EKC story
• June, 2001, Primary Care Optometry News
• Corneal subspecialist, Robert Abel, Jr., MD
• Treated 60 EKC patients with 5% Betadine
• Patients responded within 24-36 hours
• Also used a corticosteroid after Betadine treatment
• Bottom line: “Read, . . . And Heed”
Povidone-Iodine in Perspective

• “Because of its spectrum of microbiocidal activity, povidone-iodine is used widely in ophthalmology to prepare the eyelids, eyelashes, and conjunctiva before intraocular surgery to decrease the risk of endophthalmitis.”

• Povidone serves as the carrier to deliver iodine and is used widely in many hairsprays, cosmetics, and pharmaceuticals.

• “No cases of anaphylaxis related to ophthalmic use of povidone-iodine have been reported.”

• “Seafood allergy does not equate to an iodine allergy and is not a contraindication to the use of topical povidone-iodine.”

Reference: AJO. January 2011
From: DMOD
To: Ron and Randall

You know it never fails... go to a meeting and then see the very thing the lecturer was discussing. Well I had a patient with the worst EKC I had ever seen. Started in one eye then the other and now comes in wearing 2 pairs of sunglasses and miserable. I gave her the bilateral, Thomas & Melton betadine treatment late Wednesday afternoon and the staff paid close attention. (you know, does he really know what he is doing watch) She returned this morning, less than 48 hours later with only trace injection, no infiltrates, smiling, no sunglasses and headed to school!

Thanks for making me look like a genius!

DMOD
“Topical azithromycin is likely as effective for the important causes of ophthalmia neonatorum as its fellow macrolide erythromycin.”

“A controlled clinical trial comparing erythromycin, 0.5%, povidone-iodine, 2.5%, and silver nitrate, 1%, for ophthalmia neonatorum prophylaxis demonstrated that povidone-iodine was more effective than the other agents for preventing infectious conjunctivitis, including chlamydial conjunctivitis.”

“We believe povidone-iodine would be a suitable and perhaps preferable alternative to azithromycin for ophthalmia neonatorum prophylaxis.”

Rapid Pathogen Screening via the RPS AdenoPlus

- Convenient in-office, 10 minute immunoassay
- Designed exclusively for adenoviral pathogens
- Clinical Laboratory Improvement Amendment (CLIA) waived
- Has sensitivity and specificity around 91-92%
- Adenoviral infection is commonly a clinical diagnosis
- Helpful for challenging cases, and for primary care physicians
- CPT-4: 87809 QW
- Contact: www.rps-tests.com

Source: Ophthalmology, October 2006
Ganciclovir 0.15% Gel: A new Treatment for EKC

• “36 patients beginning an acute EKC were treated QID with ganciclovir 0.15% gel. All eyes were culture positive on 1-3 days.”

• “Ocular discomfort was alleviated in one week. No keratitis developed in any patient with this type 8 infection.”

• “Ganciclovir 0.15% gel must be prescribed as soon as possible. It does not blur vision owing to its water miscible property.”

Reference: Verin et al. Ophthalmic Research, 1997;29(suppl 1)12-27 (France)
Ganciclovir Effects in EKC

• “Patients treated with topical ganciclovir 0.15% ointment showed resolution of EKC within 7.7 days (range 7-12 days) compared with 18.5 days (range 7-30 days) in the control group.”

• “22% of cases developed subepithelial opacities in the treatment group compared to 77% in the control group.”

• “Conclusions: Topical ganciclovir 0.15% ophthalmic ointment is safe and effective in the treatment of adenoviral keratoconjunctivitis”

Reference: Tabbara, KF. The Eye Foundation For Research in Ophthalmology. Riyadh, Saudi Arabia
Perspective on “off-label”

“The practice of ophthalmic off-label drug use is neither uncommon nor new.”

“The prevalence and clinical importance of prescribing drugs for unlabeled uses are substantial. . . thus the prescribing of drugs for unlabeled use is often necessary for optimal patient care.”

“Good medical practice and the best interests of the patient require that physicians use legally available drugs according to their best knowledge and judgement. If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence, and to maintain records of the products’ use and effects.”

Perspective on “off-label”

“Treatment with any drug or therapy is based on a consensus between a well-informed patient and physician. This is no different in the case of the use of off-label ophthalmic medicines. The more scientifically sound the information supporting its use, the more confidently can the physician and patient assess the possible value of the proposed unapproved treatment.”

“The Ophthalmic Mutual Insurance Company recognizes that “off-label” use of approved medications is a legal and necessary part of the practice of medicine.”

Off-Label Use of Drugs and Devices Correspondence

“A drug or device becomes ‘on-label’, or approved, when a sponsor conducts a prospective multicenter clinical trial to show its safety and efficacy for a particular indication. Often these regulatory trials are of limited value, for several reasons. First, often the approved indication is of little value, whereas off-label indications are the primary use.”

Source: AJO, January 2010
“Manufacturers often take the most direct route to an approval rather than demonstrating the best use of the product in a clinical trial. For example, topical ophthalmic antibiotics universally are approved only for the treatment of bacterial conjunctivitis, a self-limiting condition with little morbidity. However, their greatest value is in the treatment of bacterial keratitis and in prophylaxis after ophthalmic surgery. These applications are proven off-label uses. The use of these agents is entirely ethical.”

Source: AJO, January 2010
“In ophthalmology, off-label drugs and devices play an enormously important role in our ability to care for patients.”

“Ophthalmology has a strong, proud, and vibrant tradition of practicing off-label.”

Source: AJO, January 2010
**Acyclovir (ACV)**

- Analog of guanosine
- Specifically targets virally-infected cells
- Minimally toxic to uninfected cells
- Best to initiate therapy within 72 hours
- **Tx:** 800 mg by mouth 5 x D for 7 days for HZO; 400 mg 5 x D for 7 days for HSK
- Main side effect: occasional nausea
- Use with caution in kidney disease
- Available generically, and as oral suspension 200 mg/5 ml for children
Valacyclovir

• Prodrug of acyclovir - greater bioavailability and longer half-life
• Rapidly and completely converted to acyclovir after oral administration
• Can be taken without regard to meals
• Side effects: nausea / headache
• Best to initiate therapy within 72 hours
• Tx: 1,000 mg caplet tid x 7 days for HZO; 500 mg tid x 7 days for HSK
• Use with caution in kidney disease
• Valtrex by Glaxo Wellcome and generically
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.”

Famciclovir

- Prodrug of penciclovir, the active antiviral drug
- Intracellular half-life of 7-10 hours
- Active against HSV and VZV
- Best to initiate therapy within 72 hours
- Can be taken without regard to meals
- Side effects: minimal/rare - mostly nausea
- Dosage: 500mg q 8 hrs x 7 d for HZO; 250 mg q 8 hrs x 7 d for HSK
- Use with caution in kidney disease
- Marketed as Famvir by Novartis and generically
<table>
<thead>
<tr>
<th>Anti-Viral</th>
</tr>
</thead>
</table>
| • Anti-Herpes Simplex:            | Topical ganciclovir  
|                                  | Oral Anti-viral       |  
| • Anti-Herpes Zoster:             | Oral Anti-viral       |
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)
Table 2. Treatment and Prophylactic Dosages for Acyclovir in Children

<table>
<thead>
<tr>
<th>Age</th>
<th>Treatment Dose Thrice Daily</th>
<th>Prophylactic Dose Twice Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants (up to 18 mos)</td>
<td>100 mg (2.5 ml)</td>
<td>100 mg (2.5 ml)</td>
</tr>
<tr>
<td>Toddlers (18 mos–3 yrs)</td>
<td>200 mg (5 ml)</td>
<td>200 mg (5 ml)</td>
</tr>
<tr>
<td>Young children (3–5 yrs)</td>
<td>300 mg (7.5 ml)</td>
<td>300 mg (7.5 ml)</td>
</tr>
<tr>
<td>Older children (6 yrs and older)</td>
<td>400 mg (10 ml)</td>
<td>400 mg (10 ml)</td>
</tr>
</tbody>
</table>

Ophthalmology, October 2012
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 sequelae of HZO, if the tissues do not respond as expected, perhaps trying a seven day course of oral antiviral could be tried.

Pregnancy and Herpetic Treatments

“Topical trifluridine used in appropriate dosages in pregnancy is unlikely to cause fetal damage.”

“There have been no reported fetal abnormalities from the use of acyclovir or valacyclovir in pregnancy. Therefore the treatment of HSV keratitis during pregnancy can be administered without modification.”

“Oral acyclovir is a pregnancy Category B drug that may also be used to treat pregnant women with epithelial keratitis.

Reference: AAO Focal Points, September 2007
Childhood Chicken Pox

If the child is at least age 2 and/or weighs greater than 40 lbs, the FDA/CDC recommended dosage is acyclovir 800 mg 4 times a day for 1 week, if medical intervention is indicated.
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
Non-Steroidal Anti-Inflammatory Drugs

- Inhibition of prostaglandin synthesis is the mechanism of action.
- They specifically inhibit the action of cyclo-oxygenase, an enzyme vital to prostaglandin synthesis.
- Prostaglandins are powerful mediators of inflammation.
  - Acular LS (Ketorolac tromethamine 0.4%)-Allergan
  - Acuvail (Ketorolac tromethamine 0.45%)-Allergan
  - Ocufen (Flurbiprofen 0.03%) by Allergan
  - Profenal (Suprofen 1%) by Alcon
  - Voltaren (Diclofenac sodium 0.1%) by Novartis
  - Bromday (Bromfenac 0.09%) by ISTA
  - Nevanac (Nepafenac 0.1%) by Alcon
Prostaglandin Synthesis Inhibitors

- Prevention of intraoperative miosis
- Prevention / treatment of cystoid macular edema
- Excellent for topical analgesia and corneal photophobia
- Not effective for ocular inflammation
The Arachidonic Acid Pathway

Trauma → Membrane Phospholipids → Phospholipase $A_2$ → Arachidonic Acid

Arachidonic Acid → Cyclo-oxygenase → Thromboxane $A_2$ → Endoperoxides

Arachidonic Acid → Lipoxygenase → Prostaglandins ($PGE_2$, $PFG_{2\alpha}$, $PGD_2$) → Prostacyclin ($PGI_2$) → Hydroperoxides → Leukotrienes and related compounds

Inhibited by nonsteroidal anti-inflammatory drugs (e.g. Voltaren, et al)

Inhibited by corticosteroids (e.g. Pred Forte, et al)
Diclofenac sodium 0.1%

- Diclofenac sodium 0.1% is a prostaglandin inhibitor used for post-op inflammation/CME
- Useful in decreasing corneal sensitivity associated with pain and photophobia
- Unlabeled indications: corneal abrasions, bullous keratopathy, non-specific corneal surface pain
- Voltaren solution by Novartis and generic
Ketorolac Tromethamine 0.4% and 0.5%

- Indication: reduction of ocular pain and burning following corneal refractive surgery
- Also used for post-surgical inflammation, pain, photophobia and ocular allergies
- Acular 0.5% and Acular LS 0.4% solution (Allergan)
- Also available in a 0.45% preservative-free unit dose to be used bid for perioperative reduction of pain and inflammation in cataract surgery
- Marketed as Acuvail by Allergan
Ketorolac Tromethamine 0.45% solution (Acuvail)

• Preservative-free formulation of ketorolac (NSAID)
• Indicated for treatment of pain and inflammation after cataract surgery
• Formulated at pH 6.8 and contains carboxymethycellulose – enables drug to adhere to ocular surface and enhance patient comfort
• Approved by FDA for bid dosing beginning the day before cataract surgery and through the first 2 weeks of the post-operative period.
• Adverse events: 1-6% increased IOP, conjunctival hyperemia, corneal edema, ocular pain, headache, tearing, and burred vision.
NSAIDs in Ophthalmology

- NSAIDs are increasingly employed to reduce miosis, pain and photophobia associated with refractive surgery, symptomatic itching, manage scleritis, and prevent and treat CME associated with cataract surgery
- This is a thorough and excellent review on this topic

Bromfenac ophthalmic solution 0.09%

• Only once daily topical NSAID indicated for treatment of post-op cataract inflammation

• Significant reduction of ocular inflammation with once daily dosing

• Lower preservative concentration (BAK) than currently available NSAIDs

• Bromday solution by ISTA 1.7 ml
NEVANAC (nepafenac 0.1%)

- NSAID pro-drug
- Effective in controlling pain and post-operative inflammation associated with cataract surgery
- Alcon suspension dosing regimen of tid
Anti-Inflammatory/Ocular Surface Pain

Voltaren
Acular LS
Bromday
Nevanac
COX-2 Inhibitor

- A nonsteroidal anti-inflammatory drug that works by inhibiting COX-2, which mediates pain and inflammation
- Does not inhibit COX-1, which regulates cell function of GI tract and platelets
- Relief of inflammation and pain of osteoarthritis and rheumatoid arthritis
  - Celebrex (celecoxib) - 100 or 200 mg bid
The cyclo-oxygenase subtype 2 (COX-2) inhibitors Celebrex and Vioxx tend to inhibit the production of the “bad” prostaglandins, while largely sparing the “helper” or physiologic effects of prostaglandins that are mediated by the COX-1 enzyme.
Selective Cyclooxygenase-2 Inhibitors

• “Both the therapeutic benefit and potential toxicity of these drugs are, in large measure, because of their shared ability to inhibit the synthesis of prostaglandins (PG) by the cyclooxygenase (COX) enzyme.”

• There are at least two distinct isoforms of cyclooxygenase: COX-1 and COX-2. COX-1 is constitutively expressed in many tissues, where it regulates physiological functions. COX-2, an inducible form, is not normally expressed by most tissues, but it is upregulated at sites of inflammation.”

Selective Cyclooxygenase-2 Inhibitors

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most widely prescribed drug class in this country. Their use is indicated for a variety of painful musculoskeletal conditions, including osteoarthritis (OA) and rheumatoid arthritis (RA). As a class, NSAIDs possess antipyretic, anti-inflammatory, and antithrombotic qualities; however, currently available NSAIDs increase the risk of peptic ulcer disease and renal insufficiency. Both the therapeutic benefit and potential toxicity of these drugs are, in large measure, because of their shared ability to inhibit the synthesis of prostaglandins (PG) by the cyclooxygenase (COX) enzyme.

There are at least two distinct isoforms of prostaglandin H synthase, or cyclooxygenase: COX-1 and COX-2. COX-1 is constitutively expressed in many tissues, where it regulates physiological functions. COX-2, an inducible form, is not normally expressed by most tissues, but is upregulated at sites of inflammation by some neoplasms and under certain physiologic circumstances. Much basic and clinical research effort has been directed at formulating selective inhibitors of the COX-2 isoform, which could have anti-inflammatory properties without the adverse gastrointestinal and renal side effects associated with current NSAIDs. This article addresses recent advances in the understanding of the role of the cyclooxygenases and the potential therapeutic value of selective inhibitors of COX-2.
Oral Analgesics

• OTC’s
• Non-narcotic Rx
• Narcotic Rx
Oral Analgesics

- OTC’s
  - Acetylsalicylic acid (ASA - aspirin)
  - Acetyl-para-aminophenol (APAP-Tylenol)
  - Ibuprofen (Advil, Nuprin)
  - Naproxen (Aleve)
Oral Analgesics

- Non-narcotic Rx
  - Ibuprofen (Motrin)
  - Indomethacin (Indocin)
  - Naproxen (Anaprox, Naprosyn)
  - Tramadol HCl (Ultram, Ultram ER)
Controlled Substances

DEA Schedules: Five schedules based on potential for abuse and physical/psychological dependence

**Schedule I:** High abuse potential (heroin, marijuana, LSD)

**Schedule II:** High abuse potential with severe dependence liability (narcotics, amphetamines)

**Schedule III:** Moderate dependence liability (certain narcotics, nonbarbiturate sedatives, etc)

**Schedule IV:** Less abuse potential than S3; limited dependence lability (nonnarcotic analgesics, antianxiety agents, etc)

**Schedule V:** Limited abuse potential (small amounts of narcotics in antitussives or antidiarrheals)
Opioid Analgesics

- Pharmacology: Centrally acting opioid receptor blockers
- SAFE and effective for acute, short-term pain
- Four Commonly used narcotics Schedule
  - Codeine (mild to moderate pain) III
  - Hydrocodone (moderate to severe pain) III
  - Oxycodone (severe pain) II
- Clinically used in combination with acetaminophen
- Generally Rx’ed as 1 tab po q4-6hrs PRN pain (disp #8)
- Onset 20 min., peak 1 hr, duration 4-6 hrs
Controlled Substances

- Prescriptions must include:
  - Name, date and address of patient
  - Name, address and DEA # of physician
  - Oral Rx’s promptly committed to writing
  - Can’t be dispensed or refilled more than 6 months after date issued or refilled more than 5 times
  - Written Rx signed by physician required for Schedule II (in emergency, signed Rx within 72 hrs)
  - Schedule II Rx’s cannot be refilled

* In many cases state laws are more restrictive than Federal laws
Schedule III Opioid Analgesics

- **Codeine**
  - Tylenol #3 (APAP 300 mg + Codeine 30 mg)

- **Hydrocodone**
  - Lortab 2.5, 5, 7.5, 10 (APAP 500 mg + Hydrocodone 2.5, 5, 7.5, 10 mg)
  - Vicodin (APAP 500 mg + Hydrocodone 5 mg)
  - Vicodin ES (APAP 500 mg + Hydrocodone 7.5 mg)
  - Vicodin HP (APAP 660 mg + Hydrocodone 10 mg)

- Hydrocodone is a better analgesic than codeine
Hydrocodone

- Used for moderate degrees of pain (schedule III)
- Commonly combined with acetaminophen
- Commonly Rx’ed as: 500 mg acetaminophen with either 2.5, 5.0, 7.5 or 10 mg hydrocodone as Lortab 5/500 (for example), or 300 mg acetaminophen with 5 mg hydrocodone (Vicodin), 7.5/300 (Vicodin ES) or 10/300 (Vicodin HP)
- Dosage: 1 or 2 tabs po q4-6hrs PRN pain
Schedule II Opioid Analgesics

• Oxycodone
  • Percocet (APAP 325 mg + Oxycodone 5 mg)
  • Percodan (ASA 325 mg + Oxycodone 4.5 mg)
  • Tylox (APAP 500 mg + Oxycodone 5 mg)

* Addiction potential is not a concern when used for less than one week.
Oxycodone

- Used for severe pain (schedule II)
- Commonly combined with acetaminophen
- Commonly Rx’ed as: 325 mg acetaminophen with 5 mg oxycodone (Percocet), or 500 mg acetaminophen with 5 mg oxycodone (Tylox)
- Dosage: 1 tab po q 6 hrs PRN pain
- Write the number to be dispensed, usually 4 to 8
Perspective on Addiction

“Clinically significant dependence develops only after several weeks of chronic treatment with relatively large doses of morphine-like opioids.”

The Medical Letter
August 21, 2000
Anti-Edema

- Any 5% NaCl Solution and/or Ointment
Ocular Prosthesis Cleaning / Lubricant

- Ophthalmic solution containing:
  - Tyloxapol 0.25% (a detergent)
  - Benzalkonium Chloride 0.02%
- Lubricates, cleans, and wets the prosthesis
- Liquefies and softens thick and solid matter
- Dosage generally qid
- Available OTC in a 15 ml bottle as Enuclene by Alcon
There is an abundance of ophthalmic medicines. All of these medicines have various degrees of clinical usefulness. This list is our attempt to identify the "cream of the crop" so as to make your task of assimilating them easier. This list is certainly not exclusive. Everyone has their favorites; these are ours.

**Antibiotic Solutions:**  
- Tobramycin  
- Fluoroquinolone  
- Trimethoprim/Polymyxin B

**Antibiotic Ointments:**  
- Polysporin

**Steroid Suspensions:**  
- Pred Forte/Durezol emulsion  
- Lotemax

**Steroid Ointments:**  
- Lotemax, fluorometholone, .1% triamcinolone

**Combination Suspensions:**  
- Zylet, TobraDex, or generic Maxitrol

**Combination Ointments:**  
- TobraDex

**Anti-inflammatory/Pain:**  
- Topical NSAID

**Anti-allergy:**  
- Antihistamine/Mast Cell Stabilizer, loteprednol
### The Melton/Thomas “Perfect Formulary”

<table>
<thead>
<tr>
<th>Category</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-glaucoma</td>
<td>Prostaglandin</td>
</tr>
<tr>
<td></td>
<td>Beta-Blocker</td>
</tr>
<tr>
<td></td>
<td>Brimonidine</td>
</tr>
<tr>
<td></td>
<td>CAI</td>
</tr>
<tr>
<td>Anti-Herpes Simplex</td>
<td>Ganciclovir</td>
</tr>
<tr>
<td>Anti-Herpes Zoster</td>
<td>Oral Antiviral</td>
</tr>
<tr>
<td>Anti-Edema</td>
<td>5% NaCl Solution and/or Ointment</td>
</tr>
<tr>
<td>Artificial Tears</td>
<td>Lipid-based</td>
</tr>
<tr>
<td>Artificial Tear Gel</td>
<td>GenTeal Gel</td>
</tr>
<tr>
<td>Artificial Tear Ointment</td>
<td>Preservative-free free brand</td>
</tr>
</tbody>
</table>
Oral Medicines: There is a multitude of oral medications that have various degrees of clinical usefulness in treating eye disease. This is our “work-horse” list of systemic drugs to make your task of assimilating them easier. This list is certainly not exclusive. Everyone has their favorites; these are ours.

Antibiotic: Cephalexin
    Augmentin
    Doxycycline

Anti-Inflammatory: Prednisone

Anti-Viral: Acyclovir – generic 5 x D
    Valacyclovir (generic) TID

Acute Angle Closure: Acetazolamide (Diamox)

Anti-Pain: Hydrocodone/acetaminophen
Dapiprazole Hydrochloride 0.5%  

- Brand name: NU-REV  
- Comparable to previously available Rev-Eyes  
- Custom compounded and available through  
  - *Vision Source & Focus Labs*  
    - Fax: 501-753-6021  
    - Phone: 866-752-6006  
    - [http://vs-focus.com](http://vs-focus.com)  
  - *Leiter’s Pharmacy*  
    - Phone: 800-292-6773  
    - [www.leiterrx.com](http://www.leiterrx.com)  
- 5 ml bottle approximately $40