Course Goal
- To provide current and accurate information about key topical drugs that are used to treat eye diseases.
- Case examples
- Topical discussion

Choosing the Proper Drug Therapy
- Efficacy of Antibiosis
  - MIC = minimum inhibitory concentration
    - Lowest concentration that inhibits visible growth (growth-stopping)
    - Measures bacteriostatic activity of antimicrobials.
  - MBC = minimum bacteriocidal concentration
    - Lowest concentration that kills the microbe

Choosing the Proper Drug Therapy
- Patient considerations
  - Immune system viability
  - Kidney or liver disease
  - Pregnant or nursing, age
  - Allergy history
  - Safety profile of the drug
  - Cost considerations

Practice-building Tip
- When Rx-ing for Peds
- Place a courtesy call and send follow-up letter to pediatrician
- Especially with po meds
Topical Meds

- Absorbed directly into bloodstream, so not broken down by GI or liver.

Local (Ocular) Side Effects of Topical Medications

- Posterior Subcapsular Cataract
- Glaucoma

Systemic Side Effects of Topical Medications

- The eye is not an isolated organ.
- All topical agents should be considered as potentially systemically potent.
- To avoid systemic SEs:
  - Medical Hx and current meds, vit, supp, herbs
  - Rx. lowest concentration and dose that works
  - Have patient close eyes, digital occlusion

Special populations, special Rx.

25 year old female

10 weeks pregnant
Treatment?

- **Acyclovir (Zovirax®)**
- **Acute infection - 400 mg PO 5x/day X 7 d**
  - HSV Keratitis
  - Dendritic ulcer
  - HSV Blepharodermatitis
  - Lid involvement

**Pregnancy Category C**

**Pregnancy Category B**

**Questions and Comments?**

**Instillation of Medications**

Proper technique can significantly increase efficacy!

**Examples of RX writing**

**Oral Rx**
- Augmentin 500 mg tablets
- Disp: 14 tablets
- Sig: 1 tablet BID PO X 1 week

**Sol Rx**
- Timoptic XE 0.5% Ophthalmic Solution
- Disp: 10 ml bottle
- Sig: 1 drop QD OU in the AM

Remember: Refills ∅ and specific instructions – “shake well”
Our Top Topicals 9this week)
- Prednisolone Acetate 1%
- Loteprednol .5%
- Bromfenac .09%
- Tobramycin .3% + Dexamethasone .1/.05%
- Cyclosporine .05%
- Tobramycin .3%
- Alcaftadine 0.25%
- Travoprost-Z .004%
- Levobunolol HCl .25% or .5%
- Moxifloxacin .5%
- Ganciclovir 0.15%

Access and Assistance
- Rebate programs
- GoodRx.com
- Lower-priced options
  - Polytrim
  - Maxitrol
  - Acyclovir
  - Pred sodium phosphate 1% sol

Case

Describe That Image!

Muco-purulence (White Pus)

“Beefy-red Injection”
What is your (tentative) assessment?

Differential Diagnosis
a. Allergic conjunctivitis
b. Bacterial conjunctivitis
c. Acanthamoeba conjunctivitis
d. Herpetic conjunctivitis (HSV, HZV)

Management?

Describe That Image!
Objective Findings

- **VA**: c SRx OD 20/25 OS 20/80 PH NI
- **Pupils**: (-)APD, PERRLA
- **EOMS**: Smooth / Full
- **CF**: Full OD/OS
- **Lens, Vitreous**: Clear OD/OS
- **IOP**: 13 mm Hg OD, 12 mmHg OS

Objective Findings

- 3+ cell in AC OS
- Hypopyon
- Cornea epi defect w/dense, white infiltrate
  - Para-central location
  - Indistinct borders
  - Surrounding edema
- Mucopurulent discharge
- Posterior segment healthy OD/OS

Differential Diagnosis

a. Interstitial Keratitis
b. Bacterial Keratitis
c. Acanthamoeba Keratitis
d. Fungal Keratitis
e. Herpetic Keratitis (HSV, HZV)

What is your plan?

- Cornea consult same day (Why?)
- Corneal scrapings performed
- Moxeza 1 gt q30min, Tobrex 1 gt q30min, Scopolamine .25% 1 gt tid
- Daily follow-up
- Scrapings grew Pseudomonas
Bacterial Infection Management

When to Culture
- Infiltrate > 2mm w/epi defect
- Central or paracentral
- Significant tissue loss
- Hypopyon
- Suspect unusual organisms
- Poor response to initial therapy
- Post-op

Questions and Comments?

Topical Antibacterial Classes
- First-line Agents for Bacterial Infections
  - Fluoroquinolones eradicate a wide variety of ocular pathogens
  - Aminoglycosides provide broad spectrum coverage, slightly more effective against gram-negative bacteria
  - Polymyxin B combinations provide broad spectrum coverage
  - Macrolides provide broad spectrum coverage
    - Bacteriostatic

Fluoroquinolones
- Ciloxan (ciprofloxacin 0.3%, Alcon)
- Iquix (levofloxacin 1.5%, Vistakon)
- Ocufllox (ofloxacin 0.3%, Allergan)
- Quixin (levofloxacin 0.5%, Vistakon)
- Moxeza (moxifloxacin 0.5%, Alcon)
- Zymaxid (gatifloxacin 0.5%, Allergan)
- Besivance (besifloxacin 0.6%, B&L)

Battling Infection
- Fluoroquinolones
  - Extremely potent bacteriocidal drugs with broad spectrum activity
Third Generation FQ
- Levofloxacin 1.5%
- On-label Tx of BK

Fourth Generation FQs
- Interfere with 2 enzymes needed for bacterial DNA synthesis
  - DNA gyrase
  - Topoisomerase IV
- Thus, two separate mutations needed for resistance.

Fluoroquinolones
- Besifloxacin .6% susp
- FDA indication for bact. conj., including Pseudomonas
- Durasite vehicle
  - Lengthens ocular surface contact time
  - No systemic counterpart; decreases resistance

Topical Anti-bacterials
- Moxeza (moxifloxacin .5%) Alcon
  - Xanthum gum vehicle
  - Approved for 4 months of age and up
  - Approved for bact. conj.
  - Dosed bid for 7 days
  - Well-suited for keratitis

Topical Anti-bacterials
- Zymaxid (gatifloxacin .5%)
  - Allergan increased conc. of Zymar (.3%)
  - Approved for > 1 year old
  - Approved for bact. conj.
  - Well-suited for keratitis

Steroids and Bacterial Keratitis
- What does the evidence show?
- Steroids for Corneal Ulcers Trial (SCUT)
- No significant benefit overall
- May improve outcome in severe BK (Pseudomonas)
- Add steroid after 24-48 hrs of FQ
- Not for Nocardia infection.
- Avoid steroid if:
  - Severe thinning
  - Large epi defect
  - Diabetes or immuno-suppression
  - Suspect Acanthamoeba, Fungi
“Go-to” Topical for MRSA

- Polymixin B/Trimethoprim
- Eradication of MRSA
- Besifloxacin, Tobramycin, Polysporin ung are other options for MRSA

Systemic Tx. For MRSA

- Bactrim (trimethoprim/sulfamethoxazole)
  - 1-2 tabs
  - q12h x 1 wk
  - Kills ocular, systemic MRSA
    - Not one of the FL Fourteen

WHAT’S NEW?

- Bacitracin is back!
- Fera Pharmaceuticals
- Polypeptide agent used for blepharitis (Staph)
- Indicated for superficial infections involving conjunctiva and/or cornea.
- Good for kids.

Other Antibiotic Ointments

- Ciprofloxacin 0.3%
- Polymyxin B/Bacitracin

CASE: 61 Y/O WM

- CC: red, burning, sandy feeling, crusty OU
- Oc Hx: LEE 2 yrs, unremarkable
- Med Hx: Rosacea x many years
- BVA: 20/20-1, 20/20-1
- FROM, FTFC OD OS, NO APD
- SLE: see photo
- IOP: 12/12 @ 9:40am
- DFE: unremarkable OU

61 Y/O WM
What is your plan?

Azithromycin 1% sol
- AzaSite ® (Akorn)
- Macrolide AB
  - Broad-spectrum
  - Anti-inflammatory
- Approved for children >1 y/o
- Approved for bact conj only.

Azithromycin Ophthalmic Sol.
- Dosing
  - 1 drop bid for first two days
  - then 1 drop once daily for next five days.

Is topical Tx. enough for Rosacea-associated 3-4+ MGD and ant bleph?

Common Case
Questions and Comments?

What is your ocular treatment plan?

Corticosteroids!

The main feature of steroids is the fused ring system.

Moderate to Severe Inflammation
- Prednisolone acetate 1% ophthalmic suspension
- Pred Forte
- High anti-inflammatory efficacy
- Acetate suspension facilitates corneal penetration to provide increased concentrations in anterior chamber
- Main indications include anterior uveitis and severe episcleritis
For Severe Inflammation

- Difluprednate .05% emulsion (Alcon)
  - No shaking
  - Less frequent dosing
  - BAK-free
  - Derived from prednisolone
  - FDA indication for post-Sx. inflamm, pain
  - IOP rise *

Difluprednate Molecule

- Addition of the acetate ester enhances tissue penetration
- Butyrate ester enhances anti-inflammatory activity
- Fluorination increases specificity for the glucocorticoid receptor

Corticosteroids

- Ocular side effects
  - IOP rise
    - Prolonged use (>3-5 weeks)
  - Cataract formation
  - Decreased healing
  - Promotion of viral and fungal infections
    - Herpes Simplex Virus

Mild-Moderate Inflammation

- Loteprednol etabonate 0.5% (Lotemax)
  - Ophthalmic gel
  - Post-operative
  - Small tendency to increase IOP
  - Used “off-label” in DES

What’s New? Non-preserved loteprednol 0.5% ophthalmic ointment (Lotemax)

When and Why Taper?

- When a 2-grade decrease in ant chamber cells is achieved
- Why?
  - Sudden withdrawal of a steroid can result in a rebound inflammatory response.
  - This would then require a larger dose of steroid for an even longer period of time because of longer lasting inflammatory activity.
What if there is IOP rise?
Handle it.

Topical Steroid Taper
- An example: start w/1 gt q1h x 2 d, then
  - 1 drop every two hours for three days
  - 1 drop every three hours for three days
  - 1 drop 4 x a day for 4 days
  - 3 x a day for 3 days
  - twice a day for 2 days
  - finally, one drop once a day for 2 days, then
  - discontinue the steroid or have the patient apply it every other day for several more days.

Inflammation/Infection
- Phlyctenulosis
  - Small, white limbal nodules w/surrounding redness
  - Response to Staph.
  - Associated with TB
  - Good response to topical AB/steroid such as Tobradex or Zylet
  - Dose QID x 5-7 days

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Steroid-Antibiotic Combinations
- Dexamethasone alcohol .1% with tobramycin .3%
  - Moderate/severe inflammation w/risk of infection
  - Now available as a generic

What’s New?
- TobraDex ST (tobramycin/dexamethasone ophthalmic suspension) 0.3/0.05%.
  - Indicated for inflammatory ocular conditions for which a corticosteroid is indicated and where bacterial infection or risk for infection exists.
  - Formulated with a new vehicle (Xanthum gum) to enhance bioavailability to targeted tissues.
  - Useful for blepharitis/MDG

Steroid/AB Combo
Steroid-Antibiotic Combinations

- These medications are steroids and therefore may cause the same side effects
- Primary use is for control of inflammation
- Provides antibacterial prophylaxis while treating the ocular inflammation
- Examples:
  - Adenoviral KC w/sig, epi staining
  - Marginal K infiltrate

Loteprednol etabrate 0.5% + Tobramycin 0.3%

Mild-moderate inflammation and risk of infection

74 year old WM: Subjective

- **CC:** Blurred “central” vision (OD) @ distance and near
  - Onset gradual, over 3-4 days
  - Last visit 3 weeks prior showed 20/25 VA OD
- **Ocular History:** 7 weeks s/p uneventful cataract surgery with IOL OD
- **Medical History:** + HTN x 12 years,
  - Hypercholesterolemia (both under control w/meds)
- **Family Ocular History:** + AMD (mother)
- **Allergies:** None
- **Topical Meds:** artificial tears

Exam Findings: Objective

- **VA:** c Rx OD 20/70 PHNI OS 20/30 PHNI
- **Pupils:** (-)APD, PERRLA
- **EOMS:** Smooth / Full
- **SLE:** Well-centered IOL OD, 1+ CC OS
- **IOP:** 12 mm Hg OD, 14 mmHg OS
- **CF:** Full OU (periphery) Central blur OD/Amshler +
- **Vitreous:** Clear OU

Fundus Evaluation

- DFE shows macular detail obscuration
- “Honeycomb” lesion w/cystic spaces
- Macular elevation

Are there any other tests you would perform?
Optical Coherence Tomography

Additional Testing
- FA demonstrates typical petaloid appearance
- No scanning lasers at the time

What is your assessment?

Irvine-Gass Syndrome
- Post-operative Cystoid Macular Edema (CME)

Hypothesis of Mechanism
- Operative Irritation/Inflammation
- Aging
- Systemic Vasculopathy
- Glaucoma
- Prostaglandins in Aqueous & Vitreous
- Breakdown of the Blood/Aqueous Barrier & Blood/Retina Barrier
- Cystoid Macular Edema

What is your plan?

Treatment of CME

- Topical NSAID x 2-3 mon
- Topical steroid
- Topical NSAID + topical steroid
- Periocular anti-inflammatory meds

Non-Steroidal Anti-Inflammatory Drugs (NSAID)

- Effective against mild/moderate ocular inflammation
- Used post-surgically
- Common ocular side effects
  - Injection
  - Burning/stinging on instillation
  - Dryness

NSAIDs Mechanism of Action

Inhibited by Corticosteroids

Phospholipids → Phospholipase A<sub>2</sub> → Arachidonic Acid → Lipoxigenases → Leukotrienes → Thromboxane A<sub>2</sub> → PGE<sub>2</sub> → PGF<sub>2α</sub> → PGD<sub>2</sub> → Prostacyclin (PGI<sub>2</sub>)

Adverse Events Associated with Conventional NSAID Therapy

- Mild/Moderate corneal side effects<sup>1</sup>:
  - Burning and irritation
  - Superficial punctate keratitis
  - Delayed wound healing
- Severe corneal issues<sup>2</sup>
  - Thinning
  - Perforation due to melts

NSAIDs

- BROMDAY™
- ISTA
- bromfenac ophthalmic solution 0.09%
- Once-a-day dosing
  - Begin on the day before cataract surgery through two weeks post-op.

Ilevro New Generation Nepafenac

- Nepafenac
- 0.3% suspension
- 1x/day dosing
NSAIDs: What’s new?

Ilevro (Alcon)
Nepafenac Ophthalmic Suspension 0.3%

**Formulation:**
- Ophthalmic non-steroidal ___-_____
- Preservative: 0.005% BAK
- pH: 7.4 (physiologic)
- Once a day Dosing

---

**Novel Pro-Drug Structure**

- **Optimizes Penetration**
  - Upon dosing, nepafenac rapidly penetrates the intraocular tissues¹

- **Target-Specific Efficacy**
  - Nepafenac is converted to *amfenac* for optimal efficacy²:
    - Cornea
    - Iris/CB
    - Retina/Choroid


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“New” (and old) NSAID

- **Acuvail™** (Allergan)
  - Ketorolac tromethamine .45%
  - New formation of Acular .5%
  - Preservative-free
  - FDA approved for pain, post-cataract Sx
  - Dosage is bid

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NSAIDs: What’s new?

Prolensa (B&L)
bromfenac ophthalmic solution 0.07%

**Formulation:**
- Treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery.
- Once a day Dosing

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Questions and Comments?

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Dendritic Keratitis
Traditional Topical Treatment

Topical Gel for HSVK

- Zirgan (Sirion/Alcon)
  - Ganciclovir ophthalmic gel 0.15%
  - Targets replication of viral DNA in infected cells
  - Low corneal toxicity
  - Pregnancy category C
  - Approved for ages 2+
  - 1 gt 5x/d until dendrite resolves, then 1 gt tid x 7d

Side Effects

- The most common adverse reactions reported in patients were blurred vision (60%), eye irritation (20%), punctate keratitis (5%) and conjunctival hyperemia (5%).

POAG OS > OD

NFL dropout and notch OS

OCT shows inf NFL defect OS
BASELINE VF: sup nasal step OS

PROSTAGLANDINS
- PG History
  - XALATAN (1996)
  - TRAVATAN (2001)
  - LUMIGAN (2001)

Prostaglandins
- Lipid compounds derived enzymatically from fatty acids
- Contain 20 carbon atoms, including a 5-carbon ring.
- latanoprost

Prostaglandins
- Latanoprost .005%
  - Lost patent protection in 2011
- Travoprost-Z .004%
- Bimatoprost .01%

PROSTAGLANDINS
- Mechanism
  - Enhances uveoscleral outflow
- Efficacy
  - 27-34% reduction of IOP
  - IOP reduction starts in 3-4 hours
  - Maximum effect after 8-12 hours
- Dosing
  - Once a day

SIDE EFFECTS
Want longer lashes?

LATISSE solution is a prescription treatment for hypotrichosis

PG CONTRAINDICATIONS

IS THERE A DIFFERENCE?

XLT STUDY
Parrish RK, ET AL. J. O. May 2003: 688-703

IOP-Lowering Meds

- TRAVOPROST-Z .004% (2006)
  - NO BAK
  - SoZia
  - LESS HYPEREMIA
  - LESS CORNEAL TOXICITY
  - STATISTICALLY EQUIVALENT IOP REDUCTION
  - INSTILLATION AIDS
  - FUTURE USE IN COMBOS

WHAT’S NEW?

- Lumigan .01%
  - Optimized formulation with a reduced concentration of bimatoprost.
WHAT’S NEWER?

- FDA Approves ZIOPTAN™ (Merck)
- tafluprost ophthalmic solution
- Once-Daily
- Preservative-Free

Nonselective Beta-Blockers

- Timolols (maleate, hemi-hydrate)
  - timolol hemi-hydrate 0.25% or 0.5%
- Levobunolol HCl (Betagan)
  - 0.25% or 0.5%
- Most cost-effective IOP meds

WHAT’S NEW?

- Non-preserved Timolol maleate (Aton)
  - .25%, .5%

Case

- A 25 year old male states that he has hayfever each spring and has been congested recently. He complains of itchy, red, watery eyes.
- DVA OD: 20/20
  OS: 20/20
- Ocular assessment of the conjunctiva is remarkable for moderate redness and a watery/mucous discharge, no corneal staining

Seasonal Allergic Conjunctivitis

Case

- Diagnosis? Management?
- Ocular allergy
- Since he is symptomatic and reported seasonal recurrence, an antihistamine with mast cell stabilizing properties would provide both immediate and long term relief with continued use.
Allergic Conjunctivitis

TREATMENT
- Reassurance
- No rubbing!
- Avoidance
- Cold compresses
- Artificial tears
- Olopatadine
- Ketotifen fumarate (OTC)
- Loteprednol

Allergies
- Olopatadine .1 %
- Dual-action drug: Antihistamine/Mast Cell Stabilizer
  - Very safe
  - Very comfortable
  - BID dosing or qd (Pataday .2%)

Bepreve (ISTA Pharm)
- Bepotastine besilate ophthalmic solution 1.5%
  - H-1 receptor antagonist
  - Inhibitor of the release of histamine from mast cells.
  - Bid dosing
  - 10 ml bottle
  - Pregnancy Category C
  - Approved for children >2 y/o

What’s new in the treatment of allergic conjunctivitis?

Lastacaft
- alcaftadine .25% ophthalmic solution
- once-daily use
- H-1 receptor antagonist
  - H1, H2, and H4
- Inhibitor of the release of histamine from mast cells.
- Pregnancy Category B
- Approved for children >2 y/o
Questions and Comments?

Dry Eye Treatment
- Artificial tears Tx is the mainstay of initial topical management
  - preservative free vs. preserved
  - low viscosity (thinner consistency)
  - medium viscosity (medium consistency)
  - high viscosity (thick consistency)
  - ointments

WHAT’S NEW?
- Systane Balance (Alcon)
  - For evaporative dry eye secondary to MGD
  - Enhancement of lipid layer
  - Propylene Glycol 0.6%
  - Mineral oils
  - Oil in water emulsion
  - LipiTech System and demulcent

WHAT’S NEW?
- Soothe Xtra Hydration (Bausch and Lomb)
  - For aqueous-deficient dry eye
  - Claims enhancement of aqueous and mucin layers

Dry Eye Treatment
- Cyclosporine 0.05% (Restasis)
  - Ophthalmic emulsion
  - Provides anti-inflammatory effects for ocular surface tissues and lacrimal glands
  - Requires 3-4 months of continuous use to reach clinically significant effects and up to 6 months to achieve full therapeutic effects

Cyclosporine emulsion .05%
- RESTASIS® is not a quick fix and may take some time for maximum effect.
  - Give it 3 months
Omega-3 Fatty Acids

- Decrease inflammation
- Decrease apoptosis
- Increase tear secretion

Conclusions

- The ability to prescribe therapeutic agents has enabled optometry to establish itself as a true primary health care profession.
- “With great power comes great responsibility.”
  - Uncle Ben in Spiderman
  - Prescribe wisely!