Fall 2016 Continuing Education

Sunday, October 30, 2016
Know Your Chances
AN EVIDENCED BASED APPROACH TO CLINICAL DECISION MAKING

Jordan Keith, OD, FAAO
Minneapolis, MN

Objectives
Define a structured question

Find the best evidence and apply it clinically

See through hype in medical news and advertisements

“Science is a way to keep us from fooling ourselves”
-Richard Feynman, PhD

“The most dangerous words in medicine are ‘In my experience’”
-Mark Crislip, MD
Don’t believe everything you think

“One has only to review the graveyard of discarded therapies to discover how many patients might have benefited from being assigned to a control group.”
- Thomas Chalmers, MD

Steps of EBM
1. Formulate an answerable question
2. Find the best evidence
3. Critically appraise the evidence
4. Apply the evidence

“I see new flashes and floaters”

How often should I expect a RD?

Which patients need further monitoring?

“I see new flashes and floaters”

Acute, symptomatic PVD

At initial presentation

Meta-analysis of 1568 patients

20% retinal break
80% PVD

Follow-up?

Hemorrhage in peripheral retina
New symptoms

Hemorrhage in vitreous
1.8% delayed retinal breaks
1. Good Questions Lead to Good Answers
- What is my diagnosis?
- What are the threats to vision?
- Are there treatments for this supported by evidence?
- If so, when do we treat?
- What do I do with the patient in my chair now?

2. Find the Best Evidence
- Level 1: Randomized clinical trials (RCT) with low study errors
- Level 2: RCT with high study errors
- Level 3: Nonrandomized clinical trials
- Level 4: Intervention Case Series
- Level 5: Intervention Case Report

3. Critical Appraisal
- Who (where) did the study?
- The goal of the study?
- Outcomes used?
- How was the study carried out?
- Blind? Double blind? Randomized?
- Sample size (N) adequate?
- What did they find out?
- How does this affect us clinically?
- Are the benefits greater than the risk?

4. Apply the Evidence
- **Treatment A**: Reduced the rate of blindness by 34%
- **Treatment B**: Produced an absolute reduction in blindness of 0.06%
- **Treatment C**: Increased patients' success rate from 99.82% to 99.88%
- **Treatment D**: 1592 patients needed to be treated to prevent 1 case of blindness
Clinically Significant Macular Edema

**CSME**
- **Retinal thickening** within 500 microns of fovea
- **Exudate** within 500 microns of fovea with adjacent thickening
- **Thickening of at least one disc area** any part within one disc diameter of center of fovea

**ETDRS, Ophthalmology. 1985; 103:1796-1806**

Clinically Significant Macular Edema

**CSME**
- **Retinal thickening** within 500 microns of fovea
- **Exudate** within 500 microns of fovea with adjacent thickening
- **Thickening of at least one disc area** any part within one disc diameter of center of fovea

**ETDRS, Ophthalmology. 1987; 94: 761-774**

Treatments for DME

- **Laser**
- **Steroids**
- **Anti-VEGF**

"In patients with CSME, focal laser reduced the risk of moderate vision loss by 50%..."
Threats to vision?

What is my dx?

Diabetic Retinopathy

NPDR

PDR

Macular Disease

Ischemia

Edema

Pre-retinal/V-heme

TRD

NVG

4-2-1 Rule: Raising the (Risk) Bar

1. IRMA in 1 quadrant

2. Venous beading in 2 quadrants

3. Severe retinal hemorrhages in 4 quadrants

NPDR → PDR in 1 Year

Mild

• 5% risk of progression to PDR

Moderate

• 15% risk of progression to PDR

Severe

• 52% risk of progression to PDR

• Meets ONE criteria of 4-2-1 Rule

Very Severe

• 75% risk of progression to PDR

• Meets TWO criteria of 4-2-1 rule

Follow-up intervals in months

<table>
<thead>
<tr>
<th>Severity of NPDR</th>
<th>American Academy of Ophthalmology</th>
<th>American Optometric Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Mild</td>
<td>6-12</td>
<td>12</td>
</tr>
<tr>
<td>Moderate</td>
<td>6-12</td>
<td>12</td>
</tr>
<tr>
<td>Severe</td>
<td>2-4</td>
<td>3-4</td>
</tr>
<tr>
<td>Very Severe</td>
<td>2-4</td>
<td>2-3</td>
</tr>
</tbody>
</table>

8-year Incidence of CHD and Stroke as a Hazard Ratio (HR) in Japanese Type 2 Diabetics (N=2033)

<table>
<thead>
<tr>
<th>Retinal Finding</th>
<th>Coronary Heart Disease</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild-Mod NPDR</td>
<td>1.69 (95% CI 1.17-2.97)</td>
<td>2.69 (95% CI 1.03-4.86)</td>
</tr>
<tr>
<td>Retinal hem/MA</td>
<td>1.63 (95% CI 1.04-2.56)</td>
<td>Not associated (P=0.06)</td>
</tr>
<tr>
<td>CWS</td>
<td>Not associated (P=0.66)</td>
<td>2.39 (95% CI 1.35-4.24)</td>
</tr>
</tbody>
</table>

Communicate Diabetic Eye Exam Results to PCP!

High-Risk Characteristics

- NVD ≥ ¼ disc area
- Any NVD or NVE with pre-retinal or vitreous heme

In patients with HRC, PRP reduces the risk of profound vision loss by 50%..." (Johnson, 1976; 81:383 - 369)

What Was the Original Risk?

<table>
<thead>
<tr>
<th>No Tx</th>
<th>Tx</th>
<th>RRR</th>
<th>ARR</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>90%</td>
<td>10%</td>
<td>50%</td>
<td>5%</td>
<td>50%</td>
</tr>
<tr>
<td>90%</td>
<td>10%</td>
<td>50%</td>
<td>5%</td>
<td>50%</td>
</tr>
</tbody>
</table>

"In patients with CSME, focal laser reduced the risk of moderate vision loss by 50%..." (Johnson, 1976; 81:383 - 369)

Which Treatment is Best?

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Effect</th>
<th>Success Rate</th>
<th>Patients Needed to Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Reduced the rate of blindness by 34%</td>
<td>99.82% to 99.88%</td>
<td>1,000,000,000</td>
</tr>
<tr>
<td>B</td>
<td>Produced an absolute reduction in blindness of 0.06%</td>
<td>99.82% to 99.88%</td>
<td>20</td>
</tr>
<tr>
<td>C</td>
<td>Increased patients' success rate from 99.82% to 99.88%</td>
<td>99.82% to 99.88%</td>
<td>1,000,000,000</td>
</tr>
<tr>
<td>D</td>
<td>1592 patients needed to be treated to prevent 1 case of blindness</td>
<td>99.82% to 99.88%</td>
<td>20</td>
</tr>
</tbody>
</table>

Treatment Studies

Relative Risk Reduction (RRR)
- Efficacy of treatments commonly reported this way in headlines/media/by pharmaceutical companies
- Use caution when reading this stat: can be misleading and commonly overstates the benefit

Absolute Risk Reduction (ARR)
- Much more meaningful clinically

Number Needed to Treat (NNT)

Other Treatments for DME?

- Steroids as effective as laser but the side effects were worse

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Effect</th>
<th>Success Rate</th>
<th>Patients Needed to Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laser</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-VEGF</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Anti-VEGF Iatrogenic?
Endophthalmitis = 1%
Transient IOP increase
Monthly injections

“My vision was fine until you sent me to that retinal specialist for laser”
Patient Education

- Answer the question, “Why do I need yearly dilated eye exams?” every year even if they don’t ask.
- Help them understand their “vascular” disease.
- Encourage them to be intimately aware of their numbers (BS, HbA1C, BP, cholesterol).
- Keep in mind number one indicator of complications is duration.
- “You don’t ‘know’ how hard it is to control the disease unless you have lived with it.

Ocular HTN

- Threats to vision?
- Treatment?
- When/who do we treat?
  - Everyone?
  - No one?
  - Depends?

How Effective is Treatment?

<table>
<thead>
<tr>
<th>No Tx</th>
<th>Tx</th>
<th>RRR</th>
<th>ARR</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>90%</td>
<td>45%</td>
<td>50%</td>
<td>45%</td>
<td>2</td>
</tr>
<tr>
<td>25%</td>
<td>12.5%</td>
<td>50%</td>
<td>12.5%</td>
<td>8</td>
</tr>
<tr>
<td>10%</td>
<td>5%</td>
<td>50%</td>
<td>5%</td>
<td>20</td>
</tr>
<tr>
<td>2/million</td>
<td>1/million</td>
<td>50%</td>
<td>0.0001%</td>
<td>1,000,000</td>
</tr>
</tbody>
</table>

“Treating a patient with ocular hypertension reduces the risk of glaucoma by 50%...”

“Treating a patient with ocular hypertension reduces the risk of glaucoma by 50%...”
What Were the Outcomes Used?

- Reproducible VF abnormality
- Reproducible ONH deterioration

Surrogate endpoints vs. clinical endpoints

Kass MA et al. OHTS. Arch Ophthalmol. 2002;120:701-713

How Was Ocular HTN Defined?

- Age 40 – 80
- IOP 24-32 mmHg in one eye and 21-32 mmHg in the other
- Gonioscopically open angles
- 2 normal HVF tests each eye
- Normal ONHs

Kass MA et al. OHTS. Arch Ophthalmol. 2002;120:701-713

Treatment?

Reduction of IOP by 20% or more and reach an IOP of 24 or less

Kass MA et al. OHTS. Arch Ophthalmol. 2002;120:701-713

Treat everyone?

- Treat no one?
- It depends?

Treat everyone?

- Treat no one?
- It depends?

Iatrogenic to Treating Everyone?

$100/bottle x 12 months x 5 years x 20 NNT = $120,000

- % of patients we didn’t help = 95%
- % of complication = 100%

Treat no one?
Is there penalty in delaying treatment?

<table>
<thead>
<tr>
<th>At 5 years</th>
<th>At 7.5 years</th>
<th>At 13 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Tx = 10%</td>
<td>Start Tx</td>
<td>Delayed Tx = 22%</td>
</tr>
<tr>
<td>Tx = 5%</td>
<td>Continue Tx</td>
<td>Early Tx = 16%</td>
</tr>
</tbody>
</table>

It Depends?

- Age, health status, patient preference
- Baseline risk determined by OHTS/EGPS calculator?
  - Age
  - IOP
  - CCT
  - PSD
  - C/D

After 13 years % developing glaucoma based on initial risk

<table>
<thead>
<tr>
<th>Lowest risk at baseline (&lt;5%)</th>
<th>Moderate risk at baseline (5-15%)</th>
<th>High risk at baseline (&gt;15%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delayed Tx = 8%</td>
<td>Early Tx = 7%</td>
<td>NNT = 100</td>
</tr>
<tr>
<td>Delayed Tx = 15%</td>
<td>Early Tx = 14%</td>
<td>NNT = 20</td>
</tr>
<tr>
<td>Delayed Tx = 40%</td>
<td>Early Tx = 28%</td>
<td>NNT = 8</td>
</tr>
</tbody>
</table>

What Do I Do With this Patient?

- Assess risk
  - Age, IOP, CCT, C/D
- Testing
  - HVF, ONH/RNFL analysis, stereo ONH photos, gonioscopy, pachymetry

"Medicine is a science of uncertainty and an art of probability"
-Sir William Olser, MD
Sensitivity vs. Specificity

Positive Predictive Value vs. Negative Predictive Value

**Riddle**

Probability of breast cancer = 0.8%

- Mammography screening program of 40-50 yo women with no symptoms

What is the probability that a positive mammogram is actually breast cancer?

- Has breast cancer
  - Positive mammogram 90%
- Does not have breast cancer
  - False positive mammogram 7%

<table>
<thead>
<tr>
<th>Cancer Status</th>
<th>Positive Mammogram</th>
<th>Negative Mammogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has Cancer</td>
<td>7 (TP)</td>
<td>1 (FN)</td>
</tr>
<tr>
<td>Does Not Have Cancer</td>
<td>1 (FP)</td>
<td>992 (TN)</td>
</tr>
</tbody>
</table>

Positive Predictive Value = 7/77 = 9%

----

0.8% with breast cancer
90% sensitivity
93% specificity

<table>
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<th>Positive Mammogram</th>
<th>Negative Mammogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has Cancer</td>
<td>8 (+) cancer</td>
<td>992 (-) cancer</td>
</tr>
<tr>
<td>Does Not Have Cancer</td>
<td>7 TP</td>
<td>922 TN</td>
</tr>
</tbody>
</table>

Positive Predictive Value = 7/77 = 9%

----

1% adult population w/ glaucoma
90% sensitivity
90% specificity

<table>
<thead>
<tr>
<th>Cancer Status</th>
<th>Positive Mammogram</th>
<th>Negative Mammogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has Cancer</td>
<td>9 (TP)</td>
<td>1 (FN)</td>
</tr>
<tr>
<td>Does Not Have Cancer</td>
<td>10 (FP)</td>
<td>990 (TN)</td>
</tr>
</tbody>
</table>

Positive Predictive Value = 9/108 = 8%

----

10% adult population w/ glaucoma when IOP >21
90% sensitivity
90% specificity

<table>
<thead>
<tr>
<th>Cancer Status</th>
<th>Positive Mammogram</th>
<th>Negative Mammogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has Cancer</td>
<td>100 (TP)</td>
<td>900 (TN)</td>
</tr>
<tr>
<td>Does Not Have Cancer</td>
<td>10 (FN)</td>
<td>90 (FP)</td>
</tr>
</tbody>
</table>

Positive Predictive Value = 50%
Testing

Sensitivity vs. Specificity
- Efficacy of tests commonly reported this way
- Clinically not valuable information in isolation
- Usefulness of test depends on initial risk of population

More judicious testing leads to fewer false positives and higher positive predictive value

"In general, tests do not make a diagnosis—you do, based on the test result in the context of how likely you believed the disease was to begin with."
- Richard Gross, MD

"Because there is no need to show that an instrument has any real value in disease detection or management before it is brought to market, we have become enamored with sophisticated analysis algorithms and colorful printouts before we have studies that show what the results of the tests mean. This approach is fueled, of course, by economic interests. Industry is motivated to create product and we [ophthalmologists] provide the key opinion leaders to drive the use of what is developed . . . ."
- Paul Lichter, MD

Patient Education
- You don’t know your patient’s risk for glaucoma.
- Help them understand what the risk is for people like them.
- Empower patients to make the decision to treat or not to treat on their own.
- Acknowledge their fear and help them understand why that won’t happen.
- Have a philosophy for treating glaucoma.

“In general, tests do not make a diagnosis—you do, based on the test result in the context of how likely you believed the disease was to begin with.”
- Richard Gross, MD

“... Cynical as it seems, these devices belong in the laboratory, before they are marketed as being of value and before billing codes are established for their use, which simply drive up the costs of care without making any impact whatsoever on the critical outcome in glaucoma—preservation of vision related QOL.”
- Paul Lichter, MD
Dry AMD

Wet ARMD

Wet AMD

10/17/16

Dry AMD

Dry AMD

Wet AMD

Wet AMD

AMD

Dry 90%

90% functional vision

Wet 10%

10% severe vision loss (GA)

90% severe vision loss

Wet

AMD

Dry

90%

10% severe vision loss

90% functional vision
What is my dx?

Threats to vision?

- AMD
- Dry
- Wet
- RPE Atrophy
- CNVM

MARINA for CNVM

- 20/40 BCVA or better
  - Lucentis = 40%
  - Sham = 11%
  - NNT = 3.5

- Lost ≤ 3 lines BCVA from baseline
  - Lucentis = 94%
  - Sham = 62%
  - NNT = 3

- Improved ≥ 3 lines BCVA from baseline
  - Lucentis = 30%
  - Sham = 5%
  - NNT = 4


Iatrogenic?

- Endophthalmitis = 1%
- Transient IOP increase
- Monthly injections

“Despite the lack of convincing evidence, the marketing and use of antioxidants and zinc in eye-targeted formulations has become common practice.”

- AREDS I


“Taking AREDS I supplements reduces the risk of AMD progression by 25%...”

AREDS 1

- AMD
- Category 1: No AMD
- Category 2: Mild/borderline AMD
- Category 3: Moderate AMD
- Category 4: No signs of advanced AMD in the study eye and BCVA 20/20 in both eyes

AREDS 1

Outcome: Progression to ADV AMD at 5 years

**Table:**

<table>
<thead>
<tr>
<th>Category</th>
<th>Probability by Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.05%</td>
</tr>
<tr>
<td>2</td>
<td>1.0%</td>
</tr>
<tr>
<td>3</td>
<td>16%</td>
</tr>
<tr>
<td>4</td>
<td>66%</td>
</tr>
</tbody>
</table>

**Figure:**

- **Outcome:** Progression to ADV AMD at 5 years
- **Probability by Category:**
  - Category 1: 0.05%
  - Category 2: 1.0%
  - Category 3: 16%
  - Category 4: 66%

**Diagram:**


Outcome: 15-letter decrease from baseline at 5 years

**Table:**

<table>
<thead>
<tr>
<th>Category</th>
<th>Probability by Treatment (Placebo vs. Treatment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Data not evaluated</td>
</tr>
<tr>
<td>2</td>
<td>No sig difference</td>
</tr>
<tr>
<td>3</td>
<td>Data not reported</td>
</tr>
<tr>
<td>4</td>
<td>Data not reported</td>
</tr>
</tbody>
</table>

**Figure:**

- **Outcome:** Progression to ADV AMD at 5 years
- **Probability by Treatment (Placebo vs. Treatment):**
  - Category 1: Data not evaluated
  - Category 2: No sig difference
  - Category 3: Data not reported
  - Category 4: Data not reported

**Diagram:**


Latrogenic?

"We do not know the long-term health effects of supplementation with these high doses of vitamins and minerals"

- AREDS I

**Figure:**

- Latrogenic?
  - $142/year x 5 years x 17 NNT = $12,070
  - % of patients we didn’t help = 92-94%
  - % of complication = 100%

**Diagram:**


15
“Taking AREDS 2 supplements reduces the risk of AMD progression by 26%...”

AREDS 2

Outcome: Progression to ADV AMD at 5 years

<table>
<thead>
<tr>
<th>AREDS 1</th>
<th>+ L/Z</th>
<th>+ DHA &amp; EPA</th>
<th>+ L/Z &amp; DHA/EPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>31%</td>
<td>30%</td>
<td>31%</td>
<td>30%</td>
</tr>
</tbody>
</table>

Outcome: Moderate vision loss (≥ 3 lines of acuity) from baseline

<table>
<thead>
<tr>
<th>AREDS 1</th>
<th>No additional effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>No additional effect</td>
<td></td>
</tr>
</tbody>
</table>

Subgroup analysis: lowest dietary consumption of Lutein/Zeaxanthin

HR 0.74 (95% CI: 0.59-0.94; P=0.01)

What Do I Do With My Patient?

- Patient Education: this is common and most don’t go blind
- Lifestyle changes (diet, smoking)
- Pros/cons supplements vs. no supplements
- Home Amsler grid?


“Even when cure is impossible, healing is not necessarily impossible. While medical science has limits, hope does not.”
- Bernard Lown, MD

“To cure sometimes, to relieve often, to comfort always.”
- Edward Trudeau, MD

Objectives

- Define a structured question
- Find the best evidence and apply it clinically
- See through hype in medical news and advertisements
Resources

Contact Information
Jordan.Keith@eyecarecenters.net
The Unilateral Red Eye: Separating Dangerous from Non-Dangerous

JORDAN KEITH, OD, FAAO
MINNEAPOLIS, MN

Objectives
1. Develop a strategy for examining EVERY unilateral red eye
2. Identify five dangerous red eyes
3. Know why they are dangerous
4. Review management and treatment

A Red Eye is a Cardinal Sign of Inflammation

in·flam·ma·tion

noun: inflammation; plural noun: inflammations
A localized physical condition in which part of the body becomes reddened, swollen, hot, and often painful, especially as a reaction to injury or infection.
Inflammation
1. Pain
2. Redness
3. Swelling
4. Heat

“Patient here with a red eye”

First Decision
- Dangerous
- Non-dangerous

40 YOBM / Pain / Redness / Photophobia

Dangerous Unilateral Red Eye #1: Anterior Uveitis

Anterior Uveitis
Frequently occurs in young adults
Peak incidence: 20’s-40’s

Blood Aqueous Barrier
Uveitis = Breakdown in Blood Aqueous Barrier

Anterior uveitis diagnosed based on the presence or absence of WBC's in the anterior chamber

Threats to Vision

Periperal Anterior Synechia

Cystoid Macular Edema

Fibrin = Posterior Synechia

Fibrin in posterior chamber

Posterior synechia

Causes?
Categorization Can Help

Acute vs. Chronic
- Acute < 3 months
- Chronic > 3 months

Type of Inflammation
- Non-granulomatous
- Granulomatous

Location
- Anterior (75%)
- Intermediate (8%)
- Posterior/panuveitis (17%)

Laterality
- Unilateral
- Bilateral
- Alternating

Most Common:
Acute, unilateral, non-granulomatous, anterior uveitis

New Onset Acute Non-Granulomatous Anterior Uveitis

- 50% HLA-B27 positive
  - Crohn’s disease (+ Ucercative colitis = IBD)
  - Reactive arthritis
  - Ankylosing spondylitis
  - Psoriatic arthritis
- 50% have an associated spondyloarthropathy (CRAP)
- 80% of these patients have ankylosing spondylitis
- 50% idiopathic
Granulomatous etiology more commonly infectious

30 YOWF / Pain / Redness / Nausea / Recently Started Topamax® (topiramate)

Dangerous Unilateral Red Eye #2: Acute Angle Closure

Acute Angle Closure: Testing
- IOP (50-100 mmHg)
- Van Herick angles
- Gonioscopy
- Anterior OCT

Acute Angle Closure: Risk Factors
- Age
- Hyperopia
- Asian descent
- Medications: Topamax® (topiramate)
Acute Angle Closure: Topamax® (topiramate)

- Used to treat migraines, weight loss, epilepsy
- Causes supraciliary effusion moving the lens and iris forward
- Angle closure
- Myopic shift
- Typically occurs within first month of use or if dosage is increased

Symes RJ, et al. JAMA Ophthalmol. 2015 (Jul 9)

Acute Angle Closure: Immediate Threat to Vision?

Critical Closing Pressure = CRAO

Dangerous Unilateral Red Eye

#3: Corneal Issues

An infiltrate is a sign of your patient’s immune system attacking an antigen via antibodies
Corticosteroids for Bacterial Keratitis

The Steroids for Corneal Ulcers Trial (SCUT)

Objectives: To determine whether daily topical corticosteroids are beneficial as an adjunct to standard therapy for bacterial keratitis.

Methods: Randomized, placebo-controlled, double-masked, multicenter, prospective, randomized, patient-blinded clinical trial. 1000 patients enrolled. Bacterial cultures taken at baseline and during treatment. Statistical analysis: Chi-square, Student’s t-test, and analysis of variance (ANOVA).

Results: No overall difference in 3-month clinical outcomes with the use of adjunctive corticosteroids. No increase in adverse events were found. For bacterial ulcers, the addition of steroids to Vigamox:
- did not reduce scar formation
- did not increase re-infection rate
- did not improve VA in the overall group
- no increase in adverse events were found

Fungal Ulcer/Infectious Keratitis

Gray-white infiltrate with feathery edges: classic for Aspergillus / Fusarium

Candida ulcers can look like bacterial ulcers and be deadly!

Acanthamoeba Keratitis

- Most common protozoa found in soil and frequently in water
- Associated with inadequate contact lens hygiene
- Early: pain is severe and out of proportion of signs
- Late: Patchy anterior stromal infiltrates that can present with overlying pseudodendritic epithelial defects
- Later progress to ring ulcer

Hangover

Herpes Simplex Virus (HSV)

- Recurrent infections most common in young adults
- Ask about previous episodes and/or cold sores

Herpes Simplex Virus (HSV) in United States

- Population seropositive by 4 years of age: 25%
- Population seropositive by 60 years of age: 100%
- Lifetime prevalence of ocular manifestations in infected people: 1%

HSV is the 2nd most common cause of corneal blindness in the United States.

The “Great Mimic” of the anterior segment

HSV Dendrite

Staphylococcal Marginal Keratitis

Chronic blepharitis → Peripheral infiltrate NO NaFL staining

Staphylococcal Marginal Keratitis

Corneal scars Peripheral thinning / neovascularization / scars
Corneal Abrasion/Erosion

(-) Infiltrate (+) NaFl staining (epithelial defect)

Tree Branch Injury

Comeal Abrasion Recurrent Erosion

What about if no history of previous trauma?

Epithelial Basement Membrane Dystrophy (EBMD)

10% of EBMD patients develop corneal erosions

50% of patients with corneal erosions will have EBMD
Dangerous Unilateral Red Eye

#4: Scleritis

Scleritis (98% anterior)
- Non-necrotizing (84%)
- Necrotizing (14%)

WITH inflammation
- Highest risk of vision loss and death

WITHOUT inflammation
- Scleromalcia perforans: Chronic RA

Scleritis vs. Episcleritis

Scleritis
- Severe pain
- Diffuse deep inflamed vessels
- If nodule: immobile
- 50% associated with systemic disease

Episcleritis
- Mild/moderate pain
- Sectoral superficial inflamed vessels
- If nodule: moveable
- 25% associated with systemic disease

Dangerous Unilateral Red Eye

#5: Orbital Cellulitis

Orbital cellulitis is a serious infection that can result in a cavernous sinus thrombosis, brain abscess, and/or meningitis if not caught early and managed appropriately.

Preseptal Vs. Orbital Cellulitis

- Headache, fever, general malaise
- Optic nerve involvement
- EOM involvement
- Proptosis

PC

OC
Anterior Uveitis → AC
Acute Angle Closure → IOP
Corneal Issues → NaFl
Scleritis
Orbital Cellulitis

Dangerous Unilateral Red Eyes
Ocular Injections: Optometry’s Role
Katherine B. Lynch, OD, FAAO

Ocular Injections
• Intraocular vs. Subconjunctival/Periocular
• When we refer
• What the co-management looks like
• What we may be doing

Intraocular Injections

The statistics
• In 2001: 4,500 intravitreal injections per year
• In 2012: 2,354,753 intravitreal injections
• Lucentis = second highest Medicare Part B drug expenditure in 2012, 1/6 of the drug budget (Li, et al)

CNVM

Indications to Inject
• Choroidal Neo Vascular Membrane
• Cystoid Macular Edema 2’ Occlusion
• Proliferative Diabetic Retinopathy
• Clinically significant macular edema
• Non-infectious uveitis
• Retinopathy of Prematurity
• Others...
Diabetic Retinopathy

- **Mild**
  - at least 1 MA
  - f/u 1 year
- **Moderate**
  - H/Mas greater than 2A, soft exudates, venous beading
  - f/u 6 months
- **Severe**
  - 4:2:1 Rule H/Mas greater than 2A in 4 quadrants, VB in 2 or more quadrants, IRMA in 1
  - REFER to retina w/in 4 weeks, f/u with you 2-3 months
  - Treatment may be indicated

Proliferative Diabetic Retinopathy

- **Proliferative** — NEOVASCULARIZATION
  - Refer w/in 2-4 weeks
- **High Risk Proliferative**
  - Refer 24-48 hours
  - Neo w/in 1DD of Optic Nerve >1/4-1/3 disc area
  - Any neo within 1DD with pre-retinal/vitreous hemorrhage
  - NVE with pre-retinal or vitreous hemorrhage

Even if we can’t see it...

- Always assume proliferative disease with:
  - Pre-retinal hemorrhage
  - Vitreous hemorrhage
- Once a patient is proliferative, they are proliferative for life

CSDME

- Can occur at ANY stage
- Criteria for CSME
  - Thickening within 500 microns
  - Hard exudates within 500 microns
  - Area of thickening >1DD within 1DD of fovea
- Refer within 2 weeks

*500 microns 1/3 DD

CSME Case

It always goes back to the anatomy

- 9 layers to the Retina
- 10th layer is the RPE
- Blood vessels = inner retinal layers
- Outer plexiform has potential space
- Outer retina is supplied by the choroid
The anatomy of the CNVM

- Can appear serous or the hemorrhage may be visible
- Sub-retinal hemorrhage = between retina and RPE (bright red)
- Sub-RPE hemorrhage = between RPE and Bruchs (grey/green)
- CNVM in one eye is a risk factor for the fellow eye!

The anatomy of the vein occlusion

- May be central or branch
- Compression is the culprit
- Blood is always visible
- OCT to better image macula
- Location, location, location
- Edema and ischemia dictate need for treatment

So how about on OCT?

Timeline for the referral

- How soon?
  - THIS IS IMPORTANT
    - CNVM: 1 week
    - Macular Edema 2’ occlusion: 2 weeks
    - CSDME: 2 weeks

Types of Injections

- Lucentis (Ranibizumab)
- Avastin (Bevacizumab)
- Eylea (Aflibercept)
- Kenalog (Triamicinolone)
- Ozurdex – sustained release dexamethosone biodegradeable pellet

Anti - VEGF

- Vascular Endothelial Growth Factor
- VEGF mediated disease
- VEGF = protein
- Triggered by hypoxia
- Stimulates new vessel growth
- Increases vascular permeability
Why does it work on so many things?

Because it works on things that leak:
• Blood vessels
• Neovascularization
• Break down of the blood retinal barrier

Vein Occlusion Studies

Anti-VEGF:
• CRUISE – established Anti-VEGF as standard
• HORIZON and RETAIN – long term efficacy of Anti-VEGF
  => better visual outcome
• COPERNICUS – Aflibercept vs. sham
• GALILEO – Aflibercept vs. sham
  *Just as good as Lucentis

Steroids:
• GENEVA – Dexamethosome single dose vs. sham
• SCORE – Triamcinolone vs. observation

The bottom line in occlusion

• Anti-VEGF > Steroid > Observation

• No real comparison studies between steroids and Anti-VEGF

• 3 months is a good time to re-evaluate

AMD Studies - 2006

• ANCHOR – Ranibizumab for Classic CNVM > PDT

• MARINA – Ranibizumab for Occult CNVM > Sham

Avastin vs. Lucentis Studies

• CATT – Avastin vs. Lucentis = equivalent endpoint w/in 5 letters at 1 year

• IVAN - w/in 3.5 letters

• BRAMD – equal visual outcomes at 1 year, but more varied response with Avastin

Avastin vs. Lucentis

• Avastin $50, Lucentis $1,903
• Avastin = whole anti VEGF antibody
• Lucentis = antibody fragment
• Lucentis -> FDA approval for ocular use
• Lucentis? Greater ocular efficacy
Eyelea

• Aflibercept
• Often will have a loading dose x months
• Then Bi-monthly injection
• Comparable results to monthly injections
• Cost: $1,850

The studies on DME and Anti-VEGF

• RESOLVE – Lucentis vs. Sham = better visual gains with Anti-VEGF
• RISE & RIDE- Ranibizumab vs. sham = Reductions in ME and better acuity with Anti-VEGF
• READ -2, RESTORE, REVEAL - Lucentis vs. Laser or combo = best gains in vision and ME with Anti-VEGF

The bottom line in Anti-VEGF

• It works
• Similar results among all Anti – VEGF medications
• Superior visual outcomes are undeniable
• Many uses

Wait a minute, how about steroids?

• There is still a place for steroids in eye care!
• Often considered in recalcitrant cases
• Often in combination
• DME and occlusion

But don’t forget we use them other places too:

• Lids: Chalazion Injection
• Subconjunctival injection: recalcitrant uveitis
• Sub-Tenon’s space: CME
• Posterior Segment: DME, CME

Steroids

• Anti-inflammatory properties
• Affect capillary basal membrane composition – inhibiting angiogenesis/dissolution
• Impact VEGF formation
• Multiple action points!
Triamcinolone

- Kenalog = Corticosteroid
- Anti-inflammatory properties
- MOA: inhibits inflammatory cascade
- IOP concerns
- Floaters and blurry vision

Osurdex

- Dexamethasone biodegradable pellet
- Sustained release – 60 days
- May be used in conjunction with Anti – VEGF
- Approved for DME, CME 2’ Occlusion, Uveitis

Hello Darkness, My Old Friend...

- What about lasers?
- If there is ischemia -> Pan Retinal Photocoagulation (360’)
- Clear point of leakage/edema is not center involving -> Focal (never closer than 300 microns from fovea)

Occlusion Case

Intravitreal Injections: The Procedure

- Anesthesia
- Betadine – lids/conjunctiva
- Speculum
- Injection site
- Inject!
- Check for complications

Video
The chatter

- What kind of room should this be done in
- Should doctors and patients be wearing masks
- Should we treat all lid disease before
- Topical or subconjunctival anesthesia
- Antibiotics or no

Things to expect – this normal

- Subconjunctival hemorrhage ~ 10-40%
- "Irritated feeling eye" ~ 24 hours
- Superficial Keratitis
- Floaters – 1 in 3 people, subside w/in 1 week

Acute Follow Up

- Cell/flare- there should be none
- IOP elevated only a few hours
- Acuity ?
- Some patients are on antibiotics s/p injection

Possible Negative Complications

- Traumatic cataract
- Cataract progression
- Retinal Detachment
- Vitreous hemorrhage
- Endophthalmitis

Endophthalmitis

- 1 week
- Decrease in acuity
- Pain
- Photophobia
- Periorbital swelling
- AC reaction
  **Keratic precipitates, hypopyon, fibrin, anterior synechiae

- Likely less than 1.6 % of people
- Any uveitis is an endophthalmitis until proven otherwise
- Intraocular antibiotics/pars plana vitrectomy
- Confirmed with biopsy
The follow up
- Will often be seen in 4 weeks
- Acuity
- OCT
- Determine most appropriate injection schedule

Treat and Extend
- A more reasonable schedule
- Fewer total injections
- Once endpoint is reached add two weeks
- Maximum add is ~12 weeks
- Return to more injection with significant changes

Treat and Extend
- Mostly for AMD, fewer studies for VO or DME
- Cost and accessibility considerations
- LUCAS – Treat and Extend as effective as monthly injection

When might retina want to see them sooner?
- Vision is worse
- Possible new bleed
- Worsening appearance
- S/s of endophthalmitis or complication

What should we know as Co-managing Optometrists
- When was their injection?
- What was it for?
- When is the next scheduled appointment?
- Acuity before?
- Stable per retina?

“Dropless” Cataract Surgery
- Standard of care in many countries
- 2007 : European Society of Cataract and Refractive Surgeons
- Risk of Endophthalmitis is far less
- Antibiotics delivered via intracameral injection
The Medications

- Aprokam: Cefuroxime – commercially available intracameral antibiotic (2nd gen cephalosporin)
  - Common in Europe
  - Single use
- TriMoxi/TriMoxiVanc – transzonular injection
  - Triamcinolone (steroid)
  - Moxifloxacin (antibiotic)
- Moxifloxicin out of the bottle?
- No FDA approved intercameral drug

Benefits

- Lesser incidence of Endophthalmitis
- Greater concentration of antibiotic
- Compliance
- Cost

Concerns

- Potential allergy
- Dilution/Contamination
- Resistance
- Post operative drops?
- Best delivery system

Botulism is so in right now...

- BOTOX by Allergan

How does Botox work?

- Many medical uses – safe!
- First ocular use in 1980
- FDA approval for Blepharospasm since 1989
- Botulinum Toxin – A
- Blocks release of acetylcholine

- Prevents the muscles from contracting
- Prevents glands from secreting
- The effect is permanent!
- Works within 2-7 days
- Without contraction, you can manipulate appearance and functionality
### What it’s being using for
- Blepharospasm
- Entropion
- Strabismus
- Congenital nystagmus
- Eyelid retraction
- Lacrimal hypersecretion
- Many others...

### How long does it last?
- Effects last 2-4 months depending on dosage/location etc.
- Can develop neutralizing antibodies
- Fun fact: Apraclonidine can improve induced lid ptosis

### Optometrists and the Privilege to Inject

### What’s happening in Optometry?
- Part III National Boards: Injections Skills Exam
- Pilot in 2011-2012
- Now included in score
- Can take ISE only without skills exam
- Includes Intravenous and Intramuscular prep/performance

### Injectables in other states
- 15 states allow procedures/injections
- Wide range of scope
- Regulated by state government

### What the Bill in Illinois Proposes
- Allows injectable pharmaceuticals with limitations
- Advanced Clinical procedures as taught, including minor surgical procedures
- Has passed in the Senate, now in the House with 2 readings already
Teaching Injections

So what might that look like?
- The use of anesthetic
- Chalazion injection/removal
- Removal of eyelid lesions
- Biopsy
- FA
- Medication delivery

Injection Types

The Basics
- Needle gauge
- Needle length
- Syringe used
- Needle prep
- Cleaning the site
- Ancillary equipment (sharps container, tourniquet, clamps, forceps, etc.)

Subcutaneous Injection
- For us: local anesthesia for lesion removal or biopsy
- Famous subcutaneous injections: vaccines (MMR/HZV), insulin

Intravenous
- For us: Fluorescein Angiography
- Famous IV injections: IV antibiotics, solutions, etc.
Intralesional
- For us (and others!): Steroid to Chalazion
- Done on the palpebral conjunctival side

Subconjunctival
- Recalcitrant anterior uveitis
- Anesthesia
- ?New glaucoma medications
- Famous subconj injections: lidocaine, steroid

IM, Intradermal
- Ocular correlations?
- Famous IM: Influenza Vaccine, Penicillin
- Famous Intradermal: TB wheel

Questions?
kalynch@ico.edu