The Oh Crap Moment: When Ocular Emergencies Happen!

Patient Case #1
- 32 year old Caucasian male
- Same day referral from Windham ER, patient was hit by exploding sparkler firework into his right eye.
- Swollen, painful red eye that was shut upon presentation
- Vision was unstable with excessive tearing.
- Patient has had prior surgery twice for a previous paintball injury in the same eye.

Exam
- VA: 20/20 OS, 20/25 OD
- Positive Slit Lamp findings:
  - Upper and lower eyelid edema
  - No swelling and redness
- Open wounds on right cheek
- No subconjunctival, no flare present
- No Seidel Sign, cornea intact
- 1+ - 2 KP present
- Gonioscopic revealed multiple areas of iris and pupil defects
- IOP: 11 OD, 15 OS
- Dilated Fundus Exam:
  - Chronic Retinal detachment
  - Multifocal choroidal scars extending from CNH to nasal macula

Disclosures
- The content of this COPE Accredited CE Presentation was prepared independently by Michael Cooper, OD and Margie Recalde, OD without input from members of the ophthalmic community.
- Dr. Cooper is affiliated with Allergan, Alcon Surgical, BioTissue, Shire, JAVC, TearScience, Glaukos, Bausch & Lomb/Valient, Quibell, Merholzukum, and TearLab as a consultant/speaker.
- Dr. Recalde is affiliated with Allergan, Bausch & Lomb/Valient, and Shire as a consultant/speaker.
- There is no direct financial or proprietary interest in any companies, products or services mentioned in this presentation.
- The content and format of this course is presented without commercial bias and does not claim superiority of any commercial product or service.

Setting the Stage…

“Peek a Boo” IOL
Treatment

- Cyclo 1% bid OD
- Durezol qid OD
- Generic Cosopt tid OD (pre-existing medication)
- Bacitracin ophthalmic ointment tid for abraded skin tissue

Long Road Ahead

- Took 2-3 months for the Traumatic Iridocyclitis to resolve
  - It could take longer...
- Luckily, pressure remained low and did not spike
  - It can...
- Be mindful of retinal pathology
  - Macula
  - Peripheral
  - Acquired Optic Neuropathy

Injury Epidemiology

- Ocular injuries in children account for 20%-50% of all ocular injuries.
- Perforating eye injuries make up 21-24% of serious ocular trauma and are a significant cause of visual loss.
- It is estimated that they can be prevented in up to 90% of cases.
- There is a male predominance of 2:1

Ocular Emergency

- Immediate Appointment if any of the following:
  - Sudden, painless loss of vision
  - Sudden onset of flashes/floaters
  - Chemical burn: Have patient irrigate eye under running water for 20 minutes prior to coming
  - Potential penetrating injuries
  - Injury to head/neck or eye

Educate Staff on Emergency Protocol

- Our instincts are what guide us best...
- “By failing to prepare, you are preparing to fail.”
- Always remember to “Keep Calm”
- “Most importantly: G-d heals and the doctor takes the fee.”
2 is 1, 1 is none

- Use a systematic approach that engages front and back office staff to prepare and manage emergent cases.
- Invaluable preparations can be made in advance of any incident.
- Make effective and critical decisions that can be managed quickly (not rashly).
- All staff and doctors should know how to respond confidently.
- ADA Standard of Conduct

Section B. Emergency Optometric Care

"A request for optometric care in an emergency should receive immediate response. Once having undertaken an emergency case, an optometrist shall neither abandon nor neglect the patient." Ethics in Clinical Optometry

Patient Case #2

- 17 year old female
- 3 days ago, patient was hit OS by another person’s head while playing soccer.
- Black eye OS with swelling and tenderness upon touch
- Vision stable
- Mother concerned about internal bleeding
- Urgent care visit 3 days ago: Ice and ibuprofen

Exam

- VAsc 20/30 OD, 20/30 OS
- Positive findings:
  - Upper and Lower left lid: 2+ swelling and ecchymosis
  - Subconjunctival Hemorrhage inferior and temporal
  - IOP Ta 14mmHg OD, 16mmHg OS at 4:50 pm
- Dilated Fundus Exam: WNL OU
- All other exam findings WNL OU

Be Suspicious

- Assume the worst until it is ruled out
- Blunt Ocular Trauma: Always maintain a high index of suspicion for what is often an occult injury.
- Patients with a history of significant ocular and pericocular blunt trauma should be considered ruptured until proven otherwise.

History

- Take a careful history (clinical and legal reasons)
  - High or Low velocity injury
  - Circumstances of Injury
  - Prior Eye Surgery
  - Vision: Reduced vision and/or Diplopia
  - Pain
  - RD symptoms (flashes, floaters, curtain/veil)
  - Was patient wearing eye protection?
History

- Is patient systemically stable?
- Nausea, vomiting
- Young Patients with Blunt Trauma

White-Eyed Blowout Fractures (WEBOF)

EOM testing crucial!

Orbits

- Enophthalmos = ruptured globe

- Orbital Blowout Fracture:
  - Orbital crepitus indicates subcutaneous emphysema from an associated sinus fracture.
  - Numbness of cheek, upper lip, and/or teeth.

Protecting the Eye

- If there is suspicion of a ruptured globe:
  - Never patch the eye
  - Cover with a Fox Shield or you can MacGyver it...

Imaging Techniques

- CT scan of brain and orbits with thin cuts (1.5mm or less) (NOT MRI) to evaluate for:
  - Intraocular foreign body(IOFB)
  - Intracocular foreign body(IOFB)
  - If wood suspected, obtain MRI after CT
  - Orbital fractures
  - Other head trauma

*If CT not immediately available, obtain plain X-ray of orbits pre-operatively and CT (as above) post-operatively.
Bilateral Eyelid Bruising

Battle's Sign

Highly suggestive of basilar skull fracture, with a positive predictive value of 85%. They are most often associated with fractures of the anterior cranial fossa.

Double vision?

- Key Questions to ask for Diplopia Cases:
  - Monocular or Binocular Diplopia?
  - Comitant= angle of deviation remains the same in all gazes with no limitation to ocular movement
  - Hereditary, uncorrected refractive error
  - Incomitant= angle of deviation varies in different gazes with no limitation to ocular movement. Secondary>primary angle deviation.
  - Usually from traumatic injury or vascular disease.

Dangerous Diplopia Cases to Detect

- Diplopia due to Pupil Involving CNIII Palsy
  - Problem with more than one of the following: lid, pupil, eye movement
  - Multiple cranial neuropathy
- Diplopia variable due to weakness or fatigue
- Diplopia with onset of new kind of headaches, scalp tenderness, pain with chewing.

Pupils

- +APD
- Rx/O compressive optic neuropathy from retrobulbar hemorrhage
- STAT REFERRAL
- A peaked, teardrop-shaped, or otherwise irregular pupil suggests globe rupture.

Conjunctiva

- Conjunctival lacerations may overlie more serious scleral injuries.
- Severe subconjunctival hemorrhage (often covering 360 degrees of bulb conjunctiva)
  - retrobulbar hemorrhage
  - occult scleral rupture
  - STAT REFERRAL
**Cornea and Sclera**

- Check for Seidel’s Sign

---

**Patient Case #3**

- 25 year old Indian male
- Same day referral from UCONN Infirmary, patient was exposed to trifluoroacetic acid from a chemical experiment explosion in the laboratory.
- Swollen, painful red eye that was shut upon presentation
- Vision was relatively stable with excessive tearing.
- At laboratory bench, immediate action taken to flush with a Morgan Lens present for several minutes.

---

**Exam**

- VAsc 20/30 OD, 20/20 OS
- Positive findings:
  - 2 areas of epithelial and intrastromal central corneal defects measuring approximately 4 mm in size (~25% of the cornea)
  - 1+ – 2 bulbar and palpebral conjunctival injection/hyperemia
  - pH measurement: 7
- IOP(cc) Ta 18mmHg OD, 16mmHg OS at 2:18 pm
- No Seidel Sign: Must rule out necrotizing tissue for risk of perforation

---

**Acid vs. Basic Chemical Burn Scales**

<table>
<thead>
<tr>
<th>#</th>
<th>Acid Burns</th>
<th>Basic Burns</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Described as a “flash fire”</td>
<td>Described as a “stove top”</td>
</tr>
<tr>
<td>2</td>
<td>Instantaneous destruction of the conjunctiva, cornea, and full-thickness limbal stem cells</td>
<td>Immediate pain and inflammation</td>
</tr>
<tr>
<td>3</td>
<td>1-2 hours after exposure</td>
<td>3-4 hours after exposure</td>
</tr>
<tr>
<td>4</td>
<td>Immediate pain and 1-2 hours after exposure</td>
<td>Delayed pain and 3-4 hours after exposure</td>
</tr>
<tr>
<td>5</td>
<td>Immediate pain and 1-2 hours after exposure</td>
<td>Delayed pain and 3-4 hours after exposure</td>
</tr>
<tr>
<td>6</td>
<td>Immediate pain and 1-2 hours after exposure</td>
<td>Delayed pain and 3-4 hours after exposure</td>
</tr>
<tr>
<td>7</td>
<td>Immediate pain and 1-2 hours after exposure</td>
<td>Delayed pain and 3-4 hours after exposure</td>
</tr>
</tbody>
</table>

---

**Treatment**

**Standard Care (I/II)**
- Cyclopia
- Topical Antibiotics (ointments to fluoroquinolones)
- Topical Steroids (Yes, they do help!)
- Preservative Free AT
- Oral Vit C (2 g)
- Doxycycline (100 mg)
- Debridement

**Advanced Care (III/IV)**
- Acetic Acid (97%)
- Chlor (1%)
- Platelet Rich Plasma
- Extirpation
- Amniotic Membrane
- Limbal Stem Cell Transplant
- COMET
- Boston Keratoprosthesis
Amniotic Membranes

- Fetal Wound Healing
- Rapid uptake of nutrients and mobilization of stem cells.
- Similar to therapeutics, earlier initiation of membrane allows for better response.
- Cautionary Note
  - Wet cryopreserved = Wound Healing
  - Dry cryopreserved = Wound Coverage

Savage Commentary

“People are not Perdue Oven Stuffer Chickens with pop up timers.”

Words of Caution…

- A white and quiet eye is not always better
- Indicative of alkali burn that has caused diffuse conjunctival ischemia and blanching of vessels.

Patient Case #4

- 30 yo Caucasian female
- Windham Hospital Emergency Room for a Girl Fight at the Strip Club after candle holder with hot wax candle thrown at head.
- Swollen, painful red eye that was shut upon presentation
- Vision is significantly decreased and pain scale is...
- Let’s talk about the background to the present scenario
Exam

- VA: 20/200 OD, 20/20 OS
- Positive findings:
  - Geographic central corneal epithelial defect measuring approximately 5.5 mm round in size (~70% of the cornea)
  - 2+ bulbar conjunctival injection/hyperemia
  - Luckily, no anterior chamber reaction (Yet...)
- Unable to get IOP measurement at initial visit
- No Seidel Sign

Recurrent Corneal Erosion (Syndrome)

- Chronic relapsing disease of corneal epithelium
- Characterized by disturbance of epithelial basement membrane
- Defective adhesions
- Recurrent breakdown of corneal epithelium
- Redness, photophobia, tearing
- Usually at night or upon awakening
- May be related to REM during sleep cycle

History

- First reported in 1872
- Hansen: "Intermittent neuralgic vesicular keratitis"
- Antecedent trauma
- Szili (1900): "epithelial irregularities and gray dots"
- Stood (1900): "trauma to corneal epithelium and anterior stroma → inability of new epithelium to form normal attachments to injured anterior surface of stroma."
- Vogt (1921): "neurotrophic corneal epithelium and anterior stroma → inability of new epithelium to form normal attachments to anterior surface of stroma."

Epidemiology

- Case Series; Brown, BJO 60:84-96, 1976
- Age 24-73
- Highest incidence in 3rd and 4th decade (Avg: 42.5 yo)
- Initial abrasion to 1st recurrence: 2 days – 16 yrs
- Dominant inheritance in 3%
- 10% of cases are bilateral

Most Common Symptoms & Frustrations

- Pain
- Watering
- Blurred Vision

Management can be frustrating for both patient and doctor
- Patient discouraged because of recurrent pain and decreased vision
- Doctor disheartened by inability to cure disease
Etiology/Pathogenesis

Primary
- Epithelial basement membrane dystrophy
- Map-dot-finger
- Dystrophies involving Bowman's layer
  - Reis-Bucklers
  - Thiel-Behnke
- Stromal dystrophy
- Lattice
- Macular
- Granular

Secondary
- Degeneration
- Trauma
- Post Refractive Surgery

RCE Rapid Fire
- Incidence of RCE 1:150 cases following a traumatic abrasion
- Majority – 87% (one study) occur within the lower half of the cornea irrespective to the etiology
  - In close proximity to Hudson-Stahli line
- Tiredness, menopause, menstruation, and alcohol were recognized as aggravating factors
- EBMD cases who suffer trauma are more likely to suffer from RCE

Anatomy Dysregulation
- Reattachment of corneal epithelium following an abrasion appears faulty
- Variety of adhesion complex defects have been observed
  - Rehybridization of BM and dermal connective tissues
  - Absence of BM and remodelling
- Corneal Epithelium
  - Downregulation of cytokine activity
  - Periocular collections of edema and amorphous debris are found within the ep (due to aberrant BM)
- Leads to elevation of epithelium and accumulation of underlying debris and the further formation of abnormal BM
- Cycle self perpetuates

Epithelium separation is maximal at night due to superficial edema induced by hypotonicity of tears caused by lack of evaporation
- During lid closure, the surface tension of the tears will cause an adherence between the lids and corneal epithelium
- Opening the eyes quickly creates a shearing force, which is greater than the force of adherence of the affected epithelium which results in epithelial avulsion

How to Communicate RCE
- Skin of the eye is not healing or bonding correctly
  - Primer and Paint
  - Crumb coat and Fondant

What To Say If “Things” Go South
- More often than not, these conversations occur after the 2nd or more commonly 3rd episode.
  - Pearl: Apologize without apologizing.
- Create an actionable plan
  - Allow for patient input
  - Explain customization
- Share latest technology
  - Motivate
Diagnosis
- Hx of previous trauma to involved eye
- SLE with indirect illumination
- Retinal illumination after dilation
- Ragged greyish-staining area of epithelium
- Cellulose sponge test looking for loose epithelium
- "positive cellulose sponge test"
- Topography
- Anterior OCT Imaging

Treatment Options
Medical – (95% successfully managed, 70% remaining symptom free x 1 yr, 40% 4 years)
- Promoting epithelial regeneration
- Patching (rest)
- Bandage contact lenses
- Antibiotics, cycloplegics, hyperosmotics, corticosteroids, immunomodulation
- Oral tetracyclines and Vitamin C

Mechanical
- When medical management is not successful
- Debridement + Amniotic Membrane
- Anterior Stromal Puncture (ASP)
- Phototherapeutic Keratectomy (PTK)
- Diamond bur superficial keratectomy
- Nd:YAG Alcohol Delamination

Words of Wisdom
- Reach out to your Optometry and Ophthalmology peers for collaborative care support or 2nd opinion.
- Be wary of long term complications
  - Dry Eye Disease
  - Lid and Palpebral Conjunctiva scarring/madarosis/shortening
  - Cicatricial Ectropion/Entropion
  - Glaucoma (15-55%)

Anterior Chamber
- A shallow anterior chamber may be the only sign of occult globe rupture and is associated with a worse prognosis.
- Rule out Hyphema
- Traumatic Iritis
- Post surgical

Patient Case #5
- A 19 year old Caucasian male presents as a same day referral from the UCONN Sports Medicine department for a left eyelid and left side of nose lacerations along with blurry vision secondary to slashing during a hockey practice.
- The lacerations have been stitched (8 interrupted 6-0 nylon sutures), but the physician’s letter is concerned about the vision in his left eye.
- The patient is in moderate pain (6 of 10 pain scale), has a subconjunctival hemorrhage 270 degrees.
- Slightly opaque corneal appearance on external exam.
- ***Anxious about his prognosis due to his playing status and scholarship***

Findings
- VA: 20/20 OD; 20/100 OS (PH 20/40)
- Pupils hard to analyze due to corneal haze OS, but appear reactive without APD OU
- No Squeak Sign
- IOP: 13 OD, 22 OS
- Gonioscopy did not reveal angle recession, 3+ 360, flat iris approach, + PAS (OS)
- AC: No hyphema OU. No cell OD, 3+ 4 cell OS
- Dilation revealed no H/T/PD 360 and mild commotio retinae. Scleral haze began to clear after administration of dilation drops and Alphagan P.
- VA post dilation was 20/20 OS.
Treatment

- External picture taken for medico-legal purposes.
- Called parents after verbal agreement with patient.
- Patient was seen daily and given the following regimen:
  - Cyclo 1% bid OS
  - PredAcetate 1% bid OS for 2 days, then cycled down thereafter based on appearance.
  - Alphagan P tid OS
- Day 2
  - VA was 20/20 OD, 20/25 OS
  - IOP was 12 OD, 14 OS
  - AC reaction dropped from 3+ to 1+ cell OS
  - No stromal haze, but commotio retinae still present

Hyphema Presentation

- Micro to Eight Ball, Hypopyon may be present

Patient Case #6

- 45 year old Hispanic male presents for an emergency with a painful right eye after the cap from his Corona Light bottle popped off as a projectile into his eye. Pain scale 10 of 10.
- VA: 20/70 (PHN) OD, 20/25+2 OS
- Multiple metal fragments in cornea—central, @2, 8
- AC: 2+–3 cell OD and Grade 1 hyphema; no cell OS
- IOP: 9 OD, 12 OS
- No prior Hx of trauma and no Hx of Sickle cell anemia

Hyphema Grading Scale

- Grade 0: No visible layering, but red blood cells within the anterior chamber (microhyphema)
- Grade I: Layered blood occupying less than one third of the anterior chamber
- Grade II: Blood filling one third to one half of the anterior chamber
- Grade III: Layered blood filling one half to less than total of the anterior chamber
- Grade IV: Total filling of the anterior chamber with blood.

Findings and In Office Treatment

- Seidel Sign was negative.
- Removed all metal fragments with 30G needle and #11 Disposable scalpel. Gentle buffing with Alger Brush thereafter.
- Gonioscopy revealed 3+ 360, no angle recession or PAS
- Dilated Fundus examination revealed mild commotio retinae, PVD, no H/T/RD 360
Treatment (at home)

- Day 1
  - Cyclo 1% bid OD only
  - Pred Acetate 1% 6x/day OD only
  - Risk of rebleed in literature, so I titrated the dose
  - Besivance qid OD only
  - Bandage lens inserted and positioned
  - Pt advised no heavy lifting, bed rest, and no drinking Corona Light or any beer bottle/can until further notice

It Gets Better...

- Days 2 to 5
  - VA is 20/30+1 OD (PHNII), 20/25 OS
  - Grade 1 Hyphema slowly resolves to resolution by day 5
  - AC reaction decreases to 0+ cell by day 5
  - No commotio retinae evident on dilated examination
  - Corneal wound sites sealing in nicely. BCL was removed on Day 2.
  - Treatment was titrated as follows:
    - Cyclo 1% remained at bid
    - Pred Acetate 1% tapered from 6-4-3 to bid by day 5
    - Besivance qid until Day 10, then stopped

Then It Gets Worse...

- He cracked open another Corona Light towards his face and flew back into the same eye about 2-3 weeks later!
  - Hyphema was Grade 0-1, started same regimen.
  - I instructed him to pop the cap off in a towel or simply away from his face next time...
  - The only residual issue was his refractive error acquired astigmatism likely due to the corneal injuries.

If you do see Hypopyon...

- Suspect Herpetic Infection or Ghost Cell Glaucoma

Iris

Lens

Uveal Prolapse= Globe
65 year old patient complains of severe headaches temporally on the right side and blurry vision in the right eye for several days. Dilated exam reveals optic nerve edema but no hemorrhages.

- What other questions would you ask?
- Are we the only providers she has seen?
- What ophthalmological information is pertinent to collect?
- How would you manage and treat this patient?
Findings

- VAacu: 20/800 OD (PH 20/400), 20/40 OS (PH 20/25)
- 2+ APD OD, sluggish
- SLE WNL and No cell evident
- Pseudophakia OU w/ mild PCD
- CNH edematous OD, no disc heme present
- OS had a question of pallor vs. pseudopallor
- 1+ RPE changes, moderate sized drusen x2
- 1 Cotton-wool spot seen along the sup arcade

Diagnosis and Treatment

- AAION w/ tentative GCA/Temar Arteritis pending biopsy
- Sent to ER immediately for further evaluation and recommended administration of corticosteroids prior to biopsy even with a pending physical examination.
- Bloodwork for ESR/CRP and CBC w/ differential given to patient to hand deliver to ER team

Unfortunately, the damage was done. He survived the incident, but his vision was CF 2’ post treatment.

Urgent Care Equipment & Supplies

- Alger Brush
- Spud
- pH Indicator (0-13)
- Fox Shield
- Media for Culturing (ie. Plates, Rapid Culture Tubes)
- Betadine Wash
- Rapid Pathogen Screening
- Glaucoma Medications: topical and oral for emergencies
- Steroids and Mydriatics for Acute Iritis/Iridocyclitis
- Topical Anti-bacterial Medications

Annual Exams REQUIRED

- Ocular Trauma Patients followed for life:
  - Angle recession glaucoma
  - Cataract
  - Peripheral retinal tear
- Statistics indicate that patients who have trauma in one eye are likely to have trauma in the other eye and are more likely to die from trauma later in life.

An ounce of prevention is worth a pound of cure. -- Benjamin Franklin
Systemic and Ocular Manifestations of Lyme Disease

Presented by:
Dr. Michael Cooper, OD
Solinsky EyeCare, LLC
West Hartford, CT
coopadre@gmail.com

Disclosures
- The content of this presentation was prepared independently by Michael Cooper, OD without input from members of the ophthalmic community.
- Dr. Cooper is affiliated with Allergan, Alcon Surgical, BioTissue, Shire, JUVC, TearScience, Graebon, Bausch + Lomb/Valeant, Quidel, Menilolatum, and TearLab as a consultant/speaker.
- There is no direct financial or proprietary interest in any companies, products or services mentioned in this presentation.
- The content and format of this course is presented without commercial bias and does not claim superiority of any commercial product or service.

The Ancient Tick: Palaeoborrelia dominicana
This tick trapped in ancient amber from the Dominican Republic is between 15 million and 20 million years old. Before it died, it was carrying the type of bacteria that causes Lyme disease.
Credit: Photo by George Poirier, Jr., courtesy of Oregon State University

The Walking Dead Origin Story?

Historical Relevance
- The oldest documented case of Lyme disease in humans comes from the famous 5,300-year-old ice mummy dubbed Oetzi, discovered in the Eastern Alps about 25 years ago.
- Initially thought to be an unknown arthritis condition, the first cluster of adult and pediatric cases was noted in 1975 in Old Lyme, CT.
- By 1977, the first 51 (mostly pediatric) cases of “ Lyme arthritis” were described, and the Borrelia burgdorferi (black-legged) tick was linked to the transmission of the disease.
- In 1982, Borrelia burgdorferi was discovered, and a brochure was distributed by the arthritis Foundation for public health purposes.
- Serology testing began in 1984.
Across the Pond

- Illness consistent with Lyme disease was reported in Europe as early as 1883.
- Lyme disease is now recognized as the most common vector-borne disease in both Europe and North America.

Picking Up Steam

- In 1987, Lyme Disease became a reportable condition to the CT Department of Public Health.
- 1998 marked the beginning of national media attention to the disease as more serious cases emerged throughout the US.

Let’s back up though for a moment and consider this...

Snackable Bits

- More than 22 variants caused by tick bites
- B. Miyamotoi is resistant to doxycycline, but exceedingly rare (10/100).
- Powassan Virus is a Flavivirus, the latest to see press time—no current treatment available.
- Babesia and Anaplasma have seen tremendous incremental increase in the past 5-8 years.

B. burgdorferi Spirochetes

Case Report #1

45 year old Caucasian male presents with bilateral iridial, red eyes for the past month. He has a previous medical history of hypertension, elevated cholesterol, and a fractured left arm. Upon further questioning, the patient reveals a past social history of marijuana use with cessation approximately 10 years ago. His vision is 20/25 in the right eye and 20/20 in the left eye, but “blurry.”

1) What other questions would you ask?
2) Are we the only providers he has seen?
3) What ophthalmological information is pertinent to collect?
4) How would you manage and treat this patient?

B burgdorferi Genome

Fraser and Carriero et al. sequenced the genome in 1997-2000
- Contains a linear chromosome of 1.5 Mb.
- Contains 21 linear and circular plasmids with a combined size of <0.5 Mb.
- Consor in nature, minimal ability for recombination or transfer of plasmid (<1%).

High genetic diversity within Borrelia populations and the disparity in the genetic structure between Borrelia and its tick vector are likely consequences of strong balancing selection on local Borrelia clones.
- Evolutionary and ecological impact has led to the last ice age to modern times about 20,000 years ago.
- Ticks the shifting environment helps shape the bitewinging of tick to host.
Spirochete Tricks

Immune evasion:
- Consistent with their genomic characterization as an extracellular pathogen for which antibody, complement, and phagocytes are critical for host defense.
- A rich salivary protein to shield against host antibodies and complement. Lyme borreliosis also expresses proteins that bind host factor H to further inhibit complement-mediated lysis.
- Antigenic variation of outer surface protein B5E is required for long-term survival of the pathogen in mammalian subsets specific antibody-mediated clearance.
- As infection progresses, Lyme borreliosis may reduce surface lipoprotein expression to further impair immune clearance.

"Spirochete tricks: Remember they burrow into tissue, leading to the chronic "arthritic" effect."

B microti: What is it?

- Classified in the Phylum Apicomplexa
- It's an obligate parasite of the genus Babesia using the I. scapularis vector for host transmission.
- Although more than 150 Babesia species have been reported, relatively few have caused documented cases of human infection; these include but are not limited to B. microti, B. divergens, B. duncani, and a currently unnamed agent designated MO1.
- It's Unique and Small
  - 3 nuclear, 1 mitochondrial, and 1 apicoplast chromosomes encoding 3500 proteins; several of which are species specific.
  - The size of the organism may be tied to negative evolution from an ancestral line.
  - Genome-wide phylogenetic analysis indicate that B. microti is significantly distant from all species of Babesia and Theileria and defines a new clade.
  - Mitochondrial genome is circular; no other member of Apicomplexa illustrate this pattern.

Anaplasma Phagocytophilum

Multiplying classification:
- Anaplasmataceae, in the order Rickettsiales, and they are classified as a protozoan.
- Was referred as Ehrlichiosis until early 2000, now called Anaplasmosis.
- Obligate parasite.

Small Genome and Missing Parts:
- 0.6-1.5 Mb
- Undergone several types of reductive evolutionary processes as they have lost redundant genes.
- Developed dependence on the host cell for necessary functions.
- Gran-negative organism that lacks peptidoglycan and lipopolysaccharides.
- Makes up for this deficiency by using the host to derive cholesterol to bulk up the cell wall.
- Cholesterol-rich cell walls may also function as ligands for stimulation of innate and acquired immune responses.

Life Cycles

- B. burgdorferi (lyme)
  - The life cycle of I. scapularis generally lasts 2 years, during which the tick takes 3 blood meals, one each as larva, nymph, and adult.
  - Ticks are infected when they hatch from eggs; they acquire B burgdorferi by feeding on an infected reservoir hosts, particularly mice, shrews, other small mammals and various species of birds.
  - Infected ticks are able to transmit the pathogens during subsequent feedings to new reservoir hosts, thereby perpetuating the natural cycle. Unlike reservoir hosts, humans are incidental or dead-end hosts that do not sustain large numbers of spirochetes in their tissues.
  - Adult ticks feed preferentially on deer; which are immune to B Burgdorferi but play an important role in the ecology of disease by transporting ticks and supporting tick populations.
Life Cycles: Part 2

- Rickettsia (Rocky Mountain spotted fever):
  - Life cycle involves two hosts, which include a rodent, primarily the white-footed mouse, and a tick in the genus *Ixodes*. During a blood meal, a *Rickettsia*-infected tick introduces rickettsiae into the mouse host. Rickettsiae enter endothelial cells and undergo asexual reproduction (fission).
  - The definitive host is the tick. Once ingested by an appropriate tick, rickettsiae are reactivated and undergo a sporophorous cycle resulting in sporoblasts. Sporoblasts are transovarially transmitted to the next generation of ticks. Sporulated rickettsiae that can cause disease in humans are transmitted to the next generation of ticks.

- *Babesia* (Babesiosis):
  - Life cycle involves two hosts, which include a rodent, primarily the white-footed mouse, and a tick in the genus *Ixodes*. During a blood meal, a *Babesia*-infected tick introduces sporozoites into the rodent host. Sporozoites enter erythrocytes and undergo asexual reproduction (schizogony).
  - The definitive host is the tick. Infected erythrocytes are ingested by the next tick, which undergoes a sexual cycle involving gametocytes and oocysts. Oocysts are transovarially transmitted to the next generation of ticks.

- Humans enter the cycle when bitten by infected ticks by introducing sporozoites into the host. The route of infection is via inoculation of sporozoites into the skin. Sporozoites then enter erythrocytes, multiplying asexually.

- Humans can become infected by either a tick bite or by contact with infected blood.

- Humans usually are dead-end hosts. However, human-to-human transmission is well recognized to occur via contaminated blood transfusions.

- Became a reportable disease in 2011.
Epidemiology

- Most common reported vector-borne disease coming in at 30,000 cases per year in the US.
  **The true number is likely 10 fold higher at 300,000 cases**
- Lyme disease has been a nationally notifiable condition in the United States since 1991.
- It is important to note that surveillance data are captured by county of residence, not county of exposure.

Case definitions are reviewed periodically, as in 1996 to clarify laboratory criteria and again in 2003 to allow reporting of probable cases.

US Incidence

- During 1992 to 2013, US states and territories reported 430,540 confirmed Lyme disease cases to the CDC.
- Annual case counts increased approximately 3-fold during the period, from 9968 confirmed cases in 1992 to 27,203 confirmed and 9104 probable cases in 2013.

**For Vermont, the incidence is the highest in the US (78.8).** As of 2015, the CDC reported the number of cases confirmed is 491 and probable is 279.
- Dating back to 2005, there were only 54 reported cases.

Fast Facts

- In 2015, 95% of confirmed Lyme disease cases were reported from 14 states:
- Heavier concentration of cases are noted most in the Northeast and Upper Midwest.
- Areas of highest incidence with county-level rates in excess of 200 per 100,000 population include Windham (County in Connecticut [Where I practice]).

*Remember, this is just Borelia burgdorferi, not its 22 other brothers and sister variants globally.*

Domestic and Global "Friends"

<table>
<thead>
<tr>
<th>Name of species of Borelia burgdorferi sensu lato</th>
<th>North America</th>
<th>Europe</th>
<th>Asia</th>
</tr>
</thead>
<tbody>
<tr>
<td>D. americanae</td>
<td>D. alticola</td>
<td>D. atratus</td>
<td></td>
</tr>
<tr>
<td>D. andersoni</td>
<td>D. byssolamphus</td>
<td>D. genetica</td>
<td></td>
</tr>
<tr>
<td>D. bertholdi</td>
<td>D. caputmedusae</td>
<td>D. eruchi</td>
<td></td>
</tr>
<tr>
<td>D. burgdorferi</td>
<td>D. burgdorferi</td>
<td>D. hardia</td>
<td></td>
</tr>
<tr>
<td>D. butleri</td>
<td>D. butleri</td>
<td>D. kutscheri</td>
<td></td>
</tr>
<tr>
<td>D. definiens</td>
<td>D. definiens</td>
<td>D. mitsukurii</td>
<td></td>
</tr>
<tr>
<td>D. farmelo</td>
<td>D. farmelo</td>
<td>D. rudolphii</td>
<td></td>
</tr>
<tr>
<td>D. hawkinsi</td>
<td>D. hawkinsi</td>
<td>D. tianjinensis</td>
<td></td>
</tr>
<tr>
<td>D. huronensis</td>
<td>D. huronensis</td>
<td>D. wtoni</td>
<td></td>
</tr>
<tr>
<td>D. louisiana</td>
<td>D. louisiana</td>
<td>D. tianjinensis</td>
<td></td>
</tr>
<tr>
<td>D. scutulosa</td>
<td>D. scutulosa</td>
<td>D. tianjinensis</td>
<td></td>
</tr>
<tr>
<td>D. sylvestris</td>
<td>D. sylvestris</td>
<td>D. tianjinensis</td>
<td></td>
</tr>
<tr>
<td>D. winnepesaukee</td>
<td>D. winnepesaukee</td>
<td>D. tianjinensis</td>
<td></td>
</tr>
</tbody>
</table>

Global Incidence

Europe:
- Rabies in wild rabbits tend to be higher in Eastern Europe compared to Western Europe and the relative frequency of infection with the different genospecies seems to vary across regions.
- Ticks collected in the northern and eastern regions of Europe (eg, Scandinavia, Baltic states, Czech Republic, Slovenia, Croatia, Bulgaria) are more likely to carry D. burgdorferi, whereas those from Western Europe countries (eg, Austria, Switzerland, United Kingdom) are more likely to be infected with D. minor.
- The distribution of rickettsias also extends into the northern reaches of Morocco, Algeria, and Tunisia, where they are most often infected with D. cimexae.

**Reporting practices vary throughout the EU and non-EU countries.**
Global Incidence

Asia

- The distribution of *B. afzelii*, the principal vector in Asia, extends from Western Russia, where it overlaps with *Ixodes*, eastward through Mongolia and China to the Pacific Ocean and Japan. This species transmits *B. afzelii*, as well as Asian and European variants of *B. burgdorferi*. It is not known to transmit *B. garinii*.

- In Russia, official records on Lyme borreliosis have been kept since 1992 with reported incidence in endemic areas generally ranging from 5 to 10 per 100,000 population. However, considerably higher rates are reported in areas northeast of Moscow in Kirov region, in the Sverdlovsk (Sverdlovsk) region, and Western Siberia.

- *B. garinii* strains have been isolated from rodents and ticks in at least 20 provinces in China, including Heilongjiang in the northeast, Xinjiang in the northwest, and Guizhou, Hunan, and Hubei provinces in Southern China. *B. garinii* and *B. afzelii* are among the isolated strains, and human illness has been detailed among forestry workers in Heilongjiang Province.
**The Great Imitator**

Here are just some of the conditions that can be confused with Lyme:
- Adrenalin’s disease
- Acute disseminated encephalomyelitis
- Vedd encephalitis
- Multiple sclerosis
- Bell palsy
- NLE
- Diphtheria
- SIH
- Bipolar Disorder

---

**What I Order for Lyme**

- From my humble perspective, if a Lyme Titer even with a retest is not helpful
- Go for the Gold: The Antibodies (IgG and IgM)
- Lyme Disease: Need of at least 3 IgG bands to be a positive result

**Babesiosis Reference Range**

- Babesia microti Antibodies IgG=1:64 Babesia microti Antibodies IgM=1:20
- Anaplasma and/or Babesia: Range:
  - A. phagocytophilum IgG=1:64 A. phagocytophilum IgM=1:120
  - E. chaffeensis IgG=1:64 E. chaffeensis IgM=1:120

---

**Special Note from CDC**

Remember what I just said about the title?
- Still order the enzyme immunoassay (EIA)
- In CT, it’s automatic, but may vary by state.
- Conform to the CDC guidelines to stay within the appropriate practice patterns.
- Avoid ordering excessive bloodwork as this has been found to insufficent in diagnosis and treatment.

---

**Two-Tiered Testing for Lyme Disease**

**First Test**

- Disease N/A
- Risk factors positive
- Symptomatic Lyme

**Second Test**

- Beta-lactamase positive
- Western blot positive
- IgG and IgM negative

Consider alternate diagnosis
- Patient with symptoms consistent with Lyme disease for ≥ 90 days, consider obtaining a confirmed serum

---

**Lyme Treatment**

**Drug**

**Dosage for adults**

<table>
<thead>
<tr>
<th>Preferred oral regimens</th>
<th>Dosage for children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxycycline</td>
<td>100 mg twice per day</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>500 mg twice per day</td>
</tr>
</tbody>
</table>

**Dosage for children**

- Also recommended for children aged 5-18 years
- For children aged 5-18 years, 50 mg per day or 2 divided doses (maximum, 100 mg per day)

**Cellulosome**

- 500 mg twice per day
- 39 mg per day in 2 divided doses (maximum, 600 mg per day)

**Used alone**

- Doxycycline
- Amoxicillin

**Combination therapy**

- For recommended dosage regimens, see footnotes in table 3
- For recommended dosage regimens, see footnotes in table 3

**Alternative parenteral regimens**

- Ceftriaxone
- 1 g intravenously once per day

**Alternative parenteral regimens**

- Ceftriaxone
- 1 g intravenously every 4 h

- Penicillin G
- 250-50000 100-200000 60-90 per day

**New Drug Candidates**: Fosfomycin and FR900098

---

**Babesiosis Treatment**

- In the event of Babesiosis, give a 10-day course of oral or injectable treatment
- For patients with severe disease, a combination of doxycycline and rifampin is recommended

**Treatment Time**: 7-10 days
**Anaplasmosis Treatment**

Doxycycline is the first-line treatment for adults and children of all ages:
- **Adults:** 100 mg every 12 hours
- **Children under 40 kg (100 lbs):** 2.2 mg/kg body weight given twice a day

**Dosing Time:** 9-14 days

- **In B. burgdorferi infected children younger than 12 years:**
  - Doxycycline should be continued until the patient is afibrile for 3 days, with the remainder of the 14-day course completed with an alternative agent active against B. burgdorferi (e.g., amoxicillin or florfenicol) to minimize the risk of dental discoloration.
  - Patients who fail to respond clinically to doxycycline monotherapy after 72 hours should be evaluated for an alternative diagnosis or the possibility of Robeson co-infection.

---

**Prevention**

1. **Clothing**
   - Tight-fitting clothes
   - Hats
   - Long sleeves and pants with elastic bands

2. **Permethrin (DEET)**
   - Be wary of herbal remedies

3. **Inspecting Pets**

4. **Inspecting Young Children**
   - a) Removing ticks promptly

---

**Secret Weapon: Guinea Fowls**

African Guinea Fowls have proven to be effective in removing ticks by consumption within the grass or weeds in your yard.

*They also "fertilize" your lawn!*

---

**Proper Tick Removal Technique**

- **Wrong:** Removing the tick from the abdomen is incorrect since it will lead to the tick biting more of the parasite into the wound site.

- **Correct:**

**Be a Role Model**

1. **Techniques to share the progress with your patient**
   - Direct information is paramount.

2. **Developing a relationship with a compounding pharmacy**
   - Periodically call to ensure relationship is maintained.

3. **How to co-manage with infectious disease specialists and ICP’s**
   - Always send letters.
   - Fill out appropriate paperwork.

4. **Follow-up protocol in my practice**

---

**Intro**
Hypothetical content based on the provided images and raw text:

**Herpes Keratitis: A Review from A to Z**

Michael Cooper, OD
Solinsky EyeCare
West Hartford, CT
coopadre@gmail.com

- 35 yr old Caucasian Male
- Day 1: Blisters on lip...
- Day 2: 104°F and chills
- Threaded white lesions on tonsils, vesicles on gums, and multiple lid blisters
- Trouble Swallowing

Dx: Herpetic Pharyngotonsillitis & Gingivostomatitis

**Disclosures**

- The content of this COPE Accredited CE Presentation was prepared independently by Michael Cooper, OD without input from members of the ophthalmic community.
- Dr. Cooper is affiliated with Allergan, Alcon Surgical, BioTissue, Shire, JJVC, TearScience, GlaxoSmithKline, Bausch + Lomb/Valeant, Quidel, Mentor, and TearLab as a consultant/speaker in the past 12 months.
- There is no direct financial or proprietary interest in any companies, products or services mentioned in this presentation.
- The content and format of this course is presented without commercial bias and does not claim superiority of any commercial product or service.

**Herpesviridae**

- Members of the herpesvirus family have been identified in more than 80 different animal species.
- Eight have been identified as human pathogens.
- Herpes viruses are a leading cause of human viral disease, second only to influenza and cold viruses.
- Herpes viruses infect most of the human population and persons living past middle age usually have antibodies to many of the human herpesviruses.

**Herpesviridae Composition**

- Comprises large, DNA-containing enveloped viruses

**Infection and Location**

<table>
<thead>
<tr>
<th>Designation</th>
<th>Common Name</th>
<th>Subfamily</th>
<th>Associated Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>HHV-1</td>
<td>HSV-1</td>
<td>Alpha</td>
<td>Oral Herpes (cold sore), Genital Herpes</td>
</tr>
<tr>
<td>HHV-2</td>
<td>HSV-2</td>
<td>Alpha</td>
<td>Genital Herpes</td>
</tr>
<tr>
<td>HHV-3</td>
<td>VZV</td>
<td>Alpha</td>
<td>Chicken Pox, Shingles</td>
</tr>
<tr>
<td>HHV-4</td>
<td>EBV</td>
<td>Gamma</td>
<td>Mononucleosis, Lymphoma, Carcinoma</td>
</tr>
<tr>
<td>HHV-5</td>
<td>CMV</td>
<td>Beta</td>
<td>Mononucleosis, Retinitis, Transplant Rejection</td>
</tr>
<tr>
<td>HHV-6</td>
<td>HHV-6</td>
<td>Beta</td>
<td>Roseola infantum, Mononucleosis syndrome, Chronic fatigue syndrome, Multiple Sclerosis?</td>
</tr>
<tr>
<td>HHV-7</td>
<td>HHV-7</td>
<td>Beta</td>
<td>Roseola infantum?, Mononucleosis syndrome?</td>
</tr>
<tr>
<td>HHV-8</td>
<td>KSHV</td>
<td>Gamma</td>
<td>Kaposi’s Sarcoma</td>
</tr>
</tbody>
</table>

**Outside of the Eye World…**

- 35 yr old Caucasian Male
- Day 1: Blisters on lip...
- Day 2: 104°F and chills
- Threaded white lesions on tonsils, vesicles on gums, and multiple lid blisters
- Trouble Swallowing

Dx: Herpetic Pharyngotonsillitis & Gingivostomatitis
Pump the Brakes: How Do You Break the News?
a) Rip it off like a band aid ala 40 Year Old Virgin?
b) Sympathize and drone on for 5-10 minutes?
c) Sympathize, state the facts, and deliver your tx plan?
d) I don’t want to tell them, let’s delegate it the technician!

Pregnancy and HSV
○ Can you treat these patients?
○ What do you treat with?
○ How would you communicate these findings and to who?

α herpesviruses
○ Fast replicating (“Herpes Steroid Provocation”)  
○ Variable host range  
○ Typically destroy host cell (lysis)  
○ Latency established in sensory ganglia  
○ 90% Seropositive  
○ Initial infection is typically subclinical (6 mo – 6 yr)  
  ▪ Self limiting– Usually

Herpes Simplex virus-1 and 2  (HSV-1/HSV-2)  
Varicella-Zoster virus  (VZV)

Herpes Simplex Virus
There are two types with very similar characteristics  
○ HSV-1  (HHV-1)  
○ HSV-2  (HHV-2)  
The genome of HSV encodes a number of enzymes, including  
○ DNA-dependent DNA polymerase*  
○ Thymidine kinase*  
○ Ribonucleotide reductase  
○ Serine protease  
○ Protease, RNase  
*Since these are viral enzymes, they represent reasonable targets for drug therapy

Myth or Reality?
○ HSV-1 and HSV-2 first infect cells of the mucoepithelia, or enter through wounds.
  
  True!

○ HSV-1 is only above the waist?  
○ HSV-2 is only below the waist?
  
  False!

Latency
○ HSV also infects neurons that innervate the epithelial tissue  
○ The virus travels along the neuron (retrograde transport)  
○ Oral mucosa → trigeminal ganglia  
○ Genital mucosa → sacral ganglia  
○ A latent infection is established in the nervous tissue, but not much is known of the mechanism of the Latency Activating Transcript (LAT)
Several agents may trigger recurrence:
- Mental Stress or Fatigue
- Exposure to strong UV sunlight
- Fever
- Localized trauma (surgery)
- Hormonal changes (menstruation)
- Temperature changes
- Endogenous prostaglandins (e.g., Latanoprost)
- The virus can travel back down the nerve axon and arrive at the mucosa that was initially infected.
- Vesicles containing infectious virus are formed on the mucosa and the virus spreads.

The virus can travel back down the nerve axon and arrive at the mucosa that was initially infected. Vesicles containing infectious virus are formed on the mucosa and the virus spreads.

Recurrent Rates of ocular HSV (Liesegang et al. 1989)
- 122 patients over 33 years
- Mean age of initial onset = 37.4 years
- 36% after 5 years
- 63% after 20 years
- After a second episode, 70-80% had another recurrence within 10 years.

**Varicella-Zoster Virus (VZV)**

Zoster means girdle, from the characteristic rash that forms a belt around the thorax.

Rash along dermatomes

**Herpes Zoster Ophthalmicus**

- Human Herpes Virus 3 (HHV 3)
- Causes two distinct clinical conditions
  - Varicella (Chickenpox)
  - Herpes Zoster (Shingles)

- Following chickenpox-retrograde spread of virus along sensory nerves to dorsal root ganglia
- Trigger factors cause virus to travel via sensory nerves to skin and eye

**Reactivation**

**Recurrence by the Numbers**

- United States: 20,000 new cases annually
- 28,000 reactivations annually
- United States: Roughly 900,000 people with the disease

**Ocular Manifestations of HSV**

- Blepharitis
- Conjunctivitis
- Scleritis
- Keratitis
  - Epithelial
  - Stromal
  - Endothelitis
    - Disciform is most common
- Iridocyclitis (How would you treat here??)
- Retinitis

**Herpes Zoster Ophthalmicus**

- Ophthalmic division of trigeminal nerve
- Approximately 15% of Herpes Zoster
- Usually in elderly
  - Rare under 45, but that’s changing…
  - Consider immuno-suppression /AIDS
- Rarely with maxillary division
- Overall 50% develop ocular involvement
- Hutchinson’s sign (nasociliary nerve) in 30%
  - Correlates strongly with ocular involvement

- Blepharitis
- Conjunctivitis
- Scleritis
- Keratitis
  - Epithelial
  - Stromal
  - Endothelitis
    - Disciform is most common
- Iridocyclitis (How would you treat here??)
- Retinitis
HSV Epithelial Keratitis
- Opaque cells form coarse punctate or stellate pattern
- Desquamation of center leaves linear branching ulcer
- Day 3-5 sub-epithelial anterior stromal infiltrates
- Occasional progression to geographic ulcer
  - If undertreated
  - Healing phase - persisting pseudodendrites

Amniotic Membranes
- Fetal Wound Healing
  - Rapid uptake of nutrients and mobilization of stem cells.
  - Similar to therapeutics, earlier initiation of membrane allows for better response.
- Cautionary Note
  - Wet cryopreserved = *Wound Healing*
  - Dry cryopreserved = *Wound Coverage*

Differential Dx/Masqueraders
- Herpes Zoster Ophthalmicus
  - Typically Stellate and Peripheral (No terminal bulbs)
  - Healing corneal abrasion
  - Acanthamoeba keratitis
  - Topical drop toxicity
  - Pseudodendrite with SCL

**Pearl:** If there is any semblance of a linear branch, stain with Lissamine/Rose Bengal!

Stromal Keratitis
- Interstitial (Immune Stromal) Keratitis
- Necrotizing Stromal Keratitis
Etiology
- Immune reaction to retained viral antigen

Clinical Findings:
- Stromal haze / infiltration
- Intact epithelium
- Immune ring
- Keratic precipitates
- Previous stromal scars

Clinical Course
- Often chronic and recurrent
- May occur weeks or months after IK
- May occur w/o prior hx of IK (~2%)

Persistent inflammation may lead to:
- Scarring
- Thinning
- Neovascularization
- Lipid deposition
- Loss / distortion of vision

Stromal Keratitis with Neovascularization

Clinical Signs
- Keratic precipitates
- Overlying stromal & epithelial edema
- Iritis
- Trabeculitis with increased IOP
  - This is often the primary presentation

Subtypes
- Disciform (most common)
- Linear
- Diffuse

Necrotizing Stromal Keratitis

Etiology
- Rare manifestation of HSV
- Viral invasion of stromal with severe inflammatory reaction
- Dense stromal infiltrate with overlying epithelial defect
- Thinning and perforation

‘Perfect moment to collaborate/refer to local Cornea or Uveitis Specialist’

Endothelial Keratitis

Clinical Signs
- Keratic precipitates
- Overlying stromal & epithelial edema
- Iritis
- The most common type

Subtypes
- Disciform (most common)
- Linear
- Diffuse

Disciform Keratitis

Etiology
- Immune Hypersensitivity

Signs
- Central disciform lesion
- Epithelial edema
- Stromal thickening
- Underlying fine KP
- Mild/Moderate uveitis
- Descemet’s folds
- IOP may be elevated
- Occasional Wessely immune ring
Signs

- Progressive line of keratic precipitates
- Stromal edema follows leading edge of KP's
- Difficult to manage – requires aggressive treatment

**Linear Keratitis**

**Diffuse Keratitis**

- Signs
  - Diffuse keratic precipitates
  - Diffuse stromal and epithelial edema
  - Retrocorneal plaque

**Stepping Back from the Abyss: HEDS I and II**

- 10 yr Landmark study (start date: 1989) that erased prevalent taboos and continues to define major aspects in the clinical care of herpetic eye disease
- With this being said, it was published 20+ years ago, and our understanding of ocular herpes infection and its management have progressed dramatically in that time

**Guidance is nice, but not reality**

- Assumes clear delineation between epithelial and stromal keratitis (Not always the case in practice!)
- Medications are on the market that were not included in the HEDS study. When do we prescribe them and not acyclovir and trifluridine?:
  - Valacyclovir (Valtrex®)
  - Ganciclovir (Zidovudine®)
  - Famciclovir (Famvir®)

- No guidance given for the use of topical vs. oral antivirals in forms of herpetic eye disease where equal efficacy was shown in HEDS...
- Well, they did happen to address it over the past few years!
Dendritic Epithelial Keratitis

1. Epithelial Keratitis
   a. Dendritic
      (Therapeutic dose of topical or oral antiviral agent)

      - Acyclovir (Zovirax®): 20 mg/ml 5 times daily for 7-10 days or
      Valacyclovir (Valtrex®): 500 mg twice daily for 7-10 days or
      Famciclovir (Famvir®): 250 mg twice daily for 5-10 days or
      Trichloroacetic acid solution 3% (Vistaril®): instillation of 1 drop into affected eye(s) 8 times daily may decrease dose to 5 times daily after 7 days if ulcer is healed. Treatment should not exceed 21 days because of potential ocular toxicity.

Ganciclovir ophthalmic gel 0.15% (Zirgan®): instillation of 1 drop into affected eye(s) 3 times daily while awake until healing of corneal ulcer, followed by 1 drop 3 times a day for 7 days.

End Arouneds in the Armor

Nucleoside Analogs
- Acyclovir (Zovirax®)
- Valacyclovir (Valtrex®; L-valyl ester of acyclovir)
- Famciclovir (Famvir®; diacetyl ester of 6-deoxy penciclovir)

- All suffer from the appearance of resistant HSV mutants
- Fortunately, the mutant strains are less virulent
- The drugs are ineffective against latent virus

Acyclovir vs. Valacyclovir vs. Famciclovir: What are the Differences?

ZO'VIRAX® is the common name for acyclovir, a synthetic nucleoside analog active against herpesvirus. ZOVIRAX® Capsules, Tablets, and Topical cream formulations for oral administration. Each capsule of ZOVIRAX® contains 200 mg of acyclovir; other inactive ingredients are croscarmellose sodium, and sodium starch glycolate. The capsule shell contains sodium chloride, magnesium stearate, and hydroxypropyl methylcellulose. 500 mg the same as above.

Valacyclovir capsules contain 250 mg, 500 mg, or 1000 mg of valacyclovir hydrochloride (1000 mg Acyclovir or 125 mg of valacyclovir hydrochloride), magnesium stearate, calcium silicate, polyethylene glycol 200, and the following inactive ingredients: croscarmellose sodium, hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose, polysorbate 80, sodium chloride, and titanium dioxide.

Acyclovir (Zovirax®): 400 mg twice daily or
Valacyclovir (Valtrex®): 500 mg once daily or
Famciclovir (Famvir®): 250 mg twice daily

Stromal Keratitis Management

2. Stromal Keratitis
   a. Without epithelial ulceration
      (Therapeutic dose of topical corticosteroid PLUS prophylactic dose of oral antiviral agent)

      Prednisolone 1%: 6-8 times daily tapered over greater than 10 weeks plus
      Acyclovir (Zovirax®): 400 mg twice daily or
      Valacyclovir (Valtrex®): 500 mg once daily or
      Famciclovir (Famvir®): 250 mg twice daily

      As disease comes under control, prednisolone can be tapered slowly to the lowest possible dose and frequency as determined by the patient's clinical condition. The lower the dose and frequency of topical corticosteroid, the longer the interval between subsequent dose reduction. Oral antiviral agents in prophylactic doses (above) should be maintained during corticosteroid treatment.
I dilate every patient with suspected ocular herpes regardless of absence or severity of anterior segment findings.

I warn patients to come back immediately with any change in vision or increased floaters due to possibility of delayed onset posterior disease.

I look for localized and linear KP in all uveitis patients, especially when not in Arlt's Triangle, and subtle corneal edema in known herpes patients, even when they are relatively asymptomatic, as signs of herpes endotheliitis and need for topical steroid in addition to oral antivirals.

We are all human... Learning from our mistakes... ...just like Bruce Banner.
Diabetes: Treatment and Management

Steven Ferrucci, OD, FAAO
Chief, Optometry Sepulveda VA
Professor, SCCO/MBKU

What is diabetes?
- DM is a chronic disorder characterized by a lack of insulin or increased resistance to insulin
- Insulin is needed for proper uptake of glucose
- Clinical result is hyperglycemia
  - retinopathy
  - nephropathy
  - neuropathy

Statistics
- Approximately 9.3% of US population
- 29.1 Million Americans
- 2012: 1 out of 10
- 2050: 1 out of 5 to 1 out of 3
- Another 79 million Americans have pre-diabetes and are likely to develop diabetes if they do not change habits
  - 37% of adults age 20 or older

Cost of Care
- $172 Billion in 2007 to $245 Billion in 2012 - 41%
  - $176 Billion direct costs
  - $69 Billion indirect costs
- In CA alone, $24.5 Billion (July 2015)
- Medical cost 2.3X higher in pts with DM
- Care of people with DM accounts for 1 out 5 healthcare dollars in US

TYPE 1
- Formerly IDDM or juvenile onset
- Prevalence: 0.2%
- 10% of all DM
- Most common age of onset < 30
- Destruction of insulin producing B-cells in pancreas (auto-immune? viral?)
- Total lack of endogenous insulin
- Need to be on insulin to survive

TYPE 2
- Formerly NIDDM or adult onset
- Prevalence: ~8.0%
- 90% of all DM
- Most frequent age of onset > 40
- Often asymptomatic
- Characterized by insulin resistance
- Strong genetic predisposition
  - One parent, 50% likelihood
  - Both parents, 80%
Gestational Diabetes

- Affects 4% of all pregnancies
- High risk populations:
  - Pregnant woman greater than age 25
  - Abnormal body weight
  - Have first degree relatives with diabetes
  - Hispanic, Asian, Native American, African American descent
- Screen in 24th to 28th week of pregnancy
- NO ADDITIONAL RETINAL SCREENING NEEDED

Symptoms

- Often asymptomatic, especially Type 2
- Classic symptoms
  - polydipsia
  - polyphagia
  - polyuria
- Others: weight loss, delayed wound healing, dry mouth, dry skin, recurrent infections, refractive changes

Risk Factors

- Family history
- Specific ethnic backgrounds
  - African Americans
  - Native Americans
  - Hispanic
  - Asian American
  - Pacific islander
- Sedentary Lifestyle
- Pertinent medical history
  - obesity
  - cardiovascular disease
  - HTN
  - High cholesterol
  - Polycystic ovarian syndrome
  - Psychiatric illness
  - Gestational DM
  - IFG/IGT

Traditional Diagnosis

- Fasting blood glucose > 126 mg/dL
- OGTT > 200 mg/dL (2 hour sample)
- Any random testing >200 mg/dl should be referred for further testing
- Random testing > 200 mg/dL with symptoms very suggestive of DM

New Diagnosis Criteria

- Panel of “experts” at ADA annual meeting now recommend HbA1c be used for diagnosis of diabetes
- Glycosolated hemoglobin
- Tells blood sugar control over 3 months
  - normal range 4% to 6%

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>BS Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>120</td>
</tr>
<tr>
<td>7</td>
<td>150</td>
</tr>
<tr>
<td>8</td>
<td>180</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>BS Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>210</td>
<td>9</td>
</tr>
<tr>
<td>240</td>
<td>10</td>
</tr>
<tr>
<td>270</td>
<td>11</td>
</tr>
<tr>
<td>300</td>
<td>12</td>
</tr>
<tr>
<td>330</td>
<td>13</td>
</tr>
</tbody>
</table>

- ≥ 6.5 would be indicative of DM
  - First major change in 30 years
  - In adults and children, not pregnant women
    - Advantages:
      - Convenience: no fasting
      - More accurate: average over 3 months
    - Disadvantage:
      - Cost?
Treatment of Type 2 DM

- Goal: to produce desirable blood glucose levels with minimal adverse effects and maximal patient compliance
- Treatment begins with diet and exercise and ends with insulin
- Often, adequate control can be achieved with oral agents
  - If not, insulin is utilized

Medical Management of DM

Oral Agents

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biguanide</td>
<td>Metformin (Glumetza)</td>
</tr>
<tr>
<td>α-Glucosidase Inhibitors</td>
<td>Acarbose (Precose), miglitol (Glyset)</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>Glipizide (Glucotrol), glyburide (Micronase), glimepiride (Amaryl)</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Repaglinide (Prandin), nateglinide (Starlix)</td>
</tr>
<tr>
<td>TZDs</td>
<td>Pioglitazone (Actos), rosiglitazone (Avandia)</td>
</tr>
<tr>
<td>DPP-4 Inhibitors</td>
<td>Sitagliptin (Januvia), saxagliptin (Onglyza), linagliptin (Tradjenta), alogliptin (Nesina)</td>
</tr>
<tr>
<td>SGLT2 Inhibitors</td>
<td>Canagliflozin (Invokana), dapagliflozin (Farxiga), empagliflozin (Jardiance)</td>
</tr>
</tbody>
</table>

Injectable Non-Insulin Agents

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLP-1 Agonists</td>
<td>Liraglutide (Victoza), exenatide (Byetta), exenatide ER (Bydureon), dulaglutide (Trulicity), albiglutide (Tanzeum)</td>
</tr>
<tr>
<td>Amylin Analogs</td>
<td>Exenatide (Byetta), exenatide ER (Bydureon)</td>
</tr>
</tbody>
</table>

Insulin Therapy

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal Insulin</td>
<td>Glargine (Lantus), detemir (Levemir), glargine U-300 (Toujeo)</td>
</tr>
<tr>
<td>Rapid-Acing Insulin Analogs</td>
<td>Aspart (NovoLog), lispro (Humalog), glulisine (Apidra), lispro U-200 (Humalog U-200)</td>
</tr>
<tr>
<td>Premixed Insulin</td>
<td>70:30, 75:25, 50:50 (Humulin, Novolin)</td>
</tr>
<tr>
<td>Regular Insulin</td>
<td>U-500 (Humulin R)</td>
</tr>
<tr>
<td>Inhaled Insulin</td>
<td>Afrezza</td>
</tr>
</tbody>
</table>

Medical Management of DM

Insulin Delivery Devices

<table>
<thead>
<tr>
<th>INSULIN PUMP THERAPY COMPANY</th>
<th>EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medtronic</td>
<td>MiniMed 500G, Paradigm: Revel</td>
</tr>
<tr>
<td>Tandem</td>
<td>Linx, t:slim</td>
</tr>
<tr>
<td>Animas</td>
<td>OmniPod</td>
</tr>
<tr>
<td>Accu-chek</td>
<td>Viva, OneTouch Ring</td>
</tr>
</tbody>
</table>

Current recommendations for Treatment of DM

- Control BS levels
  - HgbA1c < 7
- Control HTN
- Control Cholesterol levels
  - Total cholesterol < 200
- No smoking
- Exercise
- Yearly foot exams, dental exams, and dilated retinal exams
**Diabetic Retinopathy**

- Leading cause of blindness 20-74 year old
- 8-12% of all new cases of legal blindness
- 50,000 Americans legally blind
- Early diagnosis and treatment can decrease vision loss by 50-60%
- Factors which influence development of DR
  - duration of disease
  - control of BS

**Duration of disease**

- Type 1 Pts:
  - Retinopathy rare in 1st 3-5 years
  - After 10 yrs, 60% have some retinopathy
  - After 20 yrs, almost always present
    - 50-60% PDR
- Type 2:
  - 20% to 39% have retinopathy at time of diagnosis
  - After 15 years, 60-80% have some retinopathy
    - 20% chance of PDR

**Control of Blood Sugar**

- DCCT Trial: 1993
  - Intensive blood glucose control reduced risk of developing retinopathy by 76%
  - Slowed the progression by 54% if already had retinopathy
- UKPDS: 1998
  - for every 1% decrease in HgbA1C there is a 35% reduction in risk for retinopathy
  - 34% reduction in retinopathy progressing with good HTN control

**Diabetic Retinopathy**

- Joslin Diabetes Center study
  - Only 60% of DM’s receive “timely eye care”
  - $624 million and 400,000 patients’ sight saved if annual eye exam and appropriate treatment
- March 2001: *Ophthalmology* 35% of DM reported no annual DFE

**Diabetic Retinopathy**

- Non-proliferative Diabetic Retinopathy (NPDR)
  - mild
  - moderate
  - severe
  - very severe
- Proliferative Diabetic Retinopathy (PDR)
  - Including high-risk

**Nonproliferative Diabetic Retinopathy (NPDR)**

- Loss of retinal capillary pericytes
- Weakens capillary walls
- Causes non-perfusion in capillary beds and hypoxia
- Divided into mild, moderate, and severe (and very severe)
Mild NPDR

- Microaneurysms (ma)
- Dot/blot hemorrhages

- Follow-up: 1 yr
  - 5-10% of pts with no retinopathy will progress to retinopathy within 1 year
  - 5-10% with mild NPDR will also progress within 1 year

Moderate NPDR

- Marked hemorrhages/ma
- Cotton wool spots (CWS)
- Venous beading (VB)
- Intraretinal microvascular abnormalities to mild degree (IRMA’s)

- Follow Up: 6 months
  - as many as 16% of pts with mod NPDR can progress to proliferative disease within 4 years

Severe/ Very Severe NPDR

- 4-2-1 Rule:
  - Marked hemes/ma in all 4 quadrants
  - VB in 2 or more quadrants
  - Marked IRMA’s in one quadrant
- Very severe: 2 of the 3 above criteria

- Follow-up: 3-4 months
  - Between 10-50% of pts with this level progress to PDR within 1 year
- Laser is sometimes recommended
  - Type 2 DM, associated with a 50% reduction in the rate of severe vision loss, vitrectomy and progression to high-risk PDR

Rate of Progression to PDR

<table>
<thead>
<tr>
<th>Severity</th>
<th>1 yr</th>
<th>5 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>5%</td>
<td>14%</td>
</tr>
<tr>
<td>Moderate</td>
<td>12-26%</td>
<td>30-48%</td>
</tr>
<tr>
<td>Severe</td>
<td>52%</td>
<td>71%</td>
</tr>
</tbody>
</table>

Proliferative Diabetic Retinopathy (PDR)

- Hallmark is retinal neovascularization
  - response to ischemia from capillary closure
  - grow onto lattice of vitreous
  - new vessels are fragile and easily rupture
- Neo divided into 2 categories
  - NVD: on or within 2 DD of optic disc
  - NVE: neovascularization elsewhere

- Follow-up: Retinal consult within 2 weeks

High Risk PDR

- NVD >1/4 to 1/3 disc area
- Any NVD with a PRH or VH
- Moderate to severe NVE with VH or PRH
- Poses very high risk of severe VH and vision loss within 2 years

- Follow-up: Immediate Retinal consult (24-48 hours)
Clinically Significant Macular Edema (CSME)

- Characteristics
  - Retinal thickening at or within 500 microns (1/3 DD) of center of macula
  - Hard exudates at or within 1/3 DD if associated with thickening of adjacent retina
  - Thickening greater than 1 DD in size part of which is within 1 DD of center of macula
- May occur at any stage of retinopathy
- Treatment: Retinal consult within 2 weeks

CSME

- Level of Retinopathy
  - Mild NPDR: 3%
  - Moderate to Severe NPDR: 40%
  - Proliferative: 71%
- Type 2: Duration and Insulin
  - No insulin
    - 10 years: 5%
    - 20 years: 15%
  - On insulin
    - 10 years: 10%
    - 20 years: 30-35%

DME

- ETDRS
  - 3711 pts, 22 centers, 10 years
  - Established focal macular laser (FML) as treatment for CSME
- PROS:
  - Reduced risk of moderate vision loss by 50%
  - 95% chance of maintaining vision when guidelines followed
- CONS:
  - 12% lost >15 letters at 3 years
  - <3% gained 15 letters
  - Diffuse, chronic, lipid deposits respond poorly

Steroids for DME

- Early 2000's, before anti-VEGF, IVT was looked at treatment for DME
  - Inhibit reduction of PGs
  - Decreases permeability
  - May Decrease VEGF proliferation
- DRCR.net Ophthalmology September 2008
  - 848 eyes with CSME and VA from 20/40 to 20/320 were evaluated
  - At 2 yrs, laser is more effective and has fewer side effects than either 1 or 4 mg intravitreal triamcinolone

antiVEGF

- Lucentis, Avastin, Eylea
- Shown in multiple studies to be beneficial for DME
  - RISE
    - 18.1% of pts in sham gained ≥ 15 letters vs. 44.8% (0.3 mg) or 39.2% (0.5 mg)
    - 2.6 letters gained in sham vs. 12.5 (0.3 mg) or 11.9 (0.5 mg)
  - RIDE
  - READ
  - VISTA
  - VIVID

Protocol - T: Lucentis vs Avastin vs Eylea

- One year
  - Eylea gained 13.3 letters
  - Lucentis 11.2
  - Avastin 9.7
  - No statistical difference
- If VA was 20/50 or worse
  - Eylea gained 18.9
  - Lucentis 14.2
  - Avastin 11.8
Protocol -T

- 2 year results
  - No statistically significant difference between 3 drugs, even in those worse than 20/50
  - But better acuity with Eylea
- Bottom line:
  - It may matter which drug
  - May matter more with worse vision
  - Economics may dictate
    - In order to justify use of lucentis/eylea vs avastin, price would have to decrease by 70-80%

PDR

- ETDRS
  - Established benefit of immediate PRP in patients with PDR
- PROS
  - Showed an overall reduction rate of severe vision loss (ie 5/200) of approximately 50% in treated vs. untreated eyes
  - <4% chance of severe vision loss in 5 years w/ tx
- CONS
  - Decreased VF
  - Decreased night vision
  - CME

Protocol S

- Non-inferior study evaluating Lucentis vs. PRP
- 55 sites, 203 pts with PRP, 191 with Lucentis, as frequent as q 4 weeks
- At 2 years:
  - VA improved 2.8 letters with Lucentis vs. 0.2 with PRP
  - More VF loss with PRP: 531db vs. 213db loss
  - More vitrectomies in PRP group: 15% vs 4%

Protocol S

- Bottom line:
  - Longer Study needed
  - Economics may dictate
  - May be best with concurrent DME
  - Pt must be compliant
  - Perhaps combo of both treatments will be best?
  - Role in severe NPDR?

LUCENTIS FDA approved April 17, 2017 for treatment of ALL forms of diabetic retinopathy

Care of the diabetic patient

- Dilated retinal exams
- Timely intervention and referral to retinal specialist
- Patient education
  - inform of ocular side effects
  - retinopathy possible even with good vision
  - report ocular symptoms associated with DM
  - advise about organizations for support
Retinal and OCT Grand Rounds

Steven Ferrucci, OD, FAAO
Chief, Optometry Sepulveda VA
Professor, SCCO/MBKU

Disclosure Statement

• Speakers bureau/Advisory Board
  – Alcon
  – B&L
  – Centervue
  – Genentech
  – MacuLogix
  – Optovue
  – Science Based Health
  – Shire

Spectral Domain: Many Options

• Ease of use
• Customer support
• Integration of other technology
  – FAF
  – Color
  – MSI
• Reputation of company

What’s new in OCT?

• MORE SCANS PER SECOND
  – Up to 70 k
• WIDEFIELD
• COMBO INSTRUMENTS
  – PHOTOS
  – FAF
  – ANTERIOR SEG
• ANGIOGRAPHY

OCT Angiography: the Next Chapter in Posterior Imaging

Images retinal microvasculature without dye injection
Displays structure and function from a single imaging system

Principles of AngioVue OCTA

OCTA uses motion contrast to detect flow from OCT data
  o Rapidly acquires multiple cross-sectional images from a single location on the retina
  o Flow is the difference in signal between two sequential B-scans

2002: Time Domain OCT
2006: Spectral Domain OCT
2014: OCTA

Difference of Two OCT B-scans
Flow Signal (Red) Overlay on
Vascular Imaging...No Referral Needed

- See retinal vasculature without referring patients out of the practice
- Visualize signs of disease earlier and make more intelligent referrals
- Manage more pathology to keep patients in the practice longer
- Elevate the practice with state-of-the-art imaging technology

A New Approach to Visualizing Blood Flow

- Patient Benefits
  - Reduces patient burden to allow more frequent imaging
  - Avoid potential side-effects of fluorescein injection
- Clinical Benefits
  - Faster than a dye-based procedure
  - Ultra-high resolution imaging of retinal microvasculature
  - 3D visualization: segments retinal vasculature into individual layers

The Utility: Applications of OCTA in the Primary Eye Care Practice

- Observing dry AMD for conversion to wet
- Monitoring diabetic patients
- Visualizing vascularization in PEDs
- Identifying CHV in central serous
- Examining glaucoma patients for vascular changes

Comparison of Vascular Imaging Modalities

<table>
<thead>
<tr>
<th></th>
<th>FA</th>
<th>ICG</th>
<th>OCTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Administration</td>
<td>Dye Injection</td>
<td>Dye Injection</td>
<td>Non-Invasive, Dye-Free, OCT Scan</td>
</tr>
<tr>
<td>Image Presentation</td>
<td>2-Dimensional</td>
<td>2-Dimensional</td>
<td>3-Dimensional, Individual Layers</td>
</tr>
<tr>
<td>Vascularite Imaged</td>
<td>Retinal Vessels</td>
<td>Choroidal Vessels</td>
<td>Retinal and Choroidal Vessels</td>
</tr>
<tr>
<td>Blood Flow Visualisation</td>
<td>Dynamic, Leakage and Pooling Visible</td>
<td>Dynamic, Leakage and Pooling Visible</td>
<td>Static, Shows Flow Information at a Fixed Point in Time</td>
</tr>
<tr>
<td>Field of View</td>
<td>30° - 150°</td>
<td>30° - 150°</td>
<td>?</td>
</tr>
<tr>
<td>Procedure Time</td>
<td>30 Minutes</td>
<td>30 Minutes</td>
<td>30 Seconds</td>
</tr>
</tbody>
</table>

Macular Hole

- Present as a circular to oval depression of varying degrees in the avascular area of the macula
  - May have surrounding cuff of edema
- Most common cause is idiopathic
  - Other causes include blunt trauma, severe myopia, solar retinopathy, CME
- Highest incidence in 7th decade of life
- Women 2x as often as men

Macular Hole

- Vision typically 20/80 to 20/200 with full-thickness hole
- If pt has macular hole in one eye, 28-44% chance of macular hole in other eye w/o a PVD
  - If PVD already, very little chance
- Watzke-Allen sign useful to differentiate true hole from similar appearance
- OCT very useful
Classic Hole Classification

- Stage I: Foveal detachment, aka Impending hole
- Stage II: Partial thickness holes
- Stage III: Full thickness hole
- Stage IV: full thickness hole with vitreous separation

New IVTS Classification

- VMA: Vitreo-Macular Adhesion (stage 0)
- VMT: Vitreo-Macular Traction (stage 1)
- LMH: Lamellar Macula Hole (Stage 2)
- FTMH: Full Thickness Macula Hole (Stage 3,4)
- Macular pseudohole

FTMH

- Definition: Full thickness macular hole that affects all macular layers from ILM to RPE
- Size
  - Small: ≤250 um
  - Medium: 250um to 400um
  - Large ≥ 400 um
- Presence or absence of VMT
- By cause
  - Primary: Initiated by VMT (formerly idiopathic)
  - Secondary: from associated disease or trauma

Macular Pseudohole

- Definition:
  - Invagination or heaped foveal edges
  - Concomitant ERM with central opening
  - Steep macular contour to the central fovea with near-normal central foveal thickness
  - No loss of retinal tissue

LMH

- Symptoms
  - mild metamorphopsia,
  - limited acuity loss
  - stable vision
- Surgery is controversial
  - 25% to 75% improved visual acuity
- Therefore, monitoring seems reasonable
**Pseudohole**
- Conservative management
- PPV with membrane peel if decreased VA
- Monitor
- HAG

**VMT: Vitreomacular Traction**
- VMT syndrome is characterized by a partial detachment of the posterior detachment with persistent adherence to the macula
  - Can lead to CME, ERM, and macular hole formation
- Once thought to be relatively rare, with advent of OCT now being seen more and more
  - In one study, 8% of pts were thought to have VMT by clinical observation only, but 30% by OCT

**VAST STUDY**
- 2,179 eyes, 1,120 asymptomatic pts >40 years of age
  - Mean age 59
  - 57% female
  - 57% hyperopes, 35% myopes, 8% emmetropes
- VMA in 31% of eyes
  - Peak age 50-59
  - Less common in AA and HA

**VMT**
- More commonly encountered in older women
  - Can occur in either sex, and age, no apparent racial predilection
- Aphakia and pseudophakia are protective, as these patient typically have a complete PVD
- Pts may report decreased vision, metamorphopsia and photopsia

**VMA vs. VMT: Duker**

**VMA**
- Evidence of vitreous cortex detachment from retinal service
- Attachment of vitreous within 3 mm of fovea
- No detectable change in foveal contour or underlying tissues
- Focal: <1500 um
- Broad: >1500 um

**VMT**
- Evidence of vitreous cortex detachment from retinal service
- Attachment of vitreous within 3 mm of fovea
- Distortion of foveal surface, intraretinal structural changes, and/or elevation of fovea, but no full thickness interruption of retinal layers

**VMT**
- Clinically, very hard to diagnose
  - PVD with adherence to macular area
  - Can present as macular surface wrinkling/striae, similar to ERM, or loss of foveal reflex
  - May also note a thickened posterior hyaloid membrane
  - Retinal blood vessel distortion straightening may be present
  - Retinal thickening /macular edema may be associated

  - OCT IS THE KEY!!!!
VMT

- Natural progression of disease is rather variable
  - Slow progression possible with near normal acuity
  - Approx 10% will have spontaneous PVD and resolution
- Therefore, close monitoring may be advised for some patients

VMT

- In patients with poor vision, or symptomatic, a pars planar vitrectomy (PPV) may be considered
  - Duration, severity should also be considered
- Literature reports up to a 75% success rate and improvement of vision following PPV

Jetrea™ (ocriplasmin)

- New(ish) treatment for VMT
- Recombinant form of human plasmin that dissolves the protein links that form between the vitreous and macula, separating them nonsurgically

Jetrea™ (ocriplasmin)

- 652 eyes, 64 with ocriplasmin, 188 with placebo. Single 125 ug injection
- At 28 days
  - VMA resolved 26.5% vs 10.1%
  - Total PVD in 13.4% vs 3.7%
  - Nonsurgical closure of macular holes: 40.6% vs 10.6%
  - VA improved three lines or more: 12.3 vs 6.4%
- At 6 mos, 17.7% of pts vs. 26.6% underwent vitrectomy

Jetrea™ (ocriplasmin)

- Adverse events: 68.4% vs. 53.3%
  - Floaters (16.8% vs. 7.7%) eye pain, photopsia, subconjunctival hemorrhage
  - Serious events were 7.7% vs. 10.7%
- COST:
  - $3950!!!

Expansile Gas injection

- 15 eyes, 14 pts with symptomatic VMT injected intravitreally with 0.3ml perfluoropropane (C3F8), expansile gas
  - At 1 mos, traction release in 40% of pts (6/14)
  - At 6 mos, traction release in 60% (9/14)
  - Foveal contour restored in 47% of eyes
  - No gain in VA
  - Only 33% of pts had to have PPV
  - Horiz diameter < 750um, foveal thickness < 500 um, and low vitreous face reflectivity were very responsive (100%)
Epi-retinal Membrane

- AKA macular pucker, cellophane maculopathy
- Can be secondary to peripheral retinal disease, such as detachment or tear; a retinal vascular disease such as BRVO; inflammation; trauma or idiopathic
- Idiopathic tend to be more mild and non-progressive vs. those after retinal tear

Epi-retinal Membrane

- VA can range from 20/20 to 20/200 or worse
  - Studies show > 5% have worse than 20/200
- Often metamorphopsia is only complaint with idiopathic ERM
- Fewer than 20% of cases are bilateral
- Surgical removal is considered if severe vision loss or distortion

<table>
<thead>
<tr>
<th>AGE</th>
<th>INCIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 60</td>
<td>1.7%</td>
</tr>
<tr>
<td>60-69</td>
<td>7.2%</td>
</tr>
<tr>
<td>70-79</td>
<td>11.6%</td>
</tr>
<tr>
<td>80+</td>
<td>9.3%</td>
</tr>
</tbody>
</table>

BLUE MOUNTAIN EYE STUDY, AUSTRALIA

Central Serous Retinopathy

- Common disorder of unknown etiology which typically affects men between age 20 and 45
  - Males to females 10:1
- Serous detachment of neurosensory retina due to leakage from small defect in RPE

Central Serous Retinopathy

- Pt typically presents with fairly recent onset of blurred VA in one eye with a scotoma, micropsia, or metamorphopsia
  - VA typically 20/30-20/70
  - Often correctable with low hyperopic RX
  - Unilateral in 70% of cases

Epi-retinal Membrane

- Consider surgery if:
  - VA 20/40 or worse
  - Symptomatic
  - Visual need of patient
- 30 minute procedure
- Make sure you have an experienced surgeon!!
Central Serous Retinopathy

- Appears as a shallow round or oval elevation of the sensory retina often outlined by a glistening reflex
- FA is helpful in providing definitive diagnosis
  - Classic Smoke stack appearance (occasionally)
  - Ink-blot appearance
- OCT shows marked elevation

CSR: Risk Factors

**TRADITIONAL**
- Male > Female 10:1
- Age: Peak 20-45
- Type A personality
- Stress
- Pregnancy

**OTHERS**
- Steroid use
  - Oral
  - Topical?
  - Inhaled?
  - Injection?
- Choroidal Thickness
- Sleep apnea?
- Genes?

Central Serous Retinopathy

- 80-90% of pts will undergo spontaneous resolution and return to normal (or near normal) VA within 1-6 mos.
  - >60% resolve back to 20/20
  - Rare to have vision remain < 20/40
- Approx 40% will get recurrence
- CNVM is VERY rare occurrence, but possible

CSR

- **When to worry/refer**
  - If VA worse than 20/70
  - If pt demographics do not support
  - If does not resolve in 6 mos
  - If gets worse rather than better
  - FA/ OCT does not support diagnosis
  - “Just doesn’t feel right”
  - Pt is unable to accept vision/prognosis

Treatment

- Observation
- PDT
- Anti-VEGF
- Anti-corticosteroids
  - Rifampin
  - Mifepristone
  - Ketoconazole
  - Spironolactone/spironolactone
  - Finasteride
- Acetazolamide
- Aspirin
- Metoprolol
- H.pylori treatment
- Methotrexate
- Behavior Modification!

Solar Maculopathy

- Damage to the outer layers retina as shown on OCT
  - Outer segment of photoreceptors and RPE
- Clinical exam, small yellowish lesion
- Acuity typically 20/40 20/60
  - Little to no correlation with appearance and acuity
- Greater risk in younger individuals who are more likely to start at sun or eclipse
  - With clear lenses
  - Also, schizophrenic pts, pts on LSD, etc.
### Macular Schisis

- Relatively new entity, ≈1999 by Takano and Kishi
  - Prior to this, misinterpreted as shallow RD or even edema
- With OCT, thought to be not uncommon in highly myopic individuals with posterior staphyloma
- Characterized by intraretinal splitting, in both inner and outer retina, with cystoid spaces

### Macular Schisis

- Fairly stable with time, with mild fluctuations in vision
- Treatment (vitrectomy) generally only recommended if vitreal traction, as may lead to macula hole
- Consider OCT in high myopes with central vision problems

### OCT: Final Thoughts

- Has ushered in a whole new understanding of retinal disease
- Fast becoming the standard of care
- Many models/makes available

• THANK YOU!!
Pain Management in Optometric Practice
Blair Lonsberry, MS, OD, MEd., FAAO
Professor of Optometry
Pacific University College of Optometry
blonsberry@pacificu.edu

Agenda
• Addiction
• Opioid epidemic
• Pain management:
  — Topical
  — Orals

Addiction
• defined as a chronic, relapsing brain disease that is characterized by compulsive drug seeking and use, despite harmful consequences.
• considered a brain disease because drugs change the brain structure and how it works.
• these brain changes can be long-lasting, and can lead to the harmful behaviors seen in people who abuse drugs.

Why Do People Take Drugs
• To Feel Good:
  — Most abused drugs produce intense feelings of pleasure
• To Feel Better:
  — People who suffer from social anxiety, stress and depression begin the use of drugs to help lessen the feelings of distress
• To Do Better:
  — Some feel pressure to enhance their physical or mental edge
  — Curiosity or because others are doing it:
    — Adolescents particular prone to this type of peer pressure

Why Do People Take Drugs
• Initial decision to take a drug is typical voluntary and they may perceive that first time as producing positive effects (and often believe they can control their use).
• With increased use of the drug, other pleasurable experiences lose their appeal and more drug is required to feel “normal” and the person quickly loses the ability for self-control (which is a hallmark of addiction).

Why Do People Take Drugs
• Brain imaging studies have demonstrated that people with addiction have physical changes in areas of the brain that are critical to judgment, decision making, learning and memory, and behavior control
• It is believed that these changes alter the way the brain works and may help explain the compulsive and destructive behaviors of addiction.
Impaired Brain Function with Long Term Drug Abuse

- Long term drug use decreases the normal dopamine production or receptors making patients feel “flat”
- Patients’ require the drug in order to feel that high and in increased levels to obtain the previous “high”

Withdrawal

- The withdrawal syndrome may be very severe (except for codeine) and includes intense dysphoria (state of unease), nausea or vomiting, muscle aches, lacrimation, rhinorrhea, mydriasis, piloerection, sweating, diarrhea, yawning, and fever.
- Beyond the withdrawal syndrome, which usually lasts no longer than a few days, individuals who have received opioids as analgesics only rarely develop addiction. In contrast, when taken for recreational purposes, opioids are highly addictive.
- The relative risk of addiction is 4 out of 5 on a scale of 1 = nonaddictive, 5 = highly addictive.
Prescription Drug Abuse

- Prescription medications, including opioid pain relievers (such as OxyContin® and Vicodin®), anti-anxiety sedatives (such as Valium® and Xanax®), and ADHD stimulants (such as Adderall® and Ritalin®), are commonly misused to self-treat for medical problems or abused for purposes of getting high or (especially with stimulants) improving performance.

Opioid Abuse

- Opioid pain relievers are frequently abused by being crushed and injected or snorted, greatly raising the risk of addiction and overdose.
- There is a common misperception that because medications are prescribed by physicians, they are safe even when used illegally or by another person than they were prescribed for.

Opioid Abuse/Overdose

- The most common drugs involved in prescription opioid overdose deaths include:
  - Methadone (long acting opioid for heroin abuse)
  - Oxycodone (such as OxyContin®)
  - Hydrocodone (such as Vicodin®)
- Overdose rates were highest among people aged 25 to 54 years.
- Overdose rates were higher among non-Hispanic whites and American Indian or Alaskan Natives, compared to non-Hispanic blacks and Hispanics.
- Men were more likely to die from overdose, but the mortality gap between men and women is closing.

Opioid Abuse/Overdose

- Prescription opioids can be used to treat moderate-to-severe pain and are often prescribed following surgery or injury, or for health conditions such as cancer.
- There has been a dramatic increase in the acceptance and use of prescription opioids for the treatment of chronic, non-cancer pain, such as back pain or osteoarthritis, despite serious risks and the lack of evidence about their long-term effectiveness.

Opioid Abuse/Overdose

- Providers wrote nearly a quarter of a billion opioid prescriptions in 2013—with wide variation across states.
  This is enough for every American adult to have their own bottle of pills
- Studies suggest that regional variation in use of prescription opioids cannot be explained by the underlying health status of the population
- To reverse this epidemic, HCP need to improve the way we treat pain. HCP must prevent abuse, addiction, and overdose before they start.

Opioid Abuse/Overdose

- Research shows that some risk factors make people particularly vulnerable to prescription opioid abuse and overdose, including:
  - Obtaining overlapping prescriptions from multiple providers and pharmacies.
  - Taking high daily dosages of prescription pain relievers.
  - Having mental illness or a history of alcohol or other substance abuse.
  - Living in rural areas and having low income.
Opioid Abuse/Overdose

Anyone who takes prescription opioids can become addicted to them.

- as many as one in four patients receiving long-term opioid therapy in a primary care setting struggles with opioid addiction.
- In 2014, nearly two million Americans either abused or were dependent on prescription opioid pain relievers.
- Taking too many prescription opioids can stop a person’s breathing—leading to death.

Opioid Abuse/Overdose

Prescription opioid overdose deaths also often involve benzodiazepines.

- Benzodiazepines are central nervous system depressants used to sedate, induce sleep, prevent seizures, and relieve anxiety.
  - Examples include alprazolam (Xanax®), diazepam (Valium®), and lorazepam (Ativan®).
- Avoid taking benzodiazepines while taking prescription opioids whenever possible.

Preventing Opioid Abuse: PDMP

A prescription drug monitoring program (PDMP) is an electronic database that tracks controlled substance prescriptions.

- PDMPs can help identify patients who may be misusing prescription opioids or other prescription drugs and who may be at risk for overdose.

Preventing Opioid Abuse: PDMP

PDMPs improve patient safety by allowing clinicians to:

- Identify patients who are obtaining opioids from multiple providers.
- Calculate the total amount of opioids prescribed per day (in MME/day-morphine milligram equivalent).
- Identify patients who are being prescribed other substances that may increase risk of opioids—such as benzodiazepines.

What if you find something suspicious in the PDMP?

Patients should not be dismissed from care based on PDMP information. Use the opportunity to provide potentially life-saving information and interventions.

- Confirm that the information in the PDMP is correct.
- Assess for possible misuse or abuse.
- Discuss any areas of concern with your patient and emphasize your interest in their safety.

Alaska Optometry Opioid Statute

Maximum dosage for opioid prescriptions.

- (a) A licensee may not issue
  - (1) an initial prescription for an opioid that exceeds a four-day supply to an adult patient for outpatient use;
  - (2) a prescription for an opioid that exceeds a four-day supply to a minor; upon issuance of a prescription for an opioid to a minor, the licensee shall discuss with the parent or guardian of the minor why the prescription is necessary and the risks associated with opioid use.
Alaska Optometry Opioid Statute

- Maximum dosage for opioid prescriptions.
- (b) Notwithstanding (a) of this section, a licensee may issue a prescription for an opioid that exceeds a four-day supply to an adult or minor patient if the licensee determines that more than a four-day supply of an opioid is necessary.
  - (1) to treat the patient’s medical condition or for chronic pain management; the licensee may write a prescription for an opioid for the quantity needed to treat the patient’s medical condition or chronic pain; the licensee shall document in the patient’s medical record the condition triggering the prescription of an opioid in a quantity that exceeds a four-day supply and indicate that a nonopioid alternative was not appropriate to address the medical condition; or

Pain Signal

- Pain occurs when specialized nerve endings in peripheral tissues (nociceptors) are stimulated.
  - Nociceptors exist in high levels in the eye and orbit.
- Nociceptors are activated in response to mechanical stimulation (trauma) and chemical compounds such as serotonin, bradykinin, and histamine.
  - Prostaglandins and leukotrienes further sensitize the nerve endings to these mediators.

Inflammatory Cascade

- Steroids are the “Gold Standard” for stopping inflammation.
  - They are Non-selective in nature, unlike NSAID’s and act on multiple areas of inflammation such as:
    - Inhibit peripheral lymphocytes (T and B Cells) and macrophages.
    - Decrease amount of circulating eosinophils, basophils, and monocytes.
    - Inhibit activity of kinins.
    - Reduce the amount of histamine released from basophils.
    - Indirectly inhibit phospholipase A₂.
Steroids act at the beginning of the Arachidonic Acid Cascade.

- Unlike steroids, NSAID’s have only one mechanism for decreasing inflammation.
  - Inhibit the enzyme cyclooxygenase which produces prostaglandins, prostacyclins, and thromboxanes from Arachidonic Acid.

**NSAID’s vs. Steroids**

- NSAID’s are very successful at limiting inflammation systemically, but topically are less successful due to the lack of effect on the lipoxygenase pathway.

Leukotrienes attract white blood cells = Infiltrates.

**Cyclooxygenase Pathway**

- NSAIDs act only on inflammation through the COX pathway blocking the formation of:
  - Prostaglandins
    - Major inflammatory mediators found in virtually all tissues of the body – act locally as chemical mediators.
  - Thromboxanes
    - Promotes platelet aggregation and causes vasoconstriction
  - Prostacyclins
    - Inhibits platelet aggregation and causes vasodilation.

- There are two main enzymes involved: COX 1 and COX 2.

**Cyclooxygenase Enzymes**

- COX 1
  - Stimulated continuously by normal body physiology
    - Major player involved in secretion of mucous in the stomach and controlling blood flow to the kidneys.

- COX 2
  - Induced as the result of an immune response to cause higher levels of prostaglandins.
Products of the COX 2 Pathway

- The COX 2 Pathway is responsible for the formation of inflammatory prostaglandins.
  - These prostaglandins play a role in many ocular conditions:
    • Postoperative inflammation
    • Uveitis
    • Allergic Conjunctivitis
    • Cystoid Macular Edema
  - They are also responsible for inducing miosis through sphincter contraction independent of cholinergic stimulation.

NSAID’s also have other properties that make them useful in optometry.

NSAIDs are primarily used for post-operative care of cataract surgery patients. However, additional uses include following FB removal or corneal abrasions as pain management. NSAIDs also act as antipyretics, but fevers are rarely a big concern in optometry.

Analgesic Medications

- Three principle categories of pain relief are seen:
  - Peripherally Acting agents
    • Act on the peripheral pain receptors and prevent sensitization and discharge of the nociceptors
    • Ex: NSAIDs
  - Anesthetic Agents
    • Interrupt the pain signal between the peripheral source and the CNS target
    • Ex: Proparacaine
  - Centrally Acting Agents
    • Interact with specific receptors in the CNS to interrupt the pain message and its emotional responses.
    • Ex: Narcotics

Question

You have a patient suffering from a thermal corneal burn and rates his pain 9/10. What would you initiate therapy with to help manage his pain?

1. Topical NSAID’s (Ilevro)
2. Topical steroid (FML, Pred Forte)
3. Cycloplegia (Atropine)
4. Extra Strength Tylenol (EST) 1000 mg every 6 hours
5. Ibuprofen (OTC) 200 mg every 4-6 hours
6. 2-Tylenol 325 mg followed by 2-Ibuprofen 200 mg 3-4 hours later and continue to alternate
7. Ibuprofen (Rx strength) 400 mg every 4-6 hours
8. Tylenol 3 every 4-6 hours
9. Vicodin every 4-6 hours

Flurbiprofen 0.03% (Ocufen)

- First FDA approved topical ophthalmic NSAID.
- FDA indication: Inhibition of intraoperative miosis due to prostaglandins.
- The first topical to begin being used for inflammation leading to macular edema and dry eye – largely replaced now due to better options.
- FYI: Another early NSAID used for cataract surgery is Suprofen (Profenal).
Ketorolac tromethamine 0.5% (Acular)

- Solution available from Allergan or as a generic.
- FDA Labeling:
  - Ocular itching due to seasonal allergic conjunctivitis
  - Post-op inflammation after cataract extraction
  - Dosage: 1 drop QID
- Major Pitfall:
  - High level of stinging upon instillation
- Corneal effects: May cause keratitis; continued use may cause severe corneal adverse effects, including corneal thinning, erosion, perforation, or ulceration; may result in loss of vision. Discontinue use in patients with evidence of corneal epithelial damage.

Ketorolac tromethamine 0.4% (Acular LS)

- Equal efficacy to Acular, without the sting.
- Most widely prescribed topical NSAID.
- FDA Labeling:
  - Reduction of ocular pain and discomfort following corneal refractive surgery.
    - Dosage: 1 drop QID for up to 4 days following surgery.
- Approved for patient 3 years +

Acuvail (Ketorolac 0.45%)

- FDA Approval in 2009
  - Very Expensive for Patient Use.
- Formulated in PF vials for use in post operative cataract surgery.
- Acuvail is formulated at pH 6.8, enabling de-ionized drug delivery on the corneal surface.
- Contains carboxymethylcellulose, a viscous molecule that enables the drug to adhere to the ocular surface.
  - Dosage: BID X 2 weeks following surgery – start one day prior.

Diclofenac sodium 0.1% (Voltaren)

- Voltaren is indicated for the treatment of postoperative inflammation:
  - Cataract Extraction: 1 drop QID beginning 24 hours after surgery and continuing for 2 weeks following
  - Corneal Refractive Surgery: 1-2 drops of prior to surgery and 1-2 drops within 15 minutes and continued QID for up to 3 days.
- Available brand name and generic.
  - Bottle Size: 2.5 and 5 mL

Voltaren and Refractive Surgery

- Voltaren has been shown to inhibit the adherence of Staphylococcus epidermidis to soft contact lenses.
  - This is especially important during PRK when patients are put in bandage contact lenses to help control pain.
- The topical NSAIDs have been shown to have better pain management for these patients than oral analgesics.

Bromfenac 0.09%

- Originally FDA approved in 2005 as Xibrom for BID Dosing.
  - Approved for postoperative cataract surgery pain and inflammation.
- In 2010, ISTA received approval for once daily dosing and changed the name to Bromday.
  - ISTA was then sold to Bausch and Lomb.
- In 2012, a generic version of bromfenac 0.09% became available – this is the same medication, but is dosed BID as Xibrom previously was.
**Bromfenac 0.07% (Prolensa)**
- FDA approved in April 2013.
- 22% less medication than Bromday, but a lower pH of 7.8 making it more bioavailable.
- Solution - Available in 1.6 and 3 mL bottles from Bausch and Lomb.
- Pregnancy Category C.
- Dosage: One Drop Daily

**Bromfenac 0.075% (Bromsite)**
- FDA approved in November 26, 2016 by Sun Pharmaceuticals.
- BromSite™ is nonsteroidal anti-inflammatory drug (NSAID) indicated for the treatment of postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery.
- approved to prevent ocular pain and treat inflammation in the eye following cataract surgery.
- Dosage: One Drop twice daily starting a day before surgery and 2 weeks after

**Nepafenac 0.1% (Nevanac)**
- FDA labeling is only for the treatment of pain and inflammation following cataract surgery.
- Manufactured by Alcon and sold in 3 mL bottles.
- Only NSAID that is a suspension.
- Dosage: TID beginning at one day prior to surgery and continuing for 2 weeks.

**Nepafenac 0.1% (Nevanac)**
- First prodrug NSAID.
  - Hydrolyzed to amfenac in the AC.
  - This provides enhanced intraocular concentrations over the other topical NSAID's.
- Using Animal Models has been shown to inhibit prostaglandin synthesis in the retina and choroid.

**Nepafenac 0.3% (Ilevro)**
- FDA Approved in 2013.
  - Use for treatment of pain and inflammation associated with cataract surgery.
- Dosage: 1 Drop Daily
- Suspension that must be shaken.

**Major Side Effect of Topical NSAID’s**
- Corneal Melt
  - Must use extreme caution in eyes with epithelial compromise.
  - NSAID’s will delay wound healing (not quite to the extent as steroids, but still increase chance for infection).
  - “Melting” Ulcers will progressively take over the entire cornea.
- Most commonly seen with generic diclofenac.
  - Has also been reported 3 times in Japan with Xibrom usage.
NOV 10/23/2018

Side Effects of Topical NSAID’s

• Minor Side Effects:
  – Burning and Stinging
  – Conjunctival hyperemia
  – Corneal SPK and Blurred Vision
  – Sub-epithelial Infiltrates

• Avoiding Problems:
  – Avoid chronic long-term use
  – Absolutely avoid in “sick” corneas...degens, Fuch’s, etc

Ocular Conditions Treated with NSAID’s

• Incidents Involving Corneal Induced Pain:
  – Corneal abrasions
  – Concurrently in office with Betadine for the treatment of EKC
  – Pre/Post foreign body removal
  – Post anterior stromal puncture

  – Pearls for Use:
    • Limit use to in office or less than 1 week to avoid corneal melt.
    • Stick to recommended FDA approved dosages.

Ocular Conditions Treated with NSAID’s

• Active Ocular Inflammation:
  – Only prescribe if steroids are contraindicated and avoid using for more than 1 week.
  – Can be added to steroids to get a synergistic effect on inflammation.
    • Allergic conjunctivitis
    • Supplemental to steroids in treating reactivation uveitis
    • Supplemental to oral NSAIDs in treating scleritis
    • Treating and/or preventing inflamed pterygia and pingueculae

NSAID’s and Macular Edema

• Cataract surgery results in the release of prostaglandins which breakdown the blood-aqueous barrier and move into the posterior pole.
• Once in the posterior pole they increase vascular permeability and breakdown the blood-retinal barrier resulting in macular edema.

NSAIDs and Ocular Therapy

• “Off-Label” use in preventing and treating macular edema.

• Dosage often depends on clinical picture and operating surgeon:
  – Recommended Pre-Treatment: 1-3 days in routine patients and up to 1 week in patients at risk.
  – Recommended Post-Treatment: 4 weeks for routine patients. May take 6-12 weeks in patients at risk.

Oral Pain Management
Pain Management: Oral Analgesics

- Conditions potentially requiring us of oral analgesics:
  - Corneal ulcers
  - Herpes simplex/zoster
  - Post-surgical
  - Trauma

Managing Pain

- NSAID’s and Aspirin are not the only mechanisms optometrists can use to help manage pain in our patients.
  - Peripherally Acting Agents: Act on the peripheral pain receptors and prevent sensitization and discharge of the nociceptors.
    - Ex) NSAIDs, Salicylates (ASA), and Acetaminophen (APAP)
  - Anesthetic Agents: Interrupt the pain signal between the peripheral source and the CNS.
    - Ex) Proparacaine
  - Centrally Acting Agents: Interact with specific receptors in the CNS to interrupt the pain message and its emotional responses.
    - Ex) Narcotics (possibly Tylenol to a small extent)

Oral Analgesics: Guidelines

- Make the proper diagnosis first (ie. Don’t prescribe without knowing what you are prescribing for!)
- Treat the underlying cause for the pain
- Treat the pain at presentation...don’t wait!
- Treat pain continuously over a 24 hour schedule
- Non-prescription drugs should be first choice and tend to be low cost
- Treat patients with the simplest and safest means to alleviate pain

Oral Analgesics: Guidelines

- Mild to moderate pain is often successfully treated with acetaminophen or NSAID
- Moderate to severe pain is best treated with opioid analgesics
- Adjunctive treatments are very valuable in pain management:
  - “RICE”: rest, ice, compression and elevation
  - Mydriatic/cycloplegic useful for ocular pain
  - Bandage CL or pressure patch

Systemic NSAID’s

- NSAID’s are the drug of choice for treating mild to moderate ocular pain.
  - Very beneficial for treating systemic inflammation as well.
- All NSAID’s are rapidly absorbed from the GI tract, highly bound in the plasma, and capable of crossing the blood-brain barrier.
- Exhibit a “ceiling effect” – there is a dosage beyond which no further analgesia occurs.
  - Produce no tolerance or dependence, increasing their safety profile.
- Variability exists in patient responses to NSAID’s
  - No definitive recommendation on treatment can be given.
    - If one NSAID does not work – TRY ANOTHER.

Major Classes of NSAID’s

- Commonly Used:
  - Aspirin (ASA) and Other Salicylates
  - Propionic Acids
  - Indole acetic Acids
  - COX-2 Inhibitors
- Rarely Used NSAIDs in Optometry Include:
  - Oxacam Derivatives
    - Piroxicam (Feldane) and Meloxicam (Mobic)
  - Fenamates
    - Mexclofenamate (Mexifene)
  - Acetic Acids
    - Ketorolac (Toradol) and Etodolac (Lodine)
**NSAID’s**

- NSAID selection depends on multiple factors:
  - Clinical experience
  - Patient convenience or preference
  - History of favorable analgesic effect
  - Side effects
  - Cost

- The medications with the most effective analgesia are generally those with rapid onset of action.

---

**Aspirin (ASA)**

- Weak organic acid.

- Oldest non-opioid analgesic available today.
  - Reduces pain by inhibiting synthesis of the prostaglandin E₂ by irreversible acetylation and inactivation.
  - Has some CNS effect on pain by acting on the hypothalamus.

- Very good anti-inflammatory and antipyretic properties.

---

**Aspirin**

- Commercially available in multiple formulations and dosages.
  - Formulations include controlled-release tablets, enteric coated, etc.
    - Add buffers to help increase GI tolerability
  - Adult Dosage: 325 – 650 mg every
    - Do not exceed 4 g/day.

---

**Aspirin**

- Additional Analgesic Use: Beneficial for use with narcotics in the treatment of severe pain.

- Most Common use of ASA: Inhibit platelet aggregation in patients with history of heart attacks and heart surgery.
  - ASA inactivates COX irreversibly, causing prolonged bleeding time of 12 – 15 days or the entire life cycle of the platelet.

---

**Aspirin**

- Largely replaced as treatment for pain associated with inflammation by the other classes of NSAID’s due to the frequent side effects.
  - GI Distress: Inhibit prostaglandin synthesis and the production of a mucous lining on the stomach leading to increased gastric acid secretion.

- Symptoms include:
  - Dyspepsia (indigestion)
  - Nausea
  - Vomiting
  - Abdominal Cramping
  - Ulcerations/Bleeding/Perforation

---

**Additional Aspirin Side Effects**

- Aspirin Hypersensitivity
  - Results in:
    - Respiratory problems
    - Type 1 hypersensitivity reactions such as itching and angioedema. (Occurs within 1 hour of ingestion).
    - ASA intolerance occurs most commonly in asthmatic patients (Up to 40% of steroid-dependent asthmatics).

- CNS effects including Headache, Tinnitus, dizziness, and deafness may occur.
ASA Contraindications
• Children/Teenagers following a viral infection.
  — Associated w/ Reye’s syndrome (post-infectious encephalopathy).
• History of upper GI disease
• History of adult onset asthma
  — Can trigger attacks of severe bronchoconstriction and nasal congestion.
• Avoid in patients with bleeding disorders
• Avoid in patients who have had recent intraocular surgeries
• Avoid in patients who consume more than 3 alcoholic beverages in a day.
• Should not be used during pregnancy.
• Chronic renal or hepatic disease.

Acetaminophen
• Mechanism of Action is not well understood.
  — Possibly some CNS component
  — Very weak inhibitor of prostaglandin synthesis
• One of the most commonly used analgesics for mild to moderate pain.
  — Equal analgesic properties to ASA unless associated with inflammation, where it is less effective.

Take home: Good for pain. Good for fever; No effect on inflammation

Acetaminophen
• Typical Adult Dosage (FDA Based):
  — 650 mg every 4 - 6 hours for Regular Strength (2 X 325)
    • Cannot take more than 10 caplets in 24 hours.
  — 1000 mg every 6 hours for Extra Strength (2 X 500)
    • Cannot take more than 6 caplets in 24 hours.
  — 1300 mg every 8 hours for Extended Release (2 X 650)
    • Cannot take more than 6 caplets in 24 hours.
• Daily dose of Extra Strength Tylenol should not exceed 3 grams!
  — This has been recently changed from 4000 mg which can be done with doctor approval.
• Should only be used for short term therapy
• Exhibits a ceiling effect, like NSAIDs and ASA.

Acetaminophen Contraindications
• Must be used in caution in all patients with chronic alcoholism or with preexisting liver impairment.
  — Should also avoid if using medications such as barbiturates, phenytoin, or rifampin due to toxicity.

Acetaminophen Side Effects
• Rare if used as recommended.
• 13 – 25 g is lethal, but > 7.5 grams leads to serious liver toxicity and possible death.
• Recommended dosages can cause liver damage in patients with pre-existing impairment.

Dangers of Acetaminophen
• Acetaminophen overdose is the leading cause of liver failure in the U.S.
  — It sends 56,000 people to the emergency room annually and causes approximately 400 deaths yearly.
• Acetaminophen is used in so many products, people are often unaware that they are taking it, leading to more overdoses.
  — Combined with agents to get wide range of symptom coverage.
    • Antihistamines such as diphenhydramine – Tylenol PM
    • Diuretics such as Pyrimidine maleate – Mirit Complete
    • Cough Suppressants such as Dextromethorphan - Nyquil
Acetaminophen in Combination
- Actifed
- Alka-Seltzer Plus
- Benadryl
- Butalbital
- CoGesic
- Contac
- Darvocet
- Excedrin
- Fioricet
- Lortab
- Midrin
- Norco
- Percocet
- Robitussin
- Sedapap
- Sinalair
- Sudafed
- TheraFlu
- Unisom With Pain
- Vick's Nyquil
- Vick's DayQuil
- Vicodin
- Wygesic
- Zydone

FDA Labeling
- FDA requires all acetaminophen products to carry a warning that individuals who consume more than three alcoholic beverages daily consult their doctors before taking the OTC medications.
  - Also seen with ASA and NSAIDs.
- As of April 2010 the FDA required labeling changes to further indicate the dangers of APAP, ASA, and NSAID use and that the medications be written clearly in bold print.

Combining Meds for More Severe Pain Relief
- Acetaminophen and Aspirin are often combined with each other and various agents to increase their analgesic effect.
  - Frequently seen in combination with narcotic analgesics.
  - Caffeine is also commonly used, especially in the treatment of migraines.
  - Excedrin Migraine
    - Acetaminophen 250 mg
    - Aspirin 250 mg
    - Caffeine 65 mg

Propionic Acids
- Most commonly used and largest class of NSAIDs.
- MOA is similar to ASA.
  - Metabolized in the liver and excreted in the urine.
- Superior analgesic efficacy over ASA with less incidence of side effects.
- Includes: Ibuprofen, Naproxen, Ketoprofen, Oxaprozin, and Fenoprofen.

Ibuprofen
- Adult analgesic dose: 200-400 mg q4hours
  - Maximum Dosage: 2400 mg/day for pain (approved for 3200 mg/day in arthritis treatment)
- OTC: 200 mg tabs
- Rx: 300, 400, 600, 800 mg tabs
  - Can prescribe 800 mg q8hrs
- Peak levels 1-2 hours
- Most renal toxic of all the NSAID’s
- Brand Names: Motrin, Advil, and Naprin

Consider Combining APAP with NSAID’s for Mild to Moderate Pain Relief
1:00 pm: Two 325mg Tylenol
3:00 pm: Two 200mg Ibuprofen
5:00 pm: Two 325mg Tylenol
7:00 pm: Two 200mg Ibuprofen
Alternated every 2 hours while awake
  - Each medication is q4 hours.
Naproxen and Naproxen Sodium
– Sodium speeds up the absorption over Naproxen (Naprosyn) alone causing it to be used more frequently.

Naproxen Sodium
– Type of Medication Determines Dosage (This is for Naproxen Sodium):
  – OTC: 220mg tablets (Aleve)
  – Rx: 275 and 550 mg tablets (Anaprox and Anaprox DS)
– Adult Dose:
  – OTC: 220 or 440 initial dose followed by 220 mg q 8 – 12 hours.
  – Rx: 550 initial dose, followed by 275mg q6-8h or 550mg q12hours.
    • Maximum Dose: 1375mg/day.

Ketoprofen
• Adult dose:
  – 50 mg q 6-8 hours for pain
  – 50 – 100 mg TID for inflammation
• Maximum Dose: 300 mg/day
  – Limited to 7-14 days
• OTC: 12.5mg (No longer Available)
• Rx: 50, 75, 200ER mg capsules

Indole Acetic Acids: Indomethacin
• Rx Only
• Available as 25, 50, 75 ER, and IV
• Adult Dosage: 25 - 50 mg TID
• Mainly used as a short term anti-inflammatory especially for conditions that do not respond to less toxic NSAIDS.
  – Indomethacin has a very high level of intolerance compared to other NSAID’s.
• Available in Canada as a topical Ophthalmic Suspension (Indocid).

Systemic NSAID Uses: Scleritis
• NSAID’s are Treatment of Choice (?)
  – Ibuprofen 400-600 mg Qid
  – Naproxen 250-500 mg BID
  – Indomethacin 25 mg TID
• Try three NSAIDs before considering treatment to be a failure and moving on to systemic steroids (?)

Side Effects of Oral NSAID’s
• Very similar to the side effect profile of ASA.
  – GI Effects
    • Profile is dependent on COX selectivity.
    • Consider using PPI’s while treating with NSAID or ASA.
  – CNS problems such as headache, confusion in the elderly, and loss of short-term memory.
  – Inhibit platelet function
    • Only while a high concentration exists in the body.
  – Risk of triggering asthma attacks is less with NSAID’s than what is found with ASA.
Side Effects of Oral NSAID’s

- NSAID’s are excreted from the body via urine. Must monitor kidney function.
- NSAID’s block prostaglandins to the kidney which causes renal blood flow to decrease and increases the retention of sodium and fluid.
  - Risk factors for kidney damage include:
    - Dehydration
    - Hypertension
    - Congestive Heart Failure
    - Use of ACE inhibitors
    - Advanced Age
  - This will effect Cardiovascular homeostasis – can exacerbate heart failure.
  - NSAID’s can cause hyperkalemia and have been linked to cardiac arrest in patients at risk.

NSAIDS Black Box Warning

- BLACK BOX WARNING:
  - May increase the risk of serious thrombotic events, MI, and stroke.
  - Increase risk of serious GI adverse effects such as bleeding, ulcer, and perforation.

NSAID Drug Interactions

- NSAID’s are well known to displace medications from sites on plasma proteins and alter their metabolism/excretion.
- NSAID’s inhibit platelet aggregation and can significantly increase the risk of bleeding if used along with anticoagulants such as warfarin.
  - Naproxen actually displaces the warfarin from plasma proteins causing increased serum levels and elevated prothrombin times.
- Antihypertensive agents such as ACE inhibitors, diuretics, and beta blockers may have decreased effectiveness.
  - Interaction is highly variable and difficult to predict.

Contraindications to NSAIDs

- Avoid in:
  - Pregnancy (especially the late trimesters)
  - Active Peptic Ulcer Disease
  - Cross Sensitivity to ASA
  - Previous Hypersensitivity to NSAIDs
  - Chronic Renal Insufficiency
- At Risk Patients Include:
  - Dehydration
  - HTN or CHF
  - Use of ACE inhibitors
  - Advanced Age

Cox-2 Inhibitors

- Selective agents for only COX-2 designed to protect the GI system from the side effects seen with NSAID’s.
- Major agent available on the market is Celecoxib (Celebrex).
  - Other agents Valdecoxib (Bextra) and Rofecoxib (Vioxx) were removed from the market due to increased risk of heart attacks and strokes.
  - It is approved for the treatment of osteoarthritis and rheumatoid arthritis.
  - Dosage: 100 mg BID or 200 mg daily

COX-2 Selective Agents

- Must avoid use in patients with cardiovascular risk factors.
  - Studies have shown that the greater the CoX-2 selectivity the greater the risk for hypertension from NSAID’s.
- Celebrex has still been shown to cause GI bleeding in patients at risk and should not be consider “safe”.
Oral Analgesics: Guidelines

- Never exceed maximum recommended dosages:
  - ASA: 8 grams/day
  - Acetaminophen: 4 grams/day
  - Ibuprofen: 1200 mg/day OTC and 2400 mg/day prescription
  - Codeine: 360 mg/day

Anesthetics

- Topical Ocular Anesthetics should not be used for pain relief outside of the clinical setting.

- However, topical skin creams do have one possible use in optometry – treatment of skin lesions caused by herpes zoster.
  - Cannot be used on open wounds – only once scabs have formed.

Anesthetic Agents for Pain Relief

- OTC Option: Zostrix Cream (Capsaicin)
- Prescription Option: EMLA Cream (lidocaine 2.5% and prilocaine 2.5%)

- Must use caution near the eye.

Narcotic Analgesics

- Also known as:
  - Opiates (Any agent derived from opium)
  - Opioids (Compounds that possess morphine-like analgesic properties)

- Morphine is the standard med used to compare the effects of all other opioids.

Opioids Mechanism of Action

- Mechanism of Action is binding to various brain, brainstem, and spinal cord receptors and mimicking the endogenous opioid peptides (Endorphins).
  - Alter the sensation of pain and the subjective distress/emotional component of pain.

- Act as agonists, partial agonists, or mixed agonist-antagonists.

Opioids Information

- Drug of first choice for the treatment of severe acute pain.
  - Block the body’s natural protective mechanism for protecting areas in pain – thus never prescribe unless you know the direct cause of the pain.

- Often administered in combination with acetaminophen or aspirin to enhance the analgesic effect.

- FDA recommended in 2011 that all prescription narcotics containing acetaminophen standardize and limit the dosage to 325 mg.
  - This is to be slowly phased in over three years (just required in January 2014).
Opioids Side Effects
• Side Effects are very hard to predict because opioids can cause CNS depression or stimulation.
  • CNS Side Effects
    – Dizziness, lightheadedness, sedation, and drowsiness are the most common.
    – Mood elevation (euphoria) and disorientation can occur in some patients.
    – Exacerbated if used in combination with alcohol, depression medications such as tricyclic antidepressants, anticholinergics, antihistamines, anti-seizure medications, or muscle relaxants, etc.
    – Visual symptoms such as blurry vision, miosis, and diplopia can occur.

Opioid Side Effects
• GI Side Effects:
  – Nausea and Vomiting (more common in ambulatory pts.)
  – Constipation
    • Opioids inhibit intestinal trace motility.
    • Very commonly found side effect.
      – Can be relieved by OTC docusate sodium (Colace).

Opioids Side Effects
• Respiratory Side Effects:
  • Respiratory Depression
    – Most serious side effect of the opioids
    – Opioids suppress the brainstem respiratory centers
      » Alter tidal volume, respiratory rate, rhythmicity, and responsiveness to CO₂
    – Does not commonly occur at therapeutic doses in healthy patients, but must use caution in patients with pulmonary disease.

Opioids Side Effects
• Cardiovascular Side Effects:
  – Peripheral vasodilation can result in orthostatic hypotension, decreased BP, and changes in pulse rate.
  • Others Include: Urinary retention, cough suppression, headaches, rashes, itching.

Tolerance to Opioids
• Patients experience shorter durations of analgesia from similar dosages, followed by increased levels of pain. Requires dosages to continually be adjusted to provide desired effects.
• Withdrawal can occur if long term use is discontinued abruptly resulting in increased heart rates and blood pressure, nausea, vomiting, dilated pupils, photophobia, shivering, etc. These symptoms peak approximately 2 to 3 days after the last dose and will subside over weeks.

Patient Education
• Avoid all depressants – especially using along with alcohol.
• Must educate all patients of risks of these symptoms and caution them for driving or operating dangerous machines.
• Stomach upset can be helped by consuming the medication with food.
• Watch for signs of breathing difficulty or changes in blood pressure.
Opioids Contraindications

- Avoid in patients with history of hypersensitivity to narcotics.
  - True allergic reactions are rare and often involve skin rashes or contact dermatitis.
- Avoid in patients with acute bronchial asthma or COPD.
- Avoid in patients with a history of depression or suicidal tendencies.
- Avoid in patients with history of addiction.
- Avoid in pregnancy (Most opioids are pregnancy category C).
  - Drug effects seem to be insignificant in nursing infants, but should recommend waiting at least 4 – 6 hours to nurse.
- Use caution in kidney or liver dysfunction due to increased accumulation of the medication.
- Must be very cautious of drug interactions and always review medications with your patient prior to prescribing.

Schedule III Opioids: Codeine

- Prodrug that relies on the cytochrome P-450 system to be metabolized to active drug morphine.
  - Schedule II medication if prescribed alone (Codeine Sulfate 15, 30, 60 mg generic.)
- Analgesic effect occurs within 20 minutes of ingestion and reaches a maximum at 1 – 2 hours.
  - Ceiling effect occurs.

Schedule II Opioids: Hydrocodone

- Approximately 6X more potent than codeine.
- Milder Side Effects than Codeine: Less constipation and sedation.
- Clinically believed to cause more euphoria than codeine, but this is not backed by clinical studies.

Scheduled Medications – Most Opioids

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Description</th>
<th>Opiometric Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Very addictive medications that are accepted for medicinal use</td>
<td>OxyContin, OxyContin (Oral), Oxycodone, Tylox, Percodan, Percodan Elixer, Percocet, Percocet Elixer, Oxycodone (Elixer), Methadone (Oral), Methadone (Subcutaneous), Methadone (Intravenous)</td>
</tr>
<tr>
<td>II</td>
<td>Significant abuse risk, but low potential for habituation</td>
<td>Codeine / APAP, Tylenol 3, Tylenol 4, Tylenol 6, Tylenol 13, Tylenol 16, Tylenol 19</td>
</tr>
<tr>
<td>III</td>
<td>Relatively low potential and limited risk</td>
<td>Propoxyphene (Elixir), Propoxyphene with APAP = Darvocet, Propoxyphene with APAP and Ibufrofen = Darvocet + Ibufrofen, Propoxyphene with APAP and Ibufrofen (Elixir) = Darvocet + Ibufrofen, Propoxyphene with APAP and Ibufrofen (Elixir) = Darvocet + Ibufrofen (Oral)</td>
</tr>
<tr>
<td>IV</td>
<td>Very limited potential. May be OTC in some states</td>
<td>Tylenol, APC, APC (Elixir)</td>
</tr>
</tbody>
</table>

Schedule III Opioids: Codeine

- Usually administered in combination with:
  - Tylenol 3 = Codeine 30 mg and Acetaminophen 300 mg
    - Dosage: 1-2 tablets every 4 hours.
  - Tylenol 4 = Codeine 60 mg and Acetaminophen 300 mg
    - Dosage: 1 tablet every 4 – 6 hours
  - Also available as generic with 15, 30, or 60 mg of Codeine with 300 mg of Acet or elixir of 12 mg codeine + 120 mg Acet. per 5 mL.
  - Elixir can be used in children for pain management if >3 years.

The FDA has mandated that all prescription medications have no more than 325 mg of APAP.
Schedule II Opioids: Oxycodone

- Approximately 10-12X more potent than codeine
  - As potent as parenteral morphine when given orally.
- Lower level of side effects in comparison to morphine, but high level of euphoria produced, thus higher level of abuse risk.

Comparing Opioids

<table>
<thead>
<tr>
<th>Drug</th>
<th>Analgesia</th>
<th>Sedation</th>
<th>N and V</th>
<th>Constipation</th>
<th>Euphoria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Propoxyphene</td>
<td>+/-</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
</tbody>
</table>

Newly Schedule IV: Tramadol (Ultram)

- Central acting narcotic
  - Synthetic analogue of codeine.
  - Binds to mu receptors and inhibits norepinephrine and serotonin reuptake.
  - Potential for abuse is very low, but has occurred.
- Available as 50 mg tablets.
- Dosage: 50 – 100 mg q4 – 6 hours.
  - Analgesia occurs after 1 hour.
  - Maximum dose: 400 mg/day

Tramadol Extended Release (Ultram ER)

- Available dosages of 100, 200, and 300 mg extended.
  - Begin taking 100 mg daily X 5 days
  - Increase by 100 mg if relief not met to 200 mg X 5 days.
  - 300 mg maximum daily.
- Does not work on all patients – some need heavy doses every 4-6 hours.
- More for chronic pain control.

Tramadol + APAP (Ultracet)

- Combination of:
  - 325 mg of APAP
  - 37.5 mg of Tramadol
- Dosage: 2 tablets every 4 – 6 hours
- Max: 8 tablets daily
Tramadol

- Must use with extreme caution in patients taking MAO inhibitors.
- Despite low risk for addiction should still use caution in patients with history of problems.
- Similar side effects to all opioids such as dizziness, nausea, dry mouth, and sedation.
- Avoid in patients with liver or renal impairment.
- Inferior pain relief with risk of side effects has limited Tramadol’s use clinically.

• First Step in Managing Acute Pain: Acetaminophen
  - If inadequate analgesia with 1000 mg TID

• Consider NSAID:
  - Ibuprofen 400 mg every 4-6 hours

• If NSAID inadequate or contraindicated:
  - Hydrocodone + APAP

• If inadequate consider in combination with ibuprofen or may need to consider stronger options/comanagement.

Opioids

- The short-term effects may include:
  - drowsiness
  - constipation
  - light-headedness and dizziness
  - mild anxiety
  - dry mouth
  - headaches
  - nausea
  - reduced appetite
  - Confusion

- may experience the following:
  - vomiting
  - rash and itchiness
  - pinpoint pupils
  - difficult urination
  - burning sensation on the skin
  - cold clammy skin
  - trouble with breathing, such as slow or shallow breathing

10/23/2018
Lattice Degeneration

- Circumferential oval lesions often with thin white blood vessels
- Pigment can vary
- Vitreous adhesion at borders
- Syneretic vitreous overlying the lesion itself
- Can have atrophic round holes without operculum typically towards end of lesions
  - Occur up to 30% of the time

Lattice Degeneration

- Most common in Superior and inferior retina
  - 2/3 cases from 5-7 or 11-1 o’clock
- Typical lesion size
  - ½ to 2.5 DD in width
  - 1-4 DD in length
- Average numbers of lesion per eye: 2
  - Range: 1-19
- Bilateral in >50% of cases

Lattice degeneration

- Most new cases discovered from 10-20 years of age
- May have hereditary component
- No apparent gender or race bias

Risk Factors

- Myopia > 3D, especially if < 30.
- Myopia > 6 D at any age
- Fellow eye has RD
- Family history of RD
- Symptoms
- Presence of traction
- High risk behavior
Follow up

- Lattice as only sign/symptom
  - Scleral depression
  - Pt ed.
  - RTC 1 year
- Lattice with symptoms of flashes floaters
  - Reexamine q 6 mos
  - Repeat DFE/scleral depression
  - Pt ed

Follow up

- Lattice with holes but no risk factors
  - Scleral depression
  - Pt ed
  - Rtc 6 mos
  - Sooner if young myope, myope > 5 D, inferior holes, or adhesion
- Lattice with risk factors for RD
  - Consider retinal consult
- Lattice with breaks at margin of lesion
  - Consider retinal consult

Retinal Breaks

- Occur in 3 to 7% of adult population
- Usually asymptomatic
- 1-2% with breaks progress to detachment
- Risk factors include lattice degeneration, high myopia, atrophic holes, aphakia/pseudophakia, and trauma

Horseshoe tears

- Common locations
  - Near lattice
  - Near pigment clumps
  - Near chorioretinal scars
- Worst locations
  - Superior
  - Near equator
  - Close to posterior pole

Treatment

- Laser treatment is used to seal the break by creating adhesion between the retinal tissue and underlying RPE
- Provides barrier to continued enlargement from vitreo-retinal traction and prevents accumulation of subretinal fluid
- Adhesion present 24 hours after surgery, and strengthens over several days

Procedure

- Topical or retrobulbar anesthesia
- Entire lesion should be enclosed by at least 3 rows in a honeycomb pattern
Follow-up

• RTC 1-2 weeks after laser for symptomatic tears
• 3-4 weeks for asymptomatic
• If large or superior, RTC even sooner
• If enlargement or new subretinal fluid, retreat with 1 week follow-up
• RTC 6-8 weeks after initial follow-up
• Yearly thereafter

Complications

• Few complications
  – inadequate burn intensity, causing ineffective adhesion
  – possible CNVM
  – intraretinal hemorrhage
  – vitreous hemorrhage
  – ERM formation

Operculated holes

• Round, red hole with overlying free operculum attached to vitreous
  – Operculum often appears smaller than hole
• Minimal risk as no traction
• Treatment sometimes
  – High myopia
  – Aphakia
  – h/o RD in the fellow eye
  – Other factors

Atrophic Retinal Holes

• Small round, red hole w/o operculum
  – May have surrounding pigment
  – Occasional edema
• 2-3% of general population
• Most often in vitreous base
• Found in atrophic retina, perhaps Z+ to vascular insufficiency

Atrophic Retinal Holes

• No traction
  – Minimal risk of detachment
• Asymptomatic holes
  – Yearly
  – Pt ed
• Asymptomatic with surrounding edema
  – Follow more closely
• Symptomatic
  – Consider consult
• Other associated issues
  • As warranted
  • Rarely treated

Treatment of Asymptomatic Lesions

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Phakic</th>
<th>High Myopia</th>
<th>RD etc in other eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphot interface</td>
<td>No</td>
<td>No</td>
<td>Rarely</td>
</tr>
<tr>
<td>Operculated hole</td>
<td>No</td>
<td>Rarely</td>
<td>Rarely</td>
</tr>
<tr>
<td>Lattice with or without hole</td>
<td>No</td>
<td>Rarely</td>
<td>Sometimes</td>
</tr>
<tr>
<td>Flap tear</td>
<td>Sometimes</td>
<td>Sometimes</td>
<td>Usually</td>
</tr>
</tbody>
</table>
Treatment of Symptomatic Lesions

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horseshoe tears</td>
<td>Yes</td>
</tr>
<tr>
<td>Operculated holes</td>
<td>Rarely</td>
</tr>
<tr>
<td>Atrophic holes</td>
<td>No</td>
</tr>
<tr>
<td>Lattice w/o holes</td>
<td>No</td>
</tr>
<tr>
<td>Lattice with holes</td>
<td>Sometimes</td>
</tr>
</tbody>
</table>

RD

- Rule-of-thumb:
  - For macula off RD, want to get it repaired in same amount of time it has been off
  - So if off for 4 days, best to try repair within 4 days!

- Macula on RD is emergency!
  - Same day referral to retinal specialist
  - Remind pt NPO until sees specialist in case same-day surgery

Retinal Detachments

- Rhegmatogenous RD occur when liquefied vitreous fluid enters the sub-retinal space through a full-thickness retinal break.
- Occurs in 1/100,000 per yr
- Treatment options include scleral buckle, pars planar vitrectomy, and pneumatic retinopexy

Retinal Detachments

- Many factors go into selecting which procedure is best for patient
  - Phakic/pseudophakic
  - Location of tear
  - Size of tear
- Experience of retinal surgeon is essential!
  - Do your homework!

PVD

- Really no consensus
- Symptomatic PVD without retinal break
  - AOA:1-2 weeks
  - AAO: depending on symptoms, risk factors and clinical findings:
    - 1-6 weeks
    - Then 6 mos to 1 year
  - Cleveland Clinic: 4-6 Weeks
  - Others: if no heme or other issues, very low risk so no need to see back

PVD

- Floaters are typically most common symptom
  - Cobwebs
  - Files
  - Hairs
- Flashes
  - Indicative of traction on retina, but not necessarily a tear or break
The Vitreous Humor

- Vitreous attached most firmly at
  - Macula
  - Vitreous base
  - Around optic nerve head
  - Weiss’ Ring
  - Also, some traction on blood vessels
    - Vit heme

Incidence of PVD

<table>
<thead>
<tr>
<th>Age</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;30</td>
<td>RARE</td>
</tr>
<tr>
<td>30-59</td>
<td>10%</td>
</tr>
<tr>
<td>60-69</td>
<td>27%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>63%</td>
</tr>
<tr>
<td>&gt;80</td>
<td>75%</td>
</tr>
</tbody>
</table>

- 65%>65 HAVE A PVD

Incidence of PVD

- Incidence may be accelerated by
  - Myopia
  - Trauma
  - Prior vitreoretinal disease
  - Surgery
  - Inflammation
- Symmetrical 90% of the time
- Happens to second eye with 1-2 years

PVDs

- Good News:
  - Retinal Tears/Breaks Relatively uncommon
    - One study: only 7-15% of symptomatic PVDs have a retinal break
- Bad news:
  - 7-15% have a retinal break

Risk Factors

- Hemorrhage
  - 90% have break
- Inflammatory cells
- Pigment
  - Schaeffer’s Sign
    - Indicates break is possible

PVD: Take Home

- DFE WITH scleral Depression!
- Council patient on signs and symptoms of RD
  - Increase in floaters
  - Increase in flashes
  - Sudden loss of vision/curtain over eye
- RTC =6 weeks as long as FLASHES are present
  - Sooner if heme or high risk
- 6 months to 1 year after
- DOCUMENT! DOCUMENT! DOCUMENT!
CHRPE

- Unifocal lesion typically appear as flat, pigmented round lesions with distinct margins
- Color ranges from light brown to jet black, depending upon amount of melanin
- Often have areas of chorioretinal atrophy within the lesion that appear window like and allow a clear view of the underlying choroid (lacunae)

CHRPE

- Typical size is 2-6 mm, but may be smaller or as large as 14 DD (21 mm)
- Can be located anywhere within the fundus, but about 70% in temporal half of fundus
- No apparent racial predisposition, although reported more in Caucasians
- May be present at birth, with reports in as young as 3 months old

CHRPE

- Lesions are almost always stable in size, but color may change.
  - Very rare instances of enlargement with time
- Typically asymptomatic, and found on routine exam, but large lesions have been shown to have VF defects

CHRPE

- Can also appear as multifocal CHRPE
  - From 3 to 30 lesions, 0.1 to 3.0 mm in size
- Benign, stationary and unilateral in 85% of the cases
- Often called bear tracks

Gardner’s Syndrome

- Multifocal CHRPE have been associated with Gardner’s Syndrome
  - AKA FAP: familial adenomatous polyposis
  - Familial condition of colonic polyps that may be precursor to colon cancer
  - However, these lesions are bilateral, have more irregular borders, and are often scattered throughout the fundus

CHRPE

- Differential includes nevi and choroidal melanoma
  - Nevi: nevi are rarely jet black and tend to have more indistinct borders
  - Melanoma tend to be greater than 2mm in thickness, where CHRPE are flat
- B-scan, serial photos and frequent monitoring of assistance
Nevus

• Common, benign tumor of the posterior fundus
• Typically slate-gray or brown in color, with somewhat indistinct borders
  – Often have overlying drusen, which signify chronicity of lesion
• Vary in size from 1/3 DD to as much as 7 DD
  – Flat or minimally elevated, < 2mm

Nevus

• Very common, with prevalence ranging from 0.2% up to 32% of patients
• More common in Caucasian population
• Asymptomatic, and usually found on routine exams
• Management consists of serial photography and frequent follow-up, with ultrasound if needed for more suspicious lesions

Nevus

• TFSOM: To Find Small Ocular Melanomas
  – T: Thickness; lesions > 2 mm
  – F: Fluid, any subretinal fluid suggestive of RD
  – S: Symptoms of photopsia or vision loss
  – O: Orange pigment overlying the lesion
  – M: Margin touching the optic nerve head
    • No factor= 3% risk of converting to melanoma in 5 yrs
    • 1 factor=8% risk
    • 2 or more factors =50% risk

CRVO/BRVO

• Refer if macula edema within 1 week
  – Laser vs. injection in BRVO
  – Injection CRVO
  – Steroids?
• Systemic workup recommended
  – DM
  – HTN
  – Cholesterol panel
  – Carotid Doppler
• Look for NV/NVI/NVA/NVG esp. in CRVO, esp. if ischemic

Retinal Plaques

• Several different types of plaques can often be visualized in the retinal vasculature
• Pt is typically elderly, has HTN, CAD, hypercholesterolemia/hyperlipidemia, and/or atherosclerotic disease
• Often totally asymptomatic and found on routine exam

RISK FACTORS

• Age
• HTN
• Vascular disease
• Past vascular surgery
• SMOKING
• High TOTAL cholesterol
• Men> women
Prevalence

- Beaver Dam Eye Study: 1.3%
  - smoking, HTN and DM
  - 9x more likely after age 75 vs. 43-54
  - after 75, 3.1% prevalence
  - Equates to 1.2 million people with emboli 43-86
  - Fatal stroke 3x as likely over 8 years in pts with emboli, adjusting for other factors
  - OD>OS
  - Bilateral very infrequently

- Blue Mountain Eye Study 1.4%
  - HTN, smoking, Vascular disease

- LA Latino Eye Study: 0.4%
  - Smoking, CAD, h/o MI, HTN

- Singapore Eye Study: 0.6%
  - Smoking, high cholesterol, h/o angina

Retinal Plaques

- May present with amarosis fugax, transient episodes of monocular blindness
- Rarely, may report transient ischemic attack (TIA), which is above with hemiparesis, parasthesia or aphasia

Retinal plaques

- Three different types of plaques, but all share strong association to significant cardiovascular disease
  - HH 80% > fibrino-platelet 14% > calcific 6%

Retinal Plaques

- Cholesterol (Hollenhorst) plaque
  - Most common
  - shiny yellow-orange in appearance
  - from plaque in the ipsilateral carotid artery
  - Rarely causes occlusion, unless multiple
  - Typically occurs at bifurcations
  - Mobile in nature

Retinal Plaques

- Fibrino-platelet
  - Appear as dull white to gray, long plugs
  - Typically within arterioles, not at bifurcations
  - May break-up and dissolve with time
  - May lead to BRAO or CRAO
  - Often associated with carotid disease or mitral valve insufficiency
Retinal Plaques

- Calcific
  - Appears more whitish than HH
  - Dull, non-reflective, white
  - Classically within arteriole, not at bifurcation
  - Typically immobile
  - Most dangerous, often cause BRAO
  - Often from cardiac arethromas of heart valves

Retinal plaques

- No direct management of plaques is needed
- Management is aimed at discovering source of embolus to decrease risk of other emboli, occlusion, or stroke
- Pts need referral to internist for complete physical

Retinal Plaques

- Assess risk factors with PCP
  - DN, HTN, lipid panels
- Carotid ultrasound
- MRA: non-invasive image with 2D/3D
- TEE: invasive, probe into esophagus to image heart valves
  - Helpful with calcific
- CTA: CT scan of arteries construct 3D images

Carotid Ultrasound

- First line screening test
- ORDER WITHIN TWO WEEKS!!
- Identifies flow rate and % stenosis
- Common, internal, and external
- Only ≈20% of asymptomatic emboli will have significant carotid stenosis

Retinal Plaques

<50-60% occlusion
- ORAL TREATMENT
  - Anti-Platelet
    - ASA
  - Anti-coagulation
    - Comadin, platelet
  - Cholesterol meds

>70-99%
- SURGICAL TREATMENT
  - Carotid endarterectomy
  - Angioplasty
  - Reduces risk of future stroke!

Retinal Plaques

- After ruling out underlying etiology, see patient regularly, q 6 -12 mos, to evaluate for additional plaques or other disease associated with vascular disease
  - BRVO/CRVO
  - BRAO/CRAO
  - NTG
Case

- 48 yr old white female presents with acute loss of vision in her right eye and decreased vision in her left.
  - She was scheduled 2 weeks previously for an eye exam on a referral from her PCP but had fallen and was unable to make that appointment.
  - She reports that her vision in her right eye seems to be getting worse over the past several weeks.
  - Was diagnosed with diabetes 1.5 years ago.
    - BS control has been erratic with range between 6.7-13.3 (120-240)
    - Last A1C: 9.1

Type 1 Diabetes Treatment

- The new HbA1c target of less than 7.5% across all pediatric age groups.
- The adult HbA1c target of less than 7%.
  - Less stringent A1C goals (such as <8%)
    - history of severe hypoglycemia,
    - limited life expectancy,
    - advanced microvascular or macrovascular complications,
    - and extensive comorbid conditions and in those with longstanding diabetes in whom the general goal is difficult to attain.
    - <6.5 for recent diagnosed or long life expectancy.

Blood Sugar

- Hypoglycemia is typically defined as plasma glucose 3.9 mmol/L (70 mg/dL) or less.
  - patients typically become symptomatic of hypoglycemia at 2.8 mmol/L (50 mg/dL) or less.

1 Recognize Symptoms Early

No matter how carefully you manage diabetes with insulin, hypoglycemia (low blood sugar) may still develop very quickly. Symptoms include:

- Sweating
- Blurry vision
- Shakiness
- Irritability
- Anxiety
- Headache
- Weakness, fatigue

Action Item

- Optometrists should have a rapid-acting carbohydrate (glucose gel or tablets, sugar-sweetened beverage or fruit juice) in their offices for use with diabetic patients who experience acute hypoglycemia during an eye examination.

Hypoglycemia

Always have a rapid-acting carbohydrate in the office (juice, sugared soda, glucose gel) for pts on meds that can cause low blood glucose.

15 gm CHO will ↑BG ~ 30-40 mg/dl (1.7-2.2 mmol/L)
**Diagnostic Test For Diabetes**

<table>
<thead>
<tr>
<th>Test</th>
<th>Criteria</th>
<th>Confirmation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Plasma Glucose (FPG)</td>
<td>≥126 mg/dL suggest DM</td>
<td>Confirm by repeat test on different day</td>
</tr>
<tr>
<td></td>
<td>100-125 mg/dL prediabetes</td>
<td></td>
</tr>
<tr>
<td>Random Plasma Glucose</td>
<td>≥ 200 mg/dL in setting of symptoms indicates DM</td>
<td>Confirm with FPG or OGTT performed on another day</td>
</tr>
<tr>
<td>2-h oral glucose tolerance test (OGTT)</td>
<td>≥200 mg/dL diagnostic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>140-199 mg/dL diabetes</td>
<td></td>
</tr>
<tr>
<td>Glycosylated hemoglobin: HbA1c</td>
<td>≥5.7 but &lt;6.5-prediabetes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥6.5 diabetes</td>
<td></td>
</tr>
</tbody>
</table>

HbA1c is a better predictor of DM than FPG Diabetes Care 2009 November; 32(11): 2027-32

**Entrance Skills/Health Assessment**

- VA: OD: finger count
- OS: 6/12 (20/40)
- CVF: OD: unable to assess
- OS: temporal hemianopsia
- Pupils sluggish reactivity with a 2+ RAPD OD
- SLE: corneal arcus noted, no other significant findings
- IOP: 16, 16 mmHG OD, OS
- DFE: see photos

**Physical Presentation**

- Upon entering the room I noted that her right hand was twitching
  - I asked her how long that had been going on and she said about 2-3 weeks
  - I asked her if she experienced headaches, to which she said she had bad headaches that even woke her up at night

**Referral**

- Contacted her PCP who reported that she had examined the patient 3 weeks prior and had not noted any of these findings
- Referred the patient for an immediate MRI
  - wasn’t able to be scheduled until the next day

**Imaging/Surgery Referral**

- MRI revealed large mass in her brain
  - Patient was diagnosed with Craniopharyngioma
  - She was referred for immediate surgery
  - Neurosurgeon reported that she removed a tangerine sized Craniopharyngioma
  - was the largest tumor she has ever removed

**Craniopharyngioma**

- Presenting signs and symptoms of increased intracranial pressure (80%)
  - Headache
  - Vomiting
  - Papilledema
  - Loss of vision and visual field (60%)
  - Diabetes (15%)
  - Mental deterioration or personality change (26%)
Craniopharyngioma

• Treatment:
  – Therapy is often unsatisfactory
  – Total resection often results in major functional deficits
  – Partial resection followed by conventional radiation therapy as a more conservative approach has been recommended

Diabetes Lab Testing

• Comprehensive medical panel will include:
  – Serum glucose
  – Electrolytes
  – Liver enzymes
  – Kidney function:
    • BUN and creatinine
      – Elevated in renal failure
    • Glomerular filtration rate
      – Reduced in chronic kidney disease/renal failure

Kidney function

• Urinalysis can be used in conjunction with blood testing to help confirm systemic etiology of conditions
  – Urine Glucose
    • Any glucose in the urine is abnormal
  – Urine Protein
    • Proteinuria is an important indicator of renal disease
  – Urine Ketones
    • Ketones are byproducts of body fat metabolism formed in the liver
    • Ketonuria occurs in patients with diabetes

Kidney Function Tests:

Serum Creatinine:

  – waste product that comes from the normal wear and tear on muscles of the body.
  – Kidney impairment results in rise of creatinine level in the blood

BUN (blood urea nitrogen):

  – if kidneys cannot filter wastes out of the blood due to disease or damage, then the level of urea in the blood will rise

Liver Tests

• Liver tests (LTs) are blood tests used to reflect the presence of damage or inflammation.
  • alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are the most commonly used tests
  • These enzymes normally found in the blood when liver cells are injured.

Liver Tests

• The ALT is felt to be a more specific indicator of liver inflammation as AST is also found in other organs such as the heart and skeletal muscle.
• In acute injury to the liver, as in viral hepatitis, the level of the ALT and AST may be used as a general measure of the degree of liver inflammation or damage.
Liver Tests

- Bilirubin is the main bile pigment in humans which, when elevated causes the yellow discoloration of the skin called jaundice.
  - the bilirubin may be elevated in many forms of liver or biliary disease, it is relatively non-specific
- Albumin is a major protein which is formed by the liver.
  - chronic liver disease causes a decrease in the amount of albumin produced

Blood Chemistry: Lipid Profiles

Consists of:
- Serum lipids,
- Cholesterol,
  - High density lipoproteins (HDL) – “good” cholesterol
  - Low density lipoproteins (LDL) – “bad” cholesterol
  - Very-low density lipoproteins (VLDL) – dangerous cholesterol
  - triglycerides

Current Recommended Lipid Levels

<table>
<thead>
<tr>
<th>Cholesterol Levels</th>
<th>&lt;200</th>
<th>200-239</th>
<th>240-499</th>
<th>&gt;500</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>&lt;5.0</td>
<td>5.2-6.1</td>
<td>&gt;6.2</td>
<td></td>
</tr>
<tr>
<td>LDL Cholesterol</td>
<td>&lt;130</td>
<td>131-160</td>
<td>&gt;160</td>
<td></td>
</tr>
<tr>
<td>HDL Cholesterol</td>
<td>&gt;40</td>
<td>&gt;45</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Case

- 30 BF presents with eye pain in both eyes for the past several days
  - Severe pain (8/10)
  - Never had eye exam before
- PMHx:
  - Has chronic bronchitis
  - Rash on legs
  - Has recently lost weight and has a fever
  - Taking aspirin for pain

Ocular Health Assessment

- VA: 6/9 (20/30) OD, OS
- PERRL
- FTFC
- EOM’s: FROM with eye pain in all quadrants
- SLE:
  - 3+ injection,
  - 3+ cells and trace flare,
  - deposits on endo (see photo)
- IOP: 18, 18 mmHg
- DFE:
  - see attached fundus image and fluorescein angiography.

Sarcoid Diagnosis

<table>
<thead>
<tr>
<th>Test</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC with differential</td>
<td>Anemia/thrombocytopenia/leukopenia</td>
</tr>
<tr>
<td>Serum calcium/24 hour calcium</td>
<td>Hypercalcemia</td>
</tr>
<tr>
<td>Liver/Kidney function tests</td>
<td>AST/ALT/BUN/creatinine elevated in hepatic disease</td>
</tr>
<tr>
<td>ACE transforming enzyme</td>
<td>Elevated in 60% of patients</td>
</tr>
<tr>
<td>Pulmonary x-rays</td>
<td>Hilir adenopathy</td>
</tr>
</tbody>
</table>
Blood Chemistry

• Angiotensin-Converting Enzyme (ACE)
  – Found mainly in lung and liver
  – Serum elevations are found in patients with sarcoidosis, and significant levels are achieved in pulmonary sarcoid
  – Cirrhosis of the liver may produce elevated ACE levels
  – Active tuberculosis infection of the lung does NOT produce elevated ACE levels

Diagnosis: Radiographic

• Radiographic involvement is seen in almost 90% of patients.
• Chest radiography is used in staging the disease:
  – Stage I disease shows bilateral hilar lymphadenopathy (BHL).
  – Stage II disease shows BHL plus pulmonary infiltrates.
  – Stage III disease shows pulmonary infiltrates without BHL.
  – Stage IV disease shows pulmonary fibrosis.

Diagnosis: Radiographic

• CT and MRI scans may be useful in finding granulomas in other organ systems
• Gallium scan-gallium 67 has been found to accumulate in active sarcoidal tissue

Stages of Syphilis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary syphilis</td>
<td>Single firm, round, small, and painless sore (chancre)</td>
</tr>
<tr>
<td>Secondary syphilis</td>
<td>Nonitchy, reddish-brown skin rash and mucous membrane lesions +/- systemic symptoms (fever, pharyngitis, headache, arthralgias)</td>
</tr>
<tr>
<td>Tertiary syphilis</td>
<td>Gumma formation (nonspecific granulomatous lesion that may infiltrate the skin, bone, or any organ or tissue)</td>
</tr>
<tr>
<td>Latent syphilis</td>
<td>Positive serologic test, but no symptoms</td>
</tr>
</tbody>
</table>

Syphilis Diagnosis

• Typical diagnosis is with blood tests using nontreponemal and/or treponemal tests.
  – Nontreponemal test are used initially and include:
    • venereal disease research laboratory (VDRL)
    • rapid plasma reagin (RPR)
    • chemiluminescent microparticle immunoassay (CMIA)***
  – Confirmation is required with a treponemal test such as:
    • treponemal pallidum particle agglutination (TPPA)
    • fluorescent treponemal antibody absorption test (FTA-Abs)
  – The FTA-ABS test checks for antibodies to the bacteria that cause syphilis and can be used to detect syphilis except during the first 3 to 4 weeks after exposure to syphilis bacteria.

*** primary screening test for patients suspected of being exposed to syphilis
Tuberculosis

• Difficult to culture the slow-growing organism in the laboratory (it may take 4 to 12 weeks for blood or sputum culture).
• A complete medical evaluation for TB must include:
  – a medical history,
  – a physical examination,
  – a chest X-ray,
  – microbiological smears,
  – and cultures.
• It may also include a tuberculin skin test, a serological test.
  – The interpretation of the tuberculin skin test depends upon the person's risk factors for infection and progression to TB disease, such as exposure to other cases of TB or immunosuppression.

Tuberculosis

• Currently, latent infection is diagnosed in a non-immunized person by a tuberculin skin test, which yields a delayed hypersensitivity type response to an extract made from M. tuberculosis.
• Those immunized for TB or with past-cleared infection will respond with delayed hypersensitivity parallel to those currently in a state of infection, so the test must be used with caution, particularly with regard to persons from countries where TB immunization is common.

Tuberculosis

• The newer interferon release assays (IGRAs) overcome many of these problems.
  – IGRAs are in vitro blood tests that are more specific than the skin test.
  – IGRAs detect the release of interferon gamma in response to mycobacterial proteins.
  – These are not affected by immunization or environmental mycobacteria, so generate fewer false positive results.

Helpful Mnemonic

• Mnemonic for acute forms of non-granulomatous uveitis: **BLAIR G**
  – B: Behcet’s disease
  – L: Lyme disease
  – A: Ankylosing spondilitis
  – I: Inflammatory bowel disease (Crohn’s)
  – R: Reactive arthritis
  – G: Glaucomatocyclitic crisis

Case

• 23 WM
  – Eye pain OD
  – Severe, started 2 days ago
  – Photophobia and redness
• POHx:
  – Had similar problem and was given drops and felt better
• PMHx:
  – Told to get back into shape and to reduce stress
• Meds:
  – Ibuprofen for lower back pain

Assessment

• VA: 6/6 (20/20), 6/6
• Entrance skills unremarkable
• SLE:
  – OD:
    • 2+ injection,
    • 2+ cell
    • Mild flare
    • Fine deposits
  – IOF: 18, 14 mm HG
• DFE: unremarkable
Ankylosing Spondylitis

• Ankylosing spondylitis is a type of arthritis that affects the spine:
  – symptoms include pain and stiffness from the neck down to the lower back.
• The vertebrae may grow or fuse together, resulting in a rigid spine.
  – these changes may be mild or severe, and may lead to a stooped-over posture.

Ankylosing Spondylitis

• Ankylosing spondylitis affects about 0.1% to 0.5% of the adult population.
• Although it can occur at any age, spondylitis most often affects men in their 20s and 30s.
  – It is less common and generally milder in women and most common in Native Americans.
• Early diagnosis and treatment helps control pain and stiffness and may reduce or prevent significant deformity.

Ankylosing Spondylitis

• Physical Exam:
  – The overall points taken into account when making an AS diagnosis are:
    • Onset is usually under 35 years of age.
    • Pain persists for more than 3 months (i.e. it is chronic).
    • The back pain and stiffness worsen with immobility, especially at night and early morning.
    • The back pain and stiffness tend to ease with physical activity and exercise.
    • Positive response to NSAIDs (nonsteroidal anti-inflammatory drugs).

Ankylosing Spondylitis

• X-rays:
  – The hallmark of AS is involvement of the sacroiliac (SI) joint
  – show erosion typical of sacroilitis (inflammation of the sacroiliac joints).
  – can take 7 to 10 years of disease progression for the changes in the SI joints to be serious enough to show up in conventional x-rays.

Psoriatic Arthritis

• Psoriasis is a scaly rash that occurs most frequently on the elbows, knees and scalp, but can cover much of the body.
• It is a chronic, inflammatory disease of the skin, scalp, nails and joints.
• A normal skin cell matures and falls off the body’s surface in 28 to 30 days, but a psoriatic skin cell takes only three to four days to mature and gathers at the surface, thus forming lesions.
Psoriatic Arthritis

• In 5-10% of those with psoriasis, arthritis also appears.
  – In most cases the psoriasis will precede the arthritis, sometimes by many years.
• When arthritis symptoms occur with psoriasis, it is called psoriatic arthritis (PsA).
  – The joints at the end of the fingers are most commonly affected causing inflammation and pain, but other joints like the wrists, knees and ankles can also become involved.
  – Usually accompanied by symptoms of the fingernails and toes, ranging from small pits in the nails to nearly complete destruction and crumbling as seen in reactive arthritis or fungal infections.

Psoriatic Arthritis

• About 20% of people who develop PsA will eventually have spinal involvement, which is called psoriatic spondylitis.
• The inflammation in the spine can lead to complete fusion - as in ankylosing spondylitis - or skip areas where, for example, only the lower back and neck are involved.
• Those with spinal involvement are most likely to test positive for the HLA-B27 genetic marker.
• Up to 40% of people with PsA have a close relative with the disease, and if an identical twin has it, there is a 75% chance that the other twin will have PsA as well.

Reactive Arthritis

• Reactive Arthritis (formerly known as Reiter’s Syndrome) is a form of arthritis that can cause inflammation and pain in the:
  – Joints, the skin, the eyes, the bladder, the genital and the mucous membranes.
• Reactive arthritis is thought to occur as a “reaction” to an infection that started elsewhere in the body, generally in the genitourinary or gastrointestinal tract.

Reactive Arthritis

• Reactive arthritis occurs after exposure / infection caused by certain types of bacteria. These include:
  – Chlamydia
  – Bacteria such as Salmonella, Shigella, Yersinia or Campylobacter, which occurs after eating spoiled or contaminated food.
  – Not everyone exposed to these bacteria will contract ReA.
  – Those who go on to develop ReA tend to test positive for the HLA-B27 genetic marker, although other genetic factors may be involved.
  – Thus, it is an interaction between an individual’s genetic make-up and the initial infection that causes Reactive Arthritis.

Reactive Arthritis

• ReA usually develops 2-4 weeks after the infection.
• A tendency exists for more severe and long-term disease in patients who do test positive for HLA-B27 as well as those who have a family history of the disease.
• Reactive Arthritis typically follows a limited course, where symptoms subsiding in 3-12 months.
  – However, the condition has a tendency to recur.
• About 15-20% of people with ReA develop a chronic, and sometimes severe, arthritis or spondylitis.

ReA Conjunctivitis

• Eye involvement occurs in about 50% of men with urogenital reactive arthritis and about 75% of men with enteric reactive arthritis.
• Conjunctivitis and uveitis can include redness of the eyes, eye pain and irritation, or blurred vision.
• Eye involvement typically occurs early in the course of reactive arthritis, and symptoms may come and go.
• Treatment includes NSAIDs and/or steroids.
Enteropathic Arthritis

• Enteropathic arthritis is a form of chronic, inflammatory arthritis associated with the occurrence of an inflammatory bowel disease (IBD):
  – the two best-known types of which are ulcerative colitis and Crohn’s disease.
• About one in five people with Crohn’s or ulcerative colitis will develop enteropathic arthritis.
• The most common areas affected by enteropathic arthritis are inflammation of the peripheral (limb) joints, as well as the abdominal pain and possibly bloody diarrhea associated with the IBD component of the disease.
• In some cases, the entire spine can become involved as well.

Enteropathic Arthritis

• The course and severity of enteropathic arthritis varies from person to person.
• The disease “flares” - the times when the disease is most active and inflammation is occurring - tend to be self-limiting, often subsiding after 6 weeks, but recurrences are common.
• In some cases the arthritis may become chronic and destructive.

Juvenile Rheumatoid Arthritis (JRA/JIA)

• “Rheumatoid like” disease with onset before age 17
• Group of arthritides responsible for significant functional loss in children
• Most common chronic disease with genetic predisposition in children.
• 2:1 female:male, with peak incidence b/w 2-4 and then 10-12

Natural History

• Pathogenesis unknown
• Immune-mediated activity directed towards Type II collagen
• RF mediated responses rarely found
• 1° involves weight bearing joints of lower extremities (knees/ankles) as well as joints of elbows/hands
• Little associated pain/tenderness observed

Diagnosis

• Synovitis that persists for at least 6 weeks is the essential criterion for diagnosis.
• Hematologic and radiographic studies are beneficial in diagnosis and classification.
• Fewer than 20% of patients have positive RF
• Radiographic evaluation of inflamed joints reveal soft tissue swelling and peri-articular osteoporosis with possible new bone formation.
• Loss of the cartilaginous space with erosions occur after long duration.

Ocular Manifestations

• Classic triad of iridocyclitis, cataract and band keratopathy
• Overall incidence of iridocyclitis is approx 20%.
• Cataract, glaucoma, and band keratopathy are seen in 50% of patients who develop persistent iridocyclitis.
Ocular Manifestations

- Severe vision loss results primarily from cataract formation and less frequently from band keratopathy.
- Insidious onset of ocular involvement, with the iridocyclitis commonly following the arthritis symptoms (though occasionally preceding).
- Patients are often asymptomatic and therefore require ocular evaluation for detection.

Ocular Manifestations

- Evidence of chronic iridocyclitis may be presenting sign leading to Dx of JIA.
- Posterior segment involvement is not commonly seen.
- Band keratopathy in children <16 is pathognomonic for JIA.
  - results from aggressive/chronic ocular inflammation (not abnormal calcium metabolism).
- JIA patients do not present with the dry eye and K sicca manifestations that are so prevalent in RA.
The Latest In Corneal Dystrophies and Degenerations

Blair Lonsberry, MS, OD, MEd, FAAO
Professor of Optometry
Pacific University College of Optometry
Portland, OR
blonsberry@pacificu.edu

Corneal Dystrophies

• Group of corneal diseases that are:
  – genetically determined and
  – have been traditionally classified with respect to the corneal layer affected
• Emerging molecular science:
  – is redefining traditional thought on the dystrophies and
  – offering potential avenues for therapeutic intervention.

CORNEAL DEGENERATION

• Non-familial, late onset
• Asymmetric, unilateral, central or peripheral
• Changes to the tissue caused by inflammation, age, or systemic disease.
• Characterized by a deposition of material, a thinning of tissue, or vascularization

Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD)

• Primary features of this “dystrophy” are:
  – abnormal corneal epithelial regeneration and maturation,
  – abnormal basement membrane
• Often considered the most common dystrophy, but may actually be an age-related degeneration.
  – large number of patients with this condition,
  – increasing prevalence with increasing age, and
  – its late onset support a degeneration vs. dystrophy.

Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD)

• Not all patients are symptomatic (range 10-69%)
• Most common symptom is mild FB sensation which is worse in dry weather, wind and air conditioning
• Blurred vision from irregular astigmatism or rapid TBUT
• Pain is usually secondary to a RCE (recurrent corneal erosion) in apprx 10%
Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD)

- Easy to overlook:
  - typically bilateral though often asymmetric,
  - females>males,
  - often first diagnosed b/w ages of 40-70

Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD)

- Most common findings are:
  - chalky patches,
  - intraepithelial microcysts, and
  - fine lines (or any combination) in the central 2/3rd of cornea

Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD)

- Often referred to as:
  - maps,
  - dots or
  - fingerprints

EBMD-Negative Staining

RCE: Treatment

- Initial treatment includes:
  - use of hyperosmotic ointment at bedtime,
  - bandage contact lens and
  - lubrication.
Recurrent Corneal Erosion: Treatment

- If severe enough to cause vision loss or repeated episodes:
  - Oral doxycycline with/without topical corticosteroid
    - Doxy 50 mg bid and FML tid for 4-8 weeks
    - Both meds inhibit key metalloproteinases important in disease pathogenesis
    - Azasite (topical azithromycin)
  - Debridement,
  - Stromal puncture, or
  - PTK
  - Latest development: amniotic membrane transplant e.g. Prokera

CORNEAL DEBRIDEMENT

- Soften epithelium
- 1-2 gtt topical anesthetic
- q 15-30 seconds for 2-3 minutes
- Use cotton swab, spatula, spud
- or jewellers forceps
- Remove flaps by pulling edges toward center
- Don’t pull directly up or out
- Remove flaps down to tight, firm edges.
- Tx abrasion (>50-100%)
  - Recurrence Rate 18%

Amniotic Membrane Transplant

- Amniotic membrane is a biologic tissue with:
  - Antiangiogenic,
  - Antiscarring,
  - Antimicrobial, and
  - Anti-inflammatory properties that promotes healing of the ocular surface
- Amniotic membrane grafts have been used for a variety of ocular conditions including:
  - Corneal burns
  - Neurotrophic ulcers
  - Stem cell damage
  - Persistent epithelial defects

Amniotic Membrane Transplant

- Traditionally, amniotic membrane grafts had to be sutured
  - With the advent of tissue adhesives, amniotic transplants can now be sutureless
- ProKera was approved by the FDA in 2003 as a Class II medical device which has a polycarbonate ring which holds a cryopreserved amniotic membrane
- ProKera is indicated in the treatment of corneal erosions, neurotrophic corneas, recalcitrant corneal inflammation, acute ocular surface burns, acute Stevens Johnson syndrome, and descemetocoeles.

Stromal Puncture

RCE and LASIK

- Patients who have a history of EBMD may not be ideal candidates for LASIK and should be carefully screened for prior to surgery.
Macular (Groenouw Type II)

- Grayish opacities in the superficial stroma
- With age:
  - extension into deeper stromal layers
  - intervening stroma becomes hazy
  - progressive loss of vision,
  - photophobia and ocular discomfort.

Macular Corneal Dystrophy

- Surgical treatment usually required by 2nd or 3rd decade of life.
  - PK
  - DALK not indicated as may have damage to Descemets

Granular Dystrophy: (Groenouw Type I)

- Discrete white granular opacities in central anterior corneal stroma.
- With age:
  - increasing number, density, size and depth of opacities
  - intervening stroma and peripheral cornea remain clear

Granular Dystrophy: (Groenouw Type I)

- RCE are common with associated pain.
- Decreased vision results from subepithelial scarring or dense stromal deposits.
- Surgical treatment includes penetrating keratoplasty or DALK (Deep Anterior Lamellar Keratoplasty).

PTK Treatment for GRANULAR

- Characteristic clinical appearance includes:
  - linear,
  - refractile,
  - branching deposits within the anterior stroma.

Lattice (Type I)
Lattice (Type I)

- The central cornea is progressively opacified resulting in scarring and deterioration of vision while the periphery remains clear.
- RCE’s often present.
- May require surgical intervention with diminished vision.
  - PK
  - DALK

Central Crystalline Dystrophy of Schnyder

- Opacities consist of:
  - small, needle-shaped refractile crystals that are either white or polychromatic
  - may extend into deeper stroma but epithelium remains normal.

Central Crystalline Dystrophy of Schnyder

- Vision is typically mildly affected though there may be associated systemic complications
  - systemic cholesterol should be evaluated

SURGICAL TREATMENTS: PK AND DALK

PK Surgery: Full Thickness Surgery

- Central trephine cut made
- Smooth Surface with only endothelial disease
- Recipient tissue removed
- Full thickness block of tissue removed just to get to the endothelium
- Donor tissue sutured into recipient
- Sutures create an irregular surface with astigmatism and blurring
Penetrating Keratoplasty

Deep Anterior Lamellar Keratoplasty (DALK)
- Removal of all tissue EXCEPT Descemet’s and endothelium
  - Most common rejection seen in PK is endothelial rejection observed in apprx 20% of low-risk cases
  - Repeated PK’s increase chance that the graft will be rejected
  - DALK can avoid risk of endothelial rejection with similar optical results as PK

Deep Anterior Lamellar Keratoplasty (DALK)
- Indicated for patients with
  - Keratoconus
  - Corneal scars
  - Corneal stromal dystrophies
  - Basically any pathology that spares the endothelium
- Contraindicated
  - Bullous keratopathy
  - Fuch’s

Deep Anterior Lamellar Keratoplasty (DALK)
- Advantages over PK:
  - No “open sky” during surgery so lesser chance of expulsive hemorrhage
  - Much decreased rejection potential because patient keeps their own endothelium
    - Stromal rejection is rare and easily treated
  - Low to no rejection risk so steroids are tapered more quickly (usually twice as fast)
  - Heals faster as steroids tapered sooner allowing sutures to be removed earlier and more rapid visual stabilization (apprx 6 months)
  - More tectonic stability as patient keeps own endo

Normal Changes to the Endothelium
- Descemet’s layer thickens from 3-17u
- There is a decrease in the # of endothelial cells
  - from 3500 cells/mm2 to 1200
  - this single layer spreads out: lacks mitosis
- High density mitochondria : 90% pump
- Lenses produce reversible polymegathism

Abnormal Changes to the Endothelium
- Endothelial cells become more irregular
- Cells secrete collagen towards Descemet’s causing multilamination = guttata
- This breaks down the barrier function and results in stromal and epithelial edema
Fuch’s Dystrophy

- Endothelium:
  - acts as both a barrier and pump function
  - responsible for maintaining corneal transparency by reducing corneal hydration
- Fuch’s:
  - occurs bilaterally,
  - AD inheritance,
  - females 3x more likely to develop condition

Fuch’s Dystrophy: Guttata

- Corneal guttata
  - excessive accumulation of abnormal endo secretions is associated with the disease process
  - usually first noticed in the central cornea in the patients 30’s and 40’s
  - corneal physiology is affected adversely by interference with pump action
  - guttata appear as small refractile “drops” on the corneal endo

Fuch’s Dystrophy: Guttata

- closer inspection with specular reflection reveals an “orange peel-like” dimpling of the endo
- with the decreased pump function, the overlying stroma becomes edematous
- long standing corneal edema may result in corneal scarring and RCE

Fuch’s Dystrophy Endothelial Mosaic

Normal Endothelial Mosaic

Fuch’s Dystrophy Endothelial Cell Count: 545 cells/mm
Fuch’s Dystrophy

- Patient symptoms vary with degree of guttata and compromised pump function
- Moderate guttata
  - may affect visual function
  - may result in light scatter (haloes)
  - typically noticed upon waking
- With increased disruption to the pump:
  - vision decreases
  - potential development of bullous keratopathy

Fuch’s: Bullous Keratopathy

Fuch’s Dystrophy: Treatment

- Treatment in early stages:
  - usually palliative with the goal of improving comfort and function
  - hyperosmotics at bedtime (e.g. muro 128 ointment) may help reduce epithelial corneal edema in the morning
  - bandage CL can be used in the presence of bullous keratopathy

Fuch’s Dystrophy: Treatment

- When visual function deteriorates to the point patient is unduly affected, surgical options are considered including:
  - penetrating keratoplasty (PK)
  - DLEK surgery (deep lamellar endothelial keratoplasty) or newer DSAEK (Descemet Stripping Automated Endothelial Keratoplasty)
  - Latest DMEK (Descemet Membrane Endothelial Keratoplasty)
- Fuch’s is leading reason for PK’s in developed countries

DLEK

- Recipient cornea is stripped of its Descemet’s membrane, endothelium and posterior stroma
- There is transplantation of the posterior stroma and endothelium of the donor cornea through a small incision
- Results in improved:
  - endothelial function,
  - corneal clarity and
  - restoring useful vision.
DLEK

- Procedure has:
  - minimal affect on refraction,
  - provides rapid visual recovery and
  - maintains structural integrity of the cornea.

DLEK Surgery: Split Thickness Surgery to replace only the diseased tissue

- Scleral incision, deep corneal pocket, and endothelium trephined with Terry Trephine or cut with Cindy Scissors
- Just endothelium on posterior stromal disc removed from pocket
- Donor tissue placed into recipient
- Endothelium replaced with no sutures, supported by air bubble in anterior chamber. Surface remains smooth with no astigmatism

DSEK vs. DSAEK:

- DSEK has the donor lamellar disc created manually
- DSAEK facilitated by the use of a blade microkeratome which cuts the donor interface with the corneal button mounted in an artificial anterior chamber

DMEK (Descemet Membrane Endothelial Keratoplasty)

- Recipient cornea is stripped of its Descemets membrane and endothelium
  - implanted tissue consists of only the donors Descemets and endothelium
  - in comparison, DSAEK has implanted tissue consisting of posterior stroma, Descemets and endothelium
  - implantation of similar tissue “components” without additional posterior stroma has resulted improved visual function and recovery

DMEK (Descemest Membrane Endothelial Keratoplasty)

- Compared to DSAEK, DMEK may have better clinical potential with 75% patients obtaining 20/25 or better within 1-3 months
  - DSAEK 38-100% patients get 20/40 or better after 6 months
  - PK has 40% patients 20/40 or better after 1 year
- Visual recovering quicker with DMEK with many patients having good vision 1 day post op and best visual recovering by 1-3 months
  - DSAEK slower visual recovery and PK the slowest
- Additionally, may have reduced endothelial cell lost post surgery

CORNEAL DEGENERATIONS
**Keratoconus**

- **Ectatic corneal dystrophy:**
  - tends to be bilateral,
  - maybe asymmetric, and
  - generally manifests in the 2nd or 3rd decade.
- ** Likely a multigenic disease:**
  - complex mode of inheritance (sporadic, AD and AR reported) and
  - manifestation likely involving environmental factors.

**Keratoconus:**

- **Proposed etiology:**
  - increased enzyme activities and decreased levels of enzyme inhibitors result in toxic by-products
  - destruction of the normal corneal matrix resulting in thinning and scarring.

**Keratoconus: Diagnosis**

- **SLE findings include:**
  - central corneal thinning,
  - Fleischer’s ring,
  - scarring at the level of Bowman’s layer or anterior stroma, and
  - vertical striae (Vogt’s lines).
- **Common refractive or topographic effects include:**
  - irregular astigmatism and
  - poor best-corrected visual acuity with specs

**Keratoconus: Diagnosis**

- Keratoconus tends to progress over 7-8 years and then stabilizes
- Severity is variable b/w patients and is often asymmetric
- Thinning can be extensive:
  - resulting rupture in Descemet’s membrane
  - triggers a sudden influx of aqueous into the cornea (Hydrops)

**Central “Nipple” Keratoconus OU**
Keratoconus Treatment

- DALK
- Intacs:
  - Arclike PMMA segments designed to be surgically inserted into deep corneal stroma to flatten the central cornea
  - Indicated for mild to moderate keratoconus with a clear optical zone and contact lens intolerant
  - May delay or eliminate the need for keratoplasty although significant refractive error may remain
  - Refractive stability has been demonstrated up to 5 years post-op in several studies
  - Does have FDA approval for the treatment of keratoconus in the US

TREATMENT OF KERATOCONUS WITH INTACS

- The goal is to improve topography:
  - Lift the ectasia to reduce irregular astigmatism
  - Flatten the soft tissue to reduce the SE
- These changes should improve the UCVA and increase contact lens or spectacle success.
- The intention is not to cure the disease, but rather to delay need for a corneal transplant.
**INTACS FOR KCN**

![INTACS FOR KCN Image]

**The Future is Here!**

- Collagen crosslinking of riboflavin and UVA-light
  - Thought to strengthen the corneal collagen matrix and stabilize the cornea
  - Stops the progression of the condition with the potential of some reversal
- Might become the standard therapy for progressive keratoconus

---

**C3-R Mechanism**

- **UVA 370nm**
- **Riboflavin .1%**
- **Corneal Collagen Crosslinking**
- **Biomechanical Stiffness**
- **Stability**

**Collagen Cross Linking**

- Clinical outcomes seem to follow a reproducible time course after treatment:
  - Visual acuity and corneal steepness worsen over the first month
  - Resolution to baseline by 3 months with continued improvement thereafter
- Several studies have evaluated the use of CXL in the pediatric population (the most likely group to require a transplant)
  - Recommended as a treatment to stabilize the cornea and to limit the progression of the condition

---

**Keratoconus-Hydrops**

- Symptoms include:
  - Sudden decrease in best corrected vision,
  - Foreign body sensation or pain
- Signs include:
  - Conjunctival hyperemia/redness,
  - Prominent central or inferior corneal edema and
  - Clouding along with conjunctival hyperemia
- Tends to be self-limiting
  - In 8-10 weeks the endothelial cells regenerate across the ruptured Descemet’s membrane

**Keratoconus-Hydrops Treatment**

- May use hyperosmotics and antibiotics to prevent secondary infections
- PK’s are indicated if resulting scarring limits correction of vision
Bilateral corneal disorder hallmarked by a thinning of the inferior, peripheral cornea
- Corneal thinning begins approx 1-2 mm above the inferior limbus and is separated by an area of uninvolved, normal cornea between the thinned zone and the limbus.
- Acute hydrops maybe seen in the area of inferior thinning
- Commonly manifests b/w ages of 20-40 with no apparent hereditary transmission and equal gender distribution
Pellucid Marginal Degeneration

- Subjective symptoms are visual secondary to a dramatic increase in against-the-rule astigmatism.
- Area of thinning is free of vascularization or lipid infiltration which differentiates this condition from Terriens marginal degeneration of Mooren's ulceration.
- Corneal mapping demonstrates inferior mid-peripheral zones of corneal steepening at 4-8 o'clock producing “butterfly wing-like” pattern which is diagnostic.

Pellucid Marginal Degeneration

- Management includes specs, CL and surgery.
- Spectacle correction is often satisfactory in the early stages due to the minimal degree of induced astigmatism.
- In more advanced stages, CL are the suggested mode of treatment.
- CL management can be difficult because of the high degree of ATR and asymmetrical astigmatism.
- Surgical intervention involves PK, a kidney-shaped PK or an inferior lamellar patch graft.

Terrien’s Marginal Degeneration

- Rare, bilateral, asymmetric disease of unknown etiology.
- Peripheral cornea, predominantly superiorly, undergoes lipid deposition, vascularization, opacification and stromal thinning leading to gutter formation, ectasia and eventual corneal perforation. Epithelium remains intact.

Terrien’s Marginal Degeneration

- May occur at any age, though typically occurs in middle-aged males.
- The eyes are typically not injected and there is little if any pain, photophobia or anterior chamber reaction.
- Increased regular and irregular astigmatism, which may produce visual changes though patients are usually asymptomatic.
Terrien’s Marginal Degeneration

- Degeneration often progresses in a circumferential pattern
- Perforation is usually only a complication of trauma.
- Etiology poorly understood though chronic inflammatory skin conditions and autoimmune mechanisms maybe possible etiology factors.

Terrien’s Management

- As most patients are asymptomatic, management is largely supportive.
- May suffer from periodic episodes of red, irritated eyes which are quickly resolved with steroids (Pred forte, Lotemax)
- Early refractive treatment includes:
  - spectacles (polycarbonate),
  - CL an option though difficult to fit due to irregular astigmatism (RGP over piggyback),
  - and when vision uncorrectable surgical intervention includes PK.

Mooren’s Ulcer

- A painful, relentless, chronic ulcerative keratitis that begins peripherally and progresses circumferentially and centrally.
- It is idiopathic; occurring in absence of any diagnosable systemic disorder that could be responsible for the progressive destruction of the cornea (e.g. peripheral corneal melt secondary to RA).

Mooren’s Ulcer

- Mooren’s divided into 3 distinct varieties:
  - Unilateral Mooren’s: painful progressive corneal ulceration in elderly
  - Bilateral Aggressive Mooren’s Ulcer: occurs in younger Px, progresses circumferentially than centrally in the cornea and
  - Bilateral Indolent Mooren’s Ulceration: occurs in middle-aged Px presenting with progressive peripheral corneal guttering in both eyes, with little inflammatory response.
Mooren’s

- Pathophysiological mechanism remains unknown but there is evidence suggesting an autoimmune process.
- Px typically present with redness, tearing, photophobia, but pain is the most outstanding feature. The pain is often incapacitating and may be out of proportion to the inflammation.
- Maybe visual disruption secondary to associated iritis, central corneal involvement, irregular astigmatism due to peripheral corneal thinning.

Mooren’s Ulcer

Mooren’s Ulcer

Mooren’s Ulcer

Mooren’s Ulcer

Mooren’s: Management

- Initial therapy includes intensive topical steroid Tx: Pred Forte hourly is association with cycloplegics (e.g. Homatropine 5%) and topical antibiotics (moxifloxacin).
- Pulse oral therapy (Prednisone 60-100 mg daily) can be considered when topical therapy ineffective after 7-10 days.
- If ulcer continues to progress, conjunctival resection should be performed.
- For those Px that continue to progress, immunosuppressive chemotherapy is required to halt the progression.
- After active ulceration halted, PK maybe performed.
Oral Pharmaceuticals in Anterior Segment Disease
Blair Lonsberry, MS, OD, ME., FAAO
Professor of Optometry
Pacific University College of Optometry
blonsberry@pacificu.edu

Herpes Simplex
- Most common virus found in humans
  - 60-99% are infected by 20 years old
- Double stranded DNA virus
  - HSV type 1 (HSV-1)
  - HSV type 2 (HSV-2)
- Primary infection
  - Occurs in childhood via droplet exposure
  - Subclinical infection in most
- Secondary infection (recurrence)

Case
- 20 year old male presents with a red painful eye
  - Started that morning when he woke up
  - Reports a watery discharge, no itching, and is not a contact lens wearer
- SLE:
  - See attached image with NaFl stain

Herpes Simplex Keratitis
- Epithelial Keratitis:
  - Symptoms:
    - Ocular irritation, redness, photophobia, watering, blurred vision
  - Signs:
    - Swollen opaque epithelial cells arranged in a course punctate or stellate pattern
    - Central desquamation results in a dendrite***
      1. Central ulceration
      2. Terminal end bulbs
    - ***Corneal sensation is reduced***

Dendritic Ulcers
Pediatric HSV Keratitis

- pediatric herpes simplex keratitis has an 80% risk of recurrence, a 75% risk of stromal disease, and a 30% rate of misdiagnosis
- 80% of children with herpes simplex keratitis develop scarring, mostly in the central cornea
  - results in the development of astigmatism
  - 25% of children have more than 2 D of astigmatism, most of which is irregular
- consider pediatric HSV when a patient has unilateral recurrent disease in the anterior segment

Herpes Simplex Keratitis Management

- **Topical:**
  - Viroptic (trifluridine) q 2h until epi healed then taper down for 10-14 days.
  - Viroptic is toxic to the cornea.
  - Zirgan (ganciclovir) available, use 5 times a day until epi healed then 3 times for a week (US only)

Anti-Viral Medication

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of Action</th>
<th>Bioavailability</th>
<th>Dosing</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir</td>
<td>Acyclovir interferes with DNA synthesis inhibiting viral replication</td>
<td>10-30% gets absorbed Short half life *Metabolized in kidneys</td>
<td>Simplex: 400 mg 5x/day Zoster: 800 mg 5x/day</td>
<td>Overall very safe, Nausea, vomiting, headaches, dizziness, confusion</td>
</tr>
<tr>
<td>Valacyclovir</td>
<td>Acyclovir pro-drug equivalent to acyclovir but better for pain management</td>
<td>95% converted to acyclovir* Better bioavailability and longer half life</td>
<td>Simplex: 500 mg tID Zoster: 1 g tID</td>
<td>Same as acyclovir*</td>
</tr>
<tr>
<td>Famciclovir</td>
<td>Inhibits DNA chain elongation It is metabolized to penciclovir where it is active 10-20x as long as acyclovir</td>
<td>Superior to acyclovir*</td>
<td>Simplex: 250 mg TID Zoster: 500 mg TID</td>
<td>Same as acyclovir*</td>
</tr>
</tbody>
</table>

HSV Stromal Disease

- HSV Stromal disease is an immune-mediated disease
- Increased risk of scarring and high risk of poor visual prognosis
- Requires corticosteroids (HEDS: corticosteroid reduced risk of progression by 68%)
  - Without epithelial defect: corticosteroids and prophylactic anti-viral dosage
  - With epithelial defect: active infection anti-viral dosage with judicious corticosteroids

How much to dose steroid?

- HEDS used QID of prednisolone phosphate
- Current Recommendations:
  - Mod – severe (especially with neo): 1% Prednisolone or Lotemax QID to 6x/day
  - Want the lowest dose needed to control the inflammation
  - AAO EBM Treatment Guideline 2014
    - Topical steroid for 10 weeks (this is based on HEDS results) with oral antiviral
Herpes Simplex Epithelial Keratitis

• Treatment Regimen:
  — Zirgan 5x/day until the ulcer heals, then 3x/day for one week
  — Oral Valtrex 500 mg 3x/day for 7-10 days
  — Artificial tears
  — L-Lysine 2 grams daily?
    • Proven to “slow down” and retard the growth of the herpes virus and inhibit viral replication
    • Prior to topical antiviral therapy debridement was treatment of choice
    • Generally try to avoid use of sharp instruments and use of cotton swab and anesthetic
  — RTC 1 day, 4 days, 7 days

Herpes Simplex Keratitis

• Prophylactic Treatment:
  — Reduces the rate of recurrence of epithelial and stromal keratitis by ≈ 50%
  — Acyclovir 400 mg BID
  — Valtrex 500 mg QD
  — Famvir 250 mg QD
  — L-lysine 1 gram/day:
    • Proven to “slow down” and retard the growth of the herpes virus and inhibit viral replication
    • Frequent debilitating recurrences, bilateral involvement, or HSV infection in a monocular patient

Prophylaxis??

• Pitfalls to Prophylaxis:
  — Reduction of recurrence does not persist once drug stopped
  — Resistance????
    • van Velzen, et. al., (2013) demonstrated that long-term ACV prophylaxis predisposes to ACV-refractory disease due to the emergence of corneal ACVR HSV-1.

Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD)

• Easy to overlook:
  — typically bilateral though often asymmetric,
  — females>males,
  — often first diagnosed b/w ages of 40-70

Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD)

• Most common findings are:
  — chalky patches,
  — intraepithelial microcysts, and
  — fine lines (or any combination) in the central 2/3rd of cornea
Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD)

- Often referred to as:
  - maps,
  - dots or
  - fingerprints

Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD): Treatment

- Typically directed towards preventing RCE
- If RCE’s develop:
  - awake with painful eye that improves as day wears on
  - chalky patches/dots in lower 2/3rd of cornea

RCE: Treatment

- Initial treatment includes:
  - use of hyperosmotic ointment at bedtime,
  - bandage contact lens and
  - lubrication.

Recurrent Corneal Erosion: Treatment

- If severe enough to cause vision loss or repeated episodes:
  - oral doxycycline with/without topical corticosteroid
    - Doxy 50 mg bid and FML tid for 4-8 weeks
    - both meds inhibit key metalloproteinases important in disease pathogenesis
  - Azasite (topical azithromycin)
  - debridement,
  - stromal puncture, or
  - PTK
  - Latest development: amniotic membrane transplant e.g. Prokera

CORNEAL DEBRIDEMENT

- Soften epithelium
- 1-2 gtt topical anesthetic
- q 15-30 seconds for 2-3 minutes
- Use cotton swab, spatula, spud
- or jewelers forceps
- Remove flaps by pulling edges toward center
- Don’t pull directly up or out
- Remove flaps down to tight, firm edges.
  - Tx abrasion (>50-100%)
    - Recurrence Rate 18%

Diamond Burr Polishing

- Removes abnormal basement membrane
- May also promote scarring
Amniotic Membrane Transplant

- Amniotic membrane is a biologic tissue with:
  - antiangiogenic,
  - antiscarring,
  - antimicrobial, and
  - anti-inflammatory properties that promotes healing of the ocular surface.
- Amniotic membrane grafts have been used for a variety of ocular conditions including:
  - Corneal burns
  - Neurotrophic ulcers
  - Stem cell damage
  - Persistent epithelial defects

Tetracyclines

- This group includes:
  - Tetracycline (250mg-500mg cap BID-QID) needs to be taken 1 hour before or 2 hours after a meal.
  - Minocycline (100mg cap BID).
  - Doxycycline (200mg-300mg cap or tab BID).
  - In Canada: Apprilon (30mg doxy + 10mg slow release doxy).

- Rules of Thumb with Doxy:
  - Do not take before lying down (>2 hours before).
  - Do not take with calcium and avoid antacids.
  - Do not take with dairy.
  - Do take with food.
  - Do recommend sun protection.

Side Effects of Tetracyclines

- Side effects include gastric discomfort, phototoxicity, affects on calcified tissues, vestibular problems, pseudotumor.
- Pregnancy Category D.
  - Tetracyclines are attracted to embryonic and growing bone tissue.
  - Depress growth of long bones in pregnant women/children.
  - Cause changes in both deciduous and permanent teeth during the time of tooth development (includes discoloration and increased cavities).
- Contraindicated in:
  - Women in the last half of pregnancy.
  - Lactating women.
  - Children under 8 years of age.

Meibomian Gland Dysfunction

- Meibomian gland dysfunction:
  - also referred to as meibomitis and patients experience dry eye problems secondary to increased evaporation of the tears.
  - Signs include noticeable capping of the glands and frothing of tear film.
- Standard treatment includes:
  - good lid hygiene with warm compresses and lid scrubs in conjunction with
  - doxycycline 50mg po BID for 2-3 months.
  - Erythromycin ung (Ilotycin) can also be used externally.

Treatment of MGD

At Home Therapy
- Warm compresses
- Eyelid Scrubs
- Self expression

In-Office Therapy
- Manual Expression, -systemic side effects
- Oral tetracycline/doxycycline -antibiotic resistance,
- Topical Antibiotics - erythrom., tobra. poor gland penetration
- Topical Steroids - dexamethasone -risk of cataract, glaucoma, poor gland penetration

Low Compliance
Hordeola

- Acute purulent inflammation
  - Internal occurs due to obstruction of MG
  - External (stye) from infection of the follicle of a cilium and the adjacent glands of Zeiss or Moll
- Painful edema and erythema,

Hordeola

- Typically caused by Staph and often associated with blepharitis
- Treatment includes:
  - hot compresses (e.g. Bruder)
  - topical antibiotics (I)
  - possibly systemic antibiotics
    - Augmentin 500 mg bid-qid
    - Doxycycline 100 mg bid
  - Treat concurrent blepharitis

Preseptal Cellulitis

- Infection and inflammation located anterior to the orbital septum and limited to the superficial periorbital tissues and eyelids.
- Usually follows sinus infection or internal hordeolum (possibly trauma)
- Eyelid swelling, redness, ptosis, pain and low grade fever.

Preseptal Cellulitis

- Tx:
  - Augmentin 500 mg TID or 875 mg BID for 5-7 days
  - Keflex 500 mg QID 5-7 days
  - or if moderate to severe IV Fortaz (ceftazidime) 1-2 g q8h.
  - If MRSA possible, consider Bactrim/Septa

Penicillins: Clavulin (Augmentin)

- Clavulin (Augmentin) is amoxicillin with potassium clavulanate (clavulanic acid 125 mg).
- Clavulanate is a B-Lactamase inhibitor which reduces a bacteria’s ability to negate the effect of the amoxicillin by inactivating penicillinase (enzyme that inactivates the antibiotic affect).
  - Dicloxacillin can also be used in infections due to penicillinase-producing staph.

Penicillins: Clavulin (Augmentin)

- Clavulin (Augmentin) is very effective for skin and skin structure infections such as:
  - dacrocystitis,
  - internal hordeola,
  - preseptal cellulitis.

  - Treatment of:
    - otitis media,
    - sinusitis,
    - lower respiratory and urinary infections.
  - Given prophylactically to dental surgery patients.
Penicillins: Clavulin (Augmentin)

- It has low:
  - GI upset,
  - allergic reaction and anaphylaxis.
- Serious complications include:
  - anemia,
  - pseudomembranous colitis and
  - Stevens-Johnson syndrome.

Penicillins: Clavulin (Augmentin)

Adults:
- 250-500 mg tab q 8 hr (tid)
  (also available in chewable tablets and suspension)
- or 675 mg q 12 hr (bid)
- 1000 mg XR: q12 hr and not for use in children <16
Peds: <3 mos 30mg/kg/day divided q12hrs using suspension
  • >3 mos 45-90mg/kg/day div q12hrs (otitis media 90mg 6 days)

Cephalosporins

- Closely related structurally and functionally to the penicillins,
  • have the same mode of action,
  - affected by the same resistance mechanisms.
- tend to be more resistant to β-lactamases.
- classified as 1st, 2nd, 3rd, and 4th generation based largely on their bacterial susceptibility patterns and resistance to β-lactamases.
- Should be avoided or used with caution in patients who are allergic to penicillin (approx 10% x-reaction with penicillin allergy has been reported but thought to be much closer to the 1-2%)
  • allergic response without allergy to penicillin is 1-2%.
- Typically administered IV or IM, poor oral absorption.

Cephalosporins

- 1st generation: cefadroxil (Duricef), cefazolin (Ancef), cephalexin (Keflex), and cephalothin
- 2nd generations: cefaclor (Ceclor), cefprozil, cefuroxime (Zinacef), cefotetan, cefoxitin
- 3rd generation: ceftriaxone (Rocephin IM/IV).
- 4th generation: cefepime
  • Keflex (cephalexin) all orally administered are effective against most gram positive pathogens and especially good for skin and soft tissue infections.

Cephalosporins

- Keflex (cephalexin):
  - treatment of respiratory, GI, skin and skin structure, and bone infections as well as otitis media
  - Adults: 250-1000 mg every 6 hours
    • typical dosing 500 every 6 hours
  - Children: 25-100 mg/kg/day divided 6-8 hours

Co-Ttrimoxazole (Bactrim/Septra)

- Combination of trimethoprim and sulfamethoxazole
  - shows greater antimicrobial activity than equivalent quantities of either drug alone.
- Has broader spectrum of action than the sulfas and is effective in treating:
  - UTIs and respiratory tract infections
  - often considered for treatment of MRSA skin infections
Co-Ttrimoxazole (Bactrim/Septra)

- Resistance is more difficult because has to develop resistance to both drugs.
- Adverse effects include:
  - severe potential for dermatologic reactions,
  - GI upset,
  - blood disorders, and
  - drug potentiation.

Co-Ttrimoxazole (Bactrim/Septra)

- Available:
  - **Bactrim/Septra tablets**
    - contains 80 mg trimethoprim and 400 mg sulfamethoxazole
    - dosing 2 tablets every 12 hours
  - **Bactrim DS/Septra DS (Double Strength)**
    - contains 160 mg trimethoprim and 800 mg sulfamethoxazole
    - Dosing 1 tablet every 12 hours

Herpes Zoster

1. Primary infection – Chicken pox (Varicella)
   - Usually in children
   - Highly contagious***
   - Very itchy maculopapular rash with vesicles that crust over after ≈ 5 days
   - 96% of people develop by 20 years of age
   - Vaccine now available

Herpes Zoster

2. Reactivation – Shingles (Herpes Zoster)
   - More often in the elderly and immunosuppressed (AIDS)
     - Systemic work-up if Zoster in someone < 40
   - Can get shingles anywhere on the body
   - Herpes Zoster Ophthalmicus (HZO)
     - Shingles involving the dermatome supplied by the ophthalmic division of the CNV (trigeminal)
     - 15% of zoster cases

Herpes Zoster

- Symptoms:
  - Generalized malaise, tiredness, fever
  - Headache, tenderness, paresthesias (tingling), and pain on one side of the scalp
    - Will often precede rash
  - Rash on one side of the forehead
  - Red eye
  - Eye pain & light sensitivity

Herpes Zoster

- Other Eye Complications (Acute):
  - Anterior uveitis (most common ocular manifestation)
  - Acute epithelial keratitis (pseudodendrites)
  - Conjunctivitis
  - Stromal (interstitial) interstitial keratitis
  - Endotheliitis (disciform keratitis)
  - Neurotrophic keratitis
Herpes Zoster

- Associated factors include increasing age, immune deficiency and stress.
- Only people who had natural infection with wild-type VZV or had varicella vaccination can develop herpes zoster.
- Children who get the varicella vaccine appear to have a lower risk of herpes zoster compared with people who were infected with wild-type VZV.

Herpes Zoster

- A person’s risk for herpes zoster increases sharply after 50 years of age.
- Almost 1 out of 3 people in the United States will develop herpes zoster during their lifetime.
- A person’s risk of developing post-herpetic neuralgia also increases sharply with age.

Herpes Zoster

- Management includes:
  - oral antivirals:
    - 800mg acyclovir 5x/day
    - valacyclovir (Valtrex) 1g TID,
    - famciclovir (Famvir) 500 mg TID
  - effectiveness of therapy is best started within 72 hours
  - oral steroids (clinical trials show variable results but often prescribed with antiviral to reduce pain)
  - management of pain (capsaicin, tricyclic antidepressants, gabapentin).
  - If ocular complications, consider topical steroids (Pred Forte QID).

NEW!! Shingrix HZ Vaccine

- Approved in US/Canada as of October 2017
- non-live antigen, to trigger a targeted immune response, with a specifically designed adjuvant to enhance this response and help address the natural age-related decline of the immune system
- Shingrix is 97% effective against shingles for people between the ages of 50 and 69 and 91% effective for people 70 or older.
- It is 91% effective against postherpetic neuralgia for people 50 and older.
- These rates are based on evidence presented to the committee from clinical trials with over 38,000 total participants.

NEW!! Shingrix HZ Vaccine

- recommended for healthy adults aged 50 years and older to prevent shingles and related complications
- recommended for adults who previously received the current shingles vaccine (Zostavax®) to prevent shingles and related complications
- the preferred vaccine for preventing shingles and related complications

Case: Gonzalez

- 33 HF presents with a painful, red right eye
  - Started a couple of days ago, deep boring pain
  - Has tried Visine but hasn’t helped the redness
- PMHx: patient reports she has been diagnosed with rheumatoid arthritis 3 years ago
  - Takes Celebrex for the joint pain
  - Patient reports she occasionally gets a skin rash when she is outdoors in the sun
- POHx: unremarkable
- PMHx: mother has rheumatoid arthritis
Case: Gonzalez

- VA: 20/30 OD, 20/20 OS
- Pupils: PERRL – APD
- VF: FTFC OH
- EOM’s: FROM OU
- BP: 130/85 mm Hg RAS
- SLE: see picture
  - 2+ cells, mild flare
- IOP’s: 16, 16 mm HG
- DFE: see fundus photo

Scleritis

- chronic, painful, and potentially blinding inflammatory disease that is characterized by edema and cellular infiltration of the scleral and episcleral tissues
- Symptoms of scleritis can include pain, tearing or photophobia, tenderness, and decreased visual acuity. The primary sign is redness.

Ocular Manifestations - Scleritis

- classified into anterior and posterior.
  - Anterior:
    - Diffuse and nodular forms
    - Necrotizing (with/without inflammation) less frequent
      - Have the most serious systemic implications
      - Scleromalacia perforans
  - Posterior:
    - characterized by flattening of the posterior aspect of the globe, thickening of the posterior coats of the eye (choroid and sclera), and retrobulbar edema.

Treatment and Management: Scleritis

- Scleritis treatment depends on both the type and severity.
- Aggressive treatment is necessary in order to prevent structural damage.
- Topical steroids (e.g. Pred Forte) have ease of use and relatively minimal side effect profile when compared to systemic therapy however, scleritis does not usually respond to topical corticosteroids alone.

Treatment and Management: Scleritis

- Oral NSAIDs:
  - considered first-line therapy for scleritis for their ease of use, cost, and relatively mild side effect profile for both anterior and posterior scleritis
  - E.g. Ibuprofen 400-600 mg QID, Naproxen 250-500 mg BID, or Indomethacin 25-50 mg TID
  - short term use of an NSAID is often well tolerated, NSAIDs can cause adverse effects which include peptic ulcer disease, hypertension, increased heart disease, bleeding, fluid retention, renal disease, and mood change
Revised Recommendations on Screening for Retinopathy

• 2002 recommendations for screening were published by Ophthalmology
• Revised recommendations on screening published in Ophthalmology 2011;118:415-42
  – Significant changes in light of new data on the prevalence of retinal toxicity and sensitivity of new diagnostic techniques
  – Risk of toxicity after years of use is higher than previously believed
    • Risk of toxicity approaches 1% for patients who exceed 5 years of exposure

“New” New Recommendations

• Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy – Ophthalmology 2016; 123:1386-1394
  – Released March 2016 from American Academy of Ophthalmology
  – revised in light of new information about the prevalence of toxicity, risk factors, fundus distribution, and effectiveness of screening tools.

2016 Recommendations

• maximum daily HCQ use of 5.0 mg/kg real weight, which correlates better with risk than ideal weight.
• risk of toxicity is dependent on daily dose and duration of use.
  – at recommended doses:
    • risk of toxicity up to 5 years is under 1%
    • up to 10 years is under 2%
    • rises to almost 20% after 20 years. However, even after 20 years, a patient without toxicity has only a 4% risk of converting in the subsequent year.

• High dose and long duration of use are the most significant risks.
  – Other major factors are concomitant renal disease, or use of tamoxifen
• A baseline fundus examination should be performed to rule out preexisting maculopathy.
• Begin annual screening after 5 years for patients on acceptable doses and without major risk factors.

2016 Recommendations

• primary screening tests are automated visual fields plus spectral-domain optical coherence tomography (SD OCT)
• most patients of Asian descent will show initial damage in a more peripheral extramacular distribution near the arcades (require a 24-2 as opposed to 10-2 and OCT scans need to be analyzed further out)
Revised Recommendations on Screening for Retinopathy

- Parafoveal loss of visual sensitivity may appear before changes are seen on fundus evaluation
  - Many instances where retinopathy was unrecognized for years as field changes were dismissed as "non-specific" until the damage was severe
  - 10-2 VF should always be repeated promptly when central or parafoveal changes are observed to determine if they are repeatable
  - Advanced toxicity shows well-developed paracentral scotoma

Paracentral Scotomas

Normal Retina: VF/OCT/ERG

Mild Maculopathy

Bull’s Eye Maculopathy

Major Risk Factors

<table>
<thead>
<tr>
<th>Table 1. Major Risk Factors for Toxic Retinopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dosage:</td>
</tr>
<tr>
<td>HCQ</td>
</tr>
<tr>
<td>CQ</td>
</tr>
<tr>
<td>Duration of use:</td>
</tr>
<tr>
<td>&gt;5 Yrs, assuming no other risk factors</td>
</tr>
<tr>
<td>Renal disease:</td>
</tr>
<tr>
<td>Subnormal glomerular filtration rate</td>
</tr>
<tr>
<td>Concomitant drugs:</td>
</tr>
<tr>
<td>Tamoxifen use</td>
</tr>
<tr>
<td>Macular disease:</td>
</tr>
<tr>
<td>May affect screening and susceptibility to HCQ/CQ</td>
</tr>
</tbody>
</table>

CQ = chloroquine; HCQ = hydroxychloroquine.
Screening Recommendations

Table 2. Screening Frequency

<table>
<thead>
<tr>
<th>Baseline Screening</th>
<th>Fundus examination within first year of use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Add visual fields and SD OCT if maculopathy is present</td>
<td></td>
</tr>
<tr>
<td>Annual Screening</td>
<td>Begin after 5 yrs of use</td>
</tr>
<tr>
<td>Sooner in the presence of major risk factors</td>
<td></td>
</tr>
</tbody>
</table>

SD OCT = spectral-domain optical coherence tomography.

30 YO WM

- **Medications:**
  - In the past week patient:
    - 2 courses of azithromycin (1 gram each)
    - Injection of rocephin
    - Injection of penicillin G
    - Currently taking doxycycline 100 mg bid
    - Valtrex 1 gram 3 times per day for 7 days (d/c 1 day ago)
    - Was on Vigamox qid for 7 days (d/c 1 day ago)
  - **VA:** 6/7.5 (20/25) OD, OS
  - Entrance skills unremarkable though some pain on eye movement

30 YO WM

- **SLE:**
  - 2+ injection conjunctival both eyes
  - 1-2+ lid edema
  - Mixed papillary and follicular response
  - 1-2+ diffuse SPK (no staining noted above infiltrates)
  - No cells or flare noted

30 YO WM

- **AdenoPlus:**
  - Performed on the right eye (patient felt that was the worst eye)
  - Negative

30 YO WM

- **Started patient on the miracle drop**
  - Tobradex 4 times per day and scheduled patient to come back the next day
- **1 day f/u**
  - Patient was feeling better
  - Less redness and much reduced photophobia and discomfort
  - No improvement on painful urination or discharge and is now seeing blood in his urine
  - Continue tobradex 4 times per day and RTC in 4 days for f/u with dilation and told to contact PCP to update on the blood in the urine
30 YO WM

- 4 day f/u:
  - Patient says his eyes are doing great and that all of his urogenital problems abruptly stopped on Saturday
  - Discussion with PCP: Kidney stone
  - What was going on with the eye?
    - Viral conjunctivitis likely EKC

What did we learn from this?

Adult Inclusion Conjunctivitis

- occurs in sexually active adults
- women are more susceptible than men,
- usually transmitted through hand-to-eye spread of infected genital secretions.
- incubation period is one to two weeks
- Signs and Symptoms:
  - ocular irritation, watering, mucopurulent discharge and positive nodes
  - often a unilateral disease but can involve both eyes
  - follicles inferior fornix, mixed papillary/follicular on upper lid, subepithelial infiltrates, SFR.

Adult Inclusion Conjunctivitis Treatment

- If left untreated, resolves spontaneously in 6-18 months
- can be treated topically with tetracycline, erythromycin, and fluoroquinolones
  - due to the high prevalence of concomitant genital tract infection, systemic antibiotic therapy is recommended
- Mainstay oral treatment is:
  - Azythromycin 1 gram dose or
  - Doxycycline 100 mg po BID or 7-10 days.
- Topical AB therapy is done concurrently.

Corneal Ulcers

- Infective bacterial and fungal corneal lesions cause severe pain and loss of vision
- Signs and Symptoms:
  - Pain, photophobia, tearing
  - Mucopurulent discharge with generalized conjunctival injection
  - Decreased VA (esp if on visual axis)
  - Possible AC reaction and hypopyon
  - Dense infiltrate
  - Satellite lesions around main lesion may indicate fungal infection
Associated Factors

- Contact lens wear, especially soft and extended wear lens
- Recent history of corneal trauma
- Topical steroid use
- History of exposure to vegetative matter (fungal etiology)

When to culture?

- 1,2,3 Rule:
  - 1 mm from visual axis
  - 2 infiltrates (or more)
  - 3 mm or greater in size
  - Nosocomial infections
  - Immuno-compromised patient
  - Post-surgical

Sterile vs Infectious Infiltrates

<table>
<thead>
<tr>
<th>Sterile Infiltrates vs. Infectious Infiltrates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sterile Infiltrates</td>
</tr>
<tr>
<td>Smaller lesion (&lt; 1 mm)</td>
</tr>
<tr>
<td>More peripheral</td>
</tr>
<tr>
<td>Minimal epithelial damage</td>
</tr>
<tr>
<td>(Defect size compared to underlying infiltrate)</td>
</tr>
<tr>
<td>No mucus discharge</td>
</tr>
<tr>
<td>Less pain and photophobia</td>
</tr>
<tr>
<td>No lid involvement</td>
</tr>
</tbody>
</table>


Peripheral (Sterile) Corneal Ulcer

Corneal Ulcers

- The Steroids for Corneal Ulcers Trial (SCUT)
- Conclusions:
  - no overall difference in 3-month BSCVA and no safety concerns with adjunctive corticosteroid therapy for bacterial corneal ulcers
  - researchers did find significant vision improvement for one specific subgroup of the study by using steroid therapy on patients with severe ulcers
- Application to Clinical Practice:
  - Adjunctive topical corticosteroid use does not improve 3-month vision in patients with bacterial corneal ulcers unless in the severe category
ARMOR

- Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR)
- Approximately 42% of isolates were determined to be MRSA
- Newer fluoroquinolones have better activity than earlier generations
- Besivance has the lowest MIC values of all the fluoroquinolones
- Vancomycin is drug of choice if MRSA present
- Azithromycin had very poor activity against Staph

Management

- Infective ulcers need to be cultured!
- If contact lens wearer, consider culture of contact lens
- Intensive topical antibiotic regimen, consider fortified preparations, subconjunctival injections.
  - loading dose of Vigamox/Moxeza/Zymaxid/Besivance 2gtts q 15 min x 1 hour,
  - 1gt q 30 min x 6 hours,
  - 1 gt q 1 hr until f/u in 24 hours.

Pseudomonas case report

“Doxycycline as an adjunctive therapy…may help to stabilize corneal breakdown and prevent subsequent perforation.”

AM. McElvanney

Sinusitis Red Eye

- Sinus infections (rhinosinusitis), are an inflammation of the nasal and sinus passages that can cause uncomfortable pressure on either side of the nose and last for weeks
- The increase in mucus creates pressure in the sinuses that leads to pain.
- The sinuses surround the ocular region
  - pressure from sinuses may feel like eye pressure.
  - swollen sinuses and nasal membranes can push against ocular nerves resulting in pain.
- Most develop during or after a cold or other upper respiratory infection, but allergens and environmental irritants may also trigger them

Sinusitis Treatment

- The infection is likely bacterial and should be treated with antibiotics if:
  - symptoms last for 10 days without improvement, or
  - include fever of 102 degrees or higher,
  - nasal discharge and facial pain lasting three to four days
- Because of increasing resistance to the antibiotic amoxicillin — the current standard of care — the ISDA recommends Augmentin
- Augmentin 250/500 TID for 5-7 days for adults, 10-14 days for children