Everything Therapeutic: San Antonio

Course Notes

To view notes for a specific lecture, click the lecture title on the agenda page to instantly progress to the appropriate section.
# Everything Therapeutic
## San Antonio

### Program Location
The Westin Riverwalk Hotel
420 West Market Street, San Antonio, Texas 78205

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
<th>Speaker Information</th>
<th>COPE ID#</th>
<th>Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:00 am - 8:00 am</td>
<td>Registration, Continental Breakfast, &amp; Visit Exhibits</td>
<td></td>
<td>65597-AS</td>
<td></td>
</tr>
<tr>
<td>8:00 am - 9:45 am</td>
<td>Clinical Challenges in Uveitis: Tales from the AC</td>
<td>David Sendrowski, OD, MS, FAAO</td>
<td>65610-GL</td>
<td>2 D/T</td>
</tr>
<tr>
<td>9:45 am - 10:15 am</td>
<td>Break &amp; Visit Exhibits</td>
<td></td>
<td>59971-AS</td>
<td>1 D/T</td>
</tr>
<tr>
<td>10:15 am - 11:05 am</td>
<td>Ocular Dermatology: Lids and Lesions</td>
<td></td>
<td>61963-AS</td>
<td>1 D/T</td>
</tr>
<tr>
<td>11:05 am - 12:00 pm</td>
<td>Anterior Segment: Herpes Simplex Infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12:00 pm - 1:00 pm</td>
<td>Lunch &amp; Visit Exhibits</td>
<td>Robert Prouty, OD, FAAO</td>
<td>65620-GL</td>
<td></td>
</tr>
<tr>
<td>1:00 pm - 2:45 pm</td>
<td>Controversies in the Basic Glaucoma Evaluation</td>
<td></td>
<td>52520-GL</td>
<td>1 D/T</td>
</tr>
<tr>
<td>2:45 pm - 3:15 pm</td>
<td>Break &amp; Visit Exhibits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3:15 pm - 4:05 pm</td>
<td>Pot Glaucoma Updates: What We All Should Know</td>
<td>Joe DeLoach, OD, FAAO</td>
<td>60627-EJ</td>
<td>1 GEN/PR</td>
</tr>
<tr>
<td>4:05 pm - 5:00 pm</td>
<td>2019 Professional Responsibility Course for Texas Optometrists</td>
<td></td>
<td>62267-NO</td>
<td>1 GEN/PR</td>
</tr>
</tbody>
</table>

### Saturday, November 23rd

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
<th>Speaker Information</th>
<th>COPE ID#</th>
<th>Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:00 am - 8:00 am</td>
<td>Registration, Continental Breakfast, &amp; Visit Exhibits</td>
<td></td>
<td>62267-NO</td>
<td></td>
</tr>
<tr>
<td>8:00 am - 9:45 am</td>
<td>Rules and Exceptions in Neuro-Ophthalmic Disease</td>
<td></td>
<td>65622-PS</td>
<td>2 D/T</td>
</tr>
<tr>
<td>9:45 am - 10:15 am</td>
<td>Break &amp; Visit Exhibits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10:15 am - 12:00 pm</td>
<td>Conversations in Optic Nerve and Retinal Vascular Disease</td>
<td></td>
<td>65612-PS</td>
<td>2 D/T</td>
</tr>
<tr>
<td>12:00 pm - 1:00 pm</td>
<td>Lunch &amp; Visit Exhibits</td>
<td>William Townsend, OD, FAAO</td>
<td>65611-PS</td>
<td>1 D/T</td>
</tr>
<tr>
<td>1:00 pm - 2:45 pm</td>
<td>Depress Your Patient: Diagnosis and Management of Vitreoretinal Anomalies</td>
<td></td>
<td>52613-AS</td>
<td>1 D/T</td>
</tr>
<tr>
<td>2:45 pm - 3:15 pm</td>
<td>Break &amp; Visit Exhibits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3:15 pm - 4:05 pm</td>
<td>Preparing the Dry Eye for Contact Lens Wear</td>
<td></td>
<td>65611-PH</td>
<td>1 D/T</td>
</tr>
<tr>
<td>4:05 pm - 5:00 pm</td>
<td>Managing Ocular Pain and Inflammation</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Clinical Challenges in Uveitis: Tales from the AC!

David P. Sendrowski, O.D., FAAO
Chief, Ophthalmology Consultation / Special Testing / Chronic Care Service
Professor/SCCO

Disclosure Information

• Lecture Bureau for:
  • Alcon Pharm.
  • Allergan Pharm.
  • VSP
  • Ista (Merck) Pharm.
  • Shire Pharm. (consultant/lecturer)

• Nor do I or any immediate family member have any personal business interests, affiliation or activity with any entity in the Optometric health care field that would give rise to a Conflict of Interest in this lecture.

• No animals were harmed or mistreated in the development of this lecture- although some were moved from the keypad and some words may not appear as intended!!

OVERVIEW OF UVEITIC DISEASE

• Classification
• Immune Response
• Laboratory Evaluation
• Treatment Philosophies
• Management
• Uveitis accounts for 10–35% of blindness in individuals under 65 years of age
• Mutton Fat KPs!!!!
New Thoughts on Autoimmunity, Autoinflammation and Infection in Uveitis

AJO, Forrester, JV, et al. May 2018

- Infection may be implicated in “idiopathic” uveitis
- TH17 “key” cytokine found to start uveitis! (2018)
- Recognition that foreign antigen, and/or reactivated infectious agents may hide in ocular tissues
- Possibility that dysregulated microbiome may generate T-cells that cause immune-related ocular inflammation has been demonstrated experimentally

UVEITIS WORK-UP

- History - **vital component**
  - Unilateral * / bilateral presentation
  - Time course (acute or limited: < 3 months / chronic or persistent > 3 or months)
  - Prior therapy (recurrent)
  - Systemic diseases - (i.e., Sarcoidosis, Herpes Simplex, Herpes Zoster)
  - STD’s - (i.e. AIDS, syphilis, chlamydia)
- Diet - (i.e. Toxoplasmosis)
- Pets - (i.e. Toxoplasmosis, Toxocariasis)
- IV drug use - (i.e. fungal)
- Family history

- Age
- Race
- Sex
- Geographic location (Ohio / Mississippi / Missouri)
- Symptoms - (i.e., photophobia, pain, redness, decreased vision, lacrimation, etc.)

Best Three Questions to ask and Document in Patients with Uveitis

1. Recent Skin Rashes: Sarcoid, Reiter’s (RA), Bechet’s, Psoriatic Arthritis.
2. Recent Respiratory Problems: Sarcoid, Histo, Coccidiomycosis, TB
3. Recent Joint Pain or Stiffness: Ankylosing Spondylitis, Reiter’s (RA), IBD, Psoriatic Arthritis.

1. dsendrowski@ketchum.edu (Uveitis questionnaire) Beacon Hill Park
“Suggested” office work up

- Physical observation peri-ocular tissues (R/o HS, HZ)
- Pupils
- Biomicroscopy
  - Corneal Endothelial (KPs) type, configuration.
  - A/C
  - Iris--look for nodules, PS, PAS (Gonioscopy!!-extra 45$)
  - Ant. Vitreous
- BIO (92225/6) (R/o Post. Uveitis)
- IOP (vital)
- Charges (99214/3 or 99204/3)

Cell and Flare Examples

Lab work-up

- First time attack- no signs & suggestive Hx. (none or minimal)
- Referral letter to M.D. for physical
- If possible - order a few tests if uveitis is recurrent/severe: other findings
- Things to ponder:
  - 50% labs come up negative
  - Should be 50% (+) certain of the disease in chair to direct lab test
Steroids

- Need a long acting steroid with good anti-inflammatory properties (Pred. Forte 1%, Lotemax, Durezol – good choices)
- Need to use the steroid aggressively in the first 7 to 14 days (q1h or q2h) – you have no idea what level the inflammation is at.
- If AC cells drop "TWO" grades (SUN paper 2005) (3+ → 1+) you may start to taper or when you note a significant reduction.
- Hit uveitis hard and fast!!!!
New Steroid

Watch out for IOP spikes:
1. Children
2. Known responders
3. Diabetics

- **Never switch steroids:** If Tx. is working but IOP elevates – uveitis patients can stay on steroid. Usually less than 5 to 10 mm Hg. About 10% go higher than that.
- If IOP > 27mm Hg (Use BB, Alpha 2, CAIs)
- Always evaluate IOP at every visit as well as corneal to R/o HS
- Taper steroid from q1h to q2h when you observe a two grade cells reduction or a minimal AC reaction.
- Inflammation does **way more damage** than IOP.

Cycloplegia

- Good for the first (3) days to reduce photophobia, PS/PAS, and helps shore up blood/ocular barrier
- If no synechiae are present D/C after 3 days
- If synchiae already there – may need to keep patient on cyclo. Tx. or if fibrin level is high in AC
- If multiple synechiae present - try atropine/scopolamine/10% Neosynepherine to break synechiae and consider longer duration cycloplegics if synechiae are 180° or greater and IOP is elevating
Few Items

- Steroids cause ptosis (1-2mm) - it goes away after D/C steroid
- Steroids cause mydriasis - it goes away after D/C steroid
- Steroids alters TBUT, corneal rigidity, tear production - returns to normal after D/C steroid
- Pressure usually goes up 10 mmHg for steroid responder (30% max. with exceptions)
- Secondary glaucoma – most handled with topical therapy, some require surgical intervention
- Three types of glaucoma: Pupillary Block Glaucoma versus secondary "steroid induced" ODs are now allowed to treat under new law / secondary CACG (PAS)

Take Home Pearl:

- In an effort to do no harm with a topical steroid, practitioners (OD's/OMD's) utilize steroids sparingly causing greater harm to the eye in the long run

Future for biological therapy for uveitis

- Biologics (i.e., Infliximab) may be in the future initial therapy
- Include AB's, soluble receptors, and cytokines
- Anti-TNF alpha – most widely employed*
- IntraVitreal Injections (Anti-Inflam. & nano)
- Biologics have tremendous potential in the treatment of ocular inflammation but studies have been limited and side-effects are not completely known.**

New and Standard Treatment Modalities

**Antimetabolites**
- Azathioprine (Imuran)
- Methotrexate (Rheumatrex)
- Mycophenolate Mofetil (Cellcept)

**T-Cell Inhibitors**
- Cyclosporine (Sandimmune, Neoral)
- Tacrolimus (Prograf)

**Alkylating Agents**
- Chlorambucil (Leukeran)
- Cyclophosphamide (Cytoxan)

**Biologics**
- Infliximab (Remicade) **
- Etanercept (Enbrel) **
- Interferon (Avonex)
- Daclizumab (Zenapax)
- Alefacept (Amevive)
- Efalizumab (Raptiva)
- Tofacitinib (Xeljanz)

---

**Key Features in Uveitis Treatment**

- Topical steroids are the mainstay of therapy for acute uveitis.
- Topical and Oral NSAIDs are steroid sparing and not primary therapy.
- Systemic corticosteroids are beneficial for bilateral, non-infectious, unresponsive uveitis.
- The initiation therapy is typically 0.5–1 mg/kg daily followed by a slow taper once the inflammation is under control.
- Periocular Steroids, Intravitreal Steroids, previously mentioned antimetabolites, Biologics, etc.
NSAIDS that can be utilized with AU and may be under utilized**

- Fenoprofen Nalfon
- Ketoprofen Oridus
- Piroxicam Feldene
- Flurbiprofen Ansaid
- Ketorolac Toradol
- Naproxen Naprosyn
- Ibuprofen Motrin, Rufen

**As prostaglandin inhibitors, NSAIDs (particularly aspirin and ibuprofen) reduce inflammation, thus are sometimes useful. In addition, NSAIDs may play a role in reducing inflammation associated with cystoid macular edema that may accompany anterior uveitis.

Top Causes / Associations of Anterior Uveitis

- Idiopathic (AKA: Undifferentiated)
- HLA- B27 related (C/R/A/P)
- Sarcoidosis
- Herpes Virus (HSV & VZV)
- Juvenile Idiopathic arthritis – associated uveitis
- Fuch’s Heterochromic Iridocyclitis (FHI)
- Posner-Schlossman Syndrome
- Syphilis
- Masquerade Syndrome

DIFFERENTIAL DIAGNOSIS AND TREATMENT OF UVEITIS
TINU: Tubulointerstitial Nephritis and Uveitis Syndrome (Dobrin syndrome)

- Accounts for 1/3 of cases of acute “bilateral” anterior uveitis in patient<20
- Slight female predominance, some texts state male pred.
- 1 to 2+ cells, BCVA (good) but 20/40 to 20/100, abdominal pain possible, may have signs of renal insufficiency.
- Tests: BUN, Urinalysis (Beta 2-microglobulin levels specifically ordered) & possible renal biopsy.
- TX: most do well on topical steroids, small % need orals for uveitis control.
- KEY: early suspicion and diagnosis of kidney disorder.
Idiopathic (Undifferentiated) Uveitis

- Etiology
  - Most common type (65 to 70%)
  - Age 18 to 50
  - Male = female
  - Unilateral presentation
  - TINU* (young pts <20)
  - Drug Induced:
    - Prostaglandins
    - Metipranolol

- Ocular presentation
  - Severe pain and moderate photophobia
  - Little to no flare
  - Red and injected eye
  - Miotic pupil
  - Synechiae possible but slow formation
• Investigation
  – Not necessary if first attack and (-) systemic signs/symptoms
  – FTA – ABS (treatable)
  – CBC with differential (Leukemia?)
  – Urinalysis (Protenuria & Diabetes)
  – CXR (PPD-treatable / Sarcoidosis)
  – Beta 2-microglobulin levels (r/o TINU)
  – Review Pt’s drug list (new drugs)

• Ocular treatment
  – Topical steroid (Q1h to Q2h initially) *(Hit HARD!!!-Hit Fast!!!)*
  – Topical cycloplegic (BID or QD)
  – Oral NSAID to reduce pain
  – Resolution in 10-21 days

• Anklyosing Spondylitis
  – Etiology
    • Disease of the axial skeleton
    • Males (3x) > females (1x)
    • Ages 20-40
    • Women – older and more
      – Peripheral joint involvement.
      – Neck pain and breast pain
• Affects 0.1% of Caucasian adults
  – Lower back pain/stiffness in morning lasting 15 min. > 3 months. Nocturnal as well.
  – Other complaints are “pain in the chest cavity and difficulty with chest expansion”
  – Anorexia, fever, malaise - systemic signs
  – “gut microbiome” - Rosenbaum &
  – Colleagues discuss AS as a microbiome-driven disease

Ocular presentation
• Anterior uveitis - usually unilateral
• Recurrence in same or other eye
• Rapid onset of pain and photophobia
• Flare may be heavy or light
• Posterior synechiae form quickly
• Episodes vary 2-6 weeks

Fibrin clots or aggregations
Posterior Synechiae

Peripheral Anterior Synechiae

Investigations

- X-rays / CT / MRI of sacroiliac joints
- (MRI for early enthesopathy if X-rays negative—enthesopathies are disorders of peripheral ligamentous or muscular attachments)
- ESR ↑ / C-reactive protein ↑
- RF (-) / ANA (-)
- Family Hx of AS (+/-)
- Alkaline phosphotase levels ↑
- HLA B27 (+) tissue typing (* + more severe ocular complications AOA news 2016)
- Vitamin D Levels –Risk of Osteoporosis
- Electrocardiogram (?) if heart Dz in the FH
Ocular / Systemic Therapy

- Topical steroids (q1h to q2h - initially)
- Topical cycloplegic agents (QD or BID)
- Periocular steroid injections for more severe cases
- NSAIDS, COX-2 inhibitors - mainstay for systemic treatment & physical therapy
- TNF inhibitors (Etanercept, Infliximab)

Can’t see. Can’t pee, Can’t Dance with Me

Reiter’s Syndrome (Reactive Arthritis)

- Etiology
  - Triad (conjunctivitis, arthritis, urethritis)
  - Anterior Uveitis in 15 to 20%
  - Males > females (9:1 / 1:1)
  - Ages 18 - 40 more common

Forms of RS

- Post venereal = conjunctivitis (30-60%)
- Arthritis (asymmetric - large weight bearing joints) presenting with anterior uveitis (15%)
- Post dysenteric: Shigella, Yersinia, Salmonella, Campylobacter
  - (usually 1 to 4 weeks after the dysentery)
- Chlamydia Trachomatis, most common agent causing the venereal disorder so look for signs of inclusion conjunctivitis or Ureaplasma urealyticum (bacterium: urethritis/bacterial vaginosis)
Ocular presentation / Systemic signs

• Inclusion conjunctivitis is most common presentation → post infection (2-4 wks → uveitis)
• Superior micropannus of cornea (if chlamydial infection)
• Anterior uveitis → arthritic form
• Systemic signs with ocular presentation:
  keratodermal blennorrhagicum, circinata blanatis (ddx: pustular psoriasis), aphthous stomatitis, rheumatologic signs: plantar fasciitis.
• Heavy flare and cells (flare may be plasmoid)
• Course is 2-6 weeks
• Glaucoma possible after repeated episodes

Investigation
• X-rays of knees, ankles, feet, heels, Achilles tendon, and sacroiliac area
• Cultures for chlamydia from conjunctiva, urethra
• HLA-B27 (++)
• Fecal cultures for post dysenteric
• ESR and CBC (leukocytosis with mild anemia ?)
• Creatinine (+) – Elevated
• CRP (+)

Investigation
• Nail pitting
• Palate / tongue ulcers
• HLA tissue typing (HLA B27)
• RF (-)
• ANA (-)
### Ocular / Systemic Treatment

- Topical steroids (Q1h to Q2h initially)
- Quick removal of steroids may cause return of inflammation
- Topical cycloplegics (QD to BID)
- Periocular steroid injections for more severe cases
- NSAIDs, second line: methotrexate & sulfasalazine, biologics (etanercept, infliximab)
- Co-management with interest for venereal; rheumatologist for arthritis is recommended

### Systemic therapy (if venereal)

- Oral tetracycline 250mg
- Oral doxycycline 100 mg
- Oral arithromycin 1000 mg (zithromax)

### Sarcoidosis

- **Etiology**
  - Usually African-American (blacks 8-10X > whites)
  - Also Euro Whites / Japanese patients
  - Women > men
  - Multi-systemic disease: hallmark, non-caseating granulomas (eval. the peri-ocular region)
  - Accounts for 3-10% of all uveitic cases
  - 50% patients develop ocular sequellae— usually anterior
  - Etiology unknown – immunological pathology
• Most commonly seen in the Atlantic Gulf Coast states
• Ages 20-40 (children under age 5) 60 to 70
• Disease has anterior and posterior involvement
• Acute / chronic presentation
• Systemic symptoms: respiratory (most common symptom) associated with fever, fatigue (27%), dyspnea, weight loss (28%)
• Patients may be asymptomatic at the time of Dx.

Ocular Presentation

Anterior uveitis, presenting either acutely or as a chronic granulomatous iridocyclitis, is the most common ocular lesion, occurring in approximately two-thirds of patients with ocular sarcoidosis.

Mutton-fat KPs, including those involving the anterior chamber angle

Koeppe and Busacca iris nodules

Although the cornea is infrequently involved, nummular corneal infiltrates and inferior corneal endothelial opacification may be seen.
• KPs are extremely large (mutton-fat)
• Iris nodules are usually present (20%)
• Cataracts and glaucoma are complications (chronic form)

• Posterior segment: (involvement is less frequent)
  – Vitreous snowballs – located inferiorly and lie on the retinal surface (vitritis)
  – "Candle wax drippings" – (en taches de bougie) venule involvement
  – Perivenous sheathing
  – Choroidal lesions (Dalen-Fuch's nodules)
- Choroidal granuloma (rare)
- Chronic cystoid macular edema
- Neovascularization of the disc (15%)
- Optic disc swelling (40%)

• Skin lesions - erythema nodosum or sarcoid nodules under the skin
• Lungs are frequently affected
• Facial nerve palsy is possible as well
Types of Ocular Sarcoidosis

- **Definite Ocul.** (+) Biopsy with associated Uveitis
- **Presumed Ocul.** Biopsy not done, (+) hilar, uveitis
- **Probable Ocul.** Biopsy not done, CXR nml, 3 ocular signs and 2 (+) lab tests
- **Possible Ocul.** Biopsy neg., 4 ocular signs, 2(+) lab tests.

Investigations

- Chest X-ray (hilar adenopathy) *Lung is the number one organ affected by the disease*
- ACE (+) > 67 u/L
- Serum lysozyme (+)
- PPD (-)
- Blood panel
- Serum amyloid A (SAA)
- Soluble interleukin-2 receptor (sIL-2R),

May present as:
- Shortness of breath
- Chest pain
- Persistent dry cough
• Gallium scan of the head and neck
• Biopsy of conjunctiva or skin or lacrimal gland nodule
• ACE and gallium scan will give false negative if patient is taking steroids
• Pulmonary function tests

Differential diagnosis

• Sickle cell disease
• Lyme Disease
• TB
• Idiopathic pars planitis
• Histoplasmosis / Coccidiomycosis

Systemic Treatment

1. Spontaneous resolution in 24-36 months (50%)
2. Low dose Corticosteroids (20-40 mg/d)
3. Cyclosporin therapy – no safe long term approach with this drug
4. Methotrexate--low dose good for long term tx (azathioprine)
5. Chloroquine (Hydrocholoroquine) for pulmonary
6. Biologics (Etanercept / Infliximab for refractory uveitis)
Ocular Treatment

- Topical steroids (q1h to q2h) depends on activity
- Topical cycloplegics (BID or QD)
- Periocular steroids if topicals are ineffective (intermediate)
- Oral steroids and histamine H2 blocker if treating intermediate / posterior uveitis, facial nerve palsies, pulmonary problems
- Cyclosporin A - effective in patients intolerant to oral steroids

- Anti-glaucoma meds (topical and oral) for 2° complications (aqueous suppressants)
- Panretinal photocoagulation for neovascularization
- Patients need to be re-examined in 3-7 days
- Asymptomatic patients seen Q 6 months
- Steroid treated patients need to be seen Q 3 months
- Children with Sarcoidosis need to be seen Q 1-3 months

Herpes Simplex Uveitis

- Etiology
  - Corneal dendritic ulcer present
  - Uveitis 2° to trigeminal involvement
  - Hx of recurrent red eye
  - Stellate and diffuse KPs
  - Increased IOP (30-60 mm HG)
  - Two types: immune/inflammation response iritis or secondary to the virus itself
HSV I vs HSV II

- Humans only natural reservoir of herpes
- DNA virus: important concept for therapy
- Sources of infection: direct contact with lesions, salivary droplets, saliva and less from fomites of asymptomatic virus shedding carriers.
- Strong suggestion that we will or may already be seeing an increase in incidence of type 2 HSV keratitis*
  - 1 in 4 in US > age 30 infected with HSV 2 *
  - Infection with type I becoming delayed in industrialized countries*
  - Changes is sexual behavior in young adults (genital HSV I infections)*


HS Uveitis

- Intraocular pressure. Most patients with acute iritis have low pressures. High IOP in a patient with acute iritis is suggestive of a herpetic etiology, although there are other causes of hypertensive uveitis. (PSG)
- Fine stellate keratic precipitates (KPs). "Fine stellate KPs are also seen in diseases such as Fuchs’ heterochromic iridocyclitis and CMV retinitis."
- Large, central, greasy KPs.
- Iris transillumination defects in a patient with iritis.
- Atrophy of the iris pigment epithelium, not just the anterior stroma.
- Presence of a dilated pupil in the absence of dilating drops.
- "No single clinical feature can make the definitive diagnosis of herpetic iritis,"

Investigation

Primary HSV I & II (clinical diagnosis)

- Lab
  - Tissue culture (2-5 days/expensive)
  - Polymerase chain reaction (specific)
  - Giemsa stain (multi-nucleated giant cells)
  - Neutralizing and complement-fixation Ab after 1 week (1º only)
Treatment: HSV I & II

- Epithelial HS uveitis:
  - Treatment
    - Debridement: Untreated: resolution occurs in 7 to 10 days; treated: resolution in 2 to 5 days
    - Trifluridine 1.0%, 5-9 x per day until healed
    - Ganciclovir gel, 0.15%, 5 x per day until healed
    - Cycloplegic (first, wait 24/48 hrs. to start top. steroid)
    - Topical Steroid (QID - start 24 hrs. after antiviral)
    - Oral Acyclovir (400mg>5x/day) off label alternative*
  - Glaucoma: aqueous suppressant


---

Posner-Schlossman (Glaucomatocyclitic crises)

- Etiology
  - Inflammatory glaucoma (Viral infection)
  - Young to middle aged adults
  - Males > females
  - Some relationship to HS virus thought to be the etiology
• Ocular presentation
  – Unilateral presentation (blurred vision)
  – Severe pain with little photophobia
  – Trace cells in AC (stellate cells on the endo)
  – No Iris heterochromia!!
  – Highly elevated IOP (40-60 mmHg) (diagnostic clue)
  – Dilated pupil - may be fixed
  – Angles are wide open to gonioscopy
  – Cornea may be edematous if IOP > 60 mmHg

• Investigation
  – None
  – Sentinel KP's and Trace AC cells
  – Clinical diagnosis - gonioscopy
• Ocular treatment
  – Topical beta-blocker (BID)
  – Topical steroid (QID) - 1 week
  – Anti-Viral Tx (AV: 400 mg/5x/D)
  – Topical α2 agonist (tid)
  – Add CAI if IOP is extremely elevated, methazolamide 25-50 mg PO 2-3x/day, or acetazolamide 500 mg PO, BID
  – Hyperosmotic agents - if IOP is dangerously high and may harm the ONH
  – Consider topical cycloplegic agent if the patient is symptomatic
OCULAR DERMATOLOGY: 
Lids and Lesions

David P. Sendrowski OD, FAAO
Professor / SCCO/ MBKU
Chief, Ophthalmology Consultation and Special
Testing Service / KH

Disclosure Information

- Lecture Bureau for:
  - Alcon Pharm.
  - Allergan Pharm.
  - VSP
  - Ista (Merck) Pharm.
  - Sucampo Pharm.
  - Shire Pharm. (consultant/lector)

- Nor do I or any immediate family member have any personal business interests, affiliation or activity with any entity in the Optometric health care field that would give rise to a Conflict of Interest in this lecture.

- No animals were harmed or mistreated in the development of this lecture- although some were moved from the keypad and some words may not appear as intended!!

Why OD’s Should Care About Dermatology?

1. About 90% of non-melanoma skin cancer is caused by ultra-violet exposure (UV-B)—southern California
2. One person dies from melanoma almost every hour in the US.
3. Skin cancer accounts for nearly 50% of all cancers combined.
4. In 2015, the latest year for which incidence data are available, 80,442 new cases of melanomas of the skin were reported, and 8,885 people died of melanomas of the skin in the United States
Why Care About Dermatology?

5. Skin cancer is most deadly for **African Americans, Asians, and Latinos**

6. One in three Caucasians will be diagnosed with skin cancer.

7. Just one bad burn in childhood increases the risk of developing melanoma later (42% of patients reported getting “sunburned” at least once a year- recent study)

8. Men are diagnosed with skin cancer more often than women. (Occupational?)

Latest Skin Cancer Data: 2015

Location of melanomas for men and woman
DERM TERMS

• Macule
• Papule
• Plaque
• Wheal

**Macule**: a circumscribed change in skin color without elevation or depression. (greater than 1 cm = patch)

Freckles are macule lesions

**Macule Examples**

• Flat Nevi
• Lentigines (Liver spots)
• Ash Leaf Macule in Tuberous Sclerosis
Treatment of Freckles

- Topical Retinoids: 0.1% tretinoin, 0.1% tazarotene, 2% 4-hydroxyanisole with 0.01% tretinoin (Solage)
- Laser Therapy
- IPL Therapy (some OD’s use them for Ocular Rosacea)!!
- Cryotherapy
- OTC: bleaching/fading creams: products with hydroquinone and kojic acid

Papule: a solid elevated lesion usually 0.5 cm or less in diameter (vary in color, and shape: dome, flat, etc.) The term "papule" is derived from Latin from "papula," a pimple

Papule Examples
Treatment of papules

• Topical Antibiotics:
  – Erythromycin or clindamycin, macrolides, with benzoyl peroxide topical gel (Cleocin T)
• Oral Antibiotics:
  – Tetracyclines (Tetra: 500 mg BID, Doxy: 50-100 mg BID, Mino: 50 Mg BID)

Plaque: a raised lesion that has a greater area as compared to its elevation above the skin surface

Treatment of Plaques

• Calcipotriene ointment 0.005% or Calcitriol ointment 0.003% (Vit. D analogs) are very good for plaque psoriasis.
• Topical corticosteroids- rapidly clears the lesion
• Topical retinoids
• Topical salicylic acid
**Wheal** (hive): a rounded or flat-topped elevated lesion formed by local dermal edema. (Many causes: meds and food, sun sensitivity, IVFA, insect bites)

**Wheal Examples and DDx**

**Treatment for Wheal (Urticaria)**

- Systemic:
  - H (1) Antihistamine (Benadryl)
  - Combination of H(1) and H(2) antihistamines
- Topical:
  - Local treatment is rarely rewarding
- Avoidance of Trigger Factors
- Diet & Activity
More Derm Terms

- **Nodule** -- a palpable solid lesion of varying size, greater than 0.5 cm and less than 2 cm in diameter.
- **Vesicle** -- a circumscribed elevated lesion which contains free fluid. Vesicles are 0.5 cm or less in diameter.
- **Pustule** -- (abscess) a circumscribed elevated lesion which contains pus.
- **Purpura** -- a non-blanching erythema or violaceous color due to extravasation of blood into the tissue. (petechiae, ecchymosis)

Purpura from Amylodosis

- **Ocular Purpura**
- **Pinch purpura**
Capillary Hemangioma

HISTORY

- Basic demographics of your patient (age, race, sex, current residency, avocation)
- Don’t forget about: PMH, FH, Occupation, hobbies, recent travel, new and current drugs, smoking & alcohol, known allergies.
- When, where, how of the skin lesion in question
- Location of lesion (head and neck)
- Exposure to UV (# sunburns, how they tan)
- Size (>6 mm-- ???)
- Time of onset-- when did pt. become aware.
- Growth rate

Skin Types (I to V) classification known as the Fitzpatrick skin type (or phototype) depends on the amount of melanin pigment in the skin. This is determined by constitutional colour (white, brown or black skin) and the result of exposure to ultraviolet radiation (tanning).
**History**

- Bleeding / ulceration / pain / weeping of lesion (most common— asymptomatic)
- Prior history of malignancy (skin* & all)
- Prior history of radiation therapy, exposure to arsenic, tar, treatments for psoriasis- UV light.

**PHYSICAL EXAMINATION**

- Tenderness, warmth, thickness, consistency
- Does it blanch with pressure, is it friable.
- Tumor Location / changes to normal tissue
- Dimensions
- Mobility of lesion
- Surface characteristics of lesion (irregularity of margins, pigmentation, homogeneity)
Putting it Into Practice

<table>
<thead>
<tr>
<th>Normal Size</th>
<th>Melanoma</th>
<th>Signs</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Regional</td>
<td>when half of the mole does not match the other half</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Border</td>
<td>when the border appears of the mole is irregular or ragged</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Color</td>
<td>when the color of the mole varies throughout</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diameter</td>
<td>if the mole diameter is larger than a pencil's eraser</td>
</tr>
</tbody>
</table>

Pressure test

Nodular melanoma
Angioma

Press suspected nodule firmly for 30 seconds; near-total involution is characteristic of hemangioma, not melanoma.

Physical examination

- Regional lymph node involvement
- Blanching
- Palpation
- Physical changes
Instrumentation – You have!!

- High illumination
- High magnification
- Good Observer

“If I look bad, I probably am bad”
“Ugly Duckling”

Eyelid Anatomy / Derm. layers

Skin of eyelid:
- Epidermis (4 layers)
  - Keratinocytes
  - Merkel cells
  - Langerhans cells
  - Melanocytes
- Dermis (vessels, nerves, lymphatics)
- Adenexal Tissue (Glandular Tissue: holocrine, apocrine, sebaceous.)
Benign Skin Lesions

- Squamous cell papillomas caused by HPV (commonly in oral mucosa)
- Squamous papillomas composed of papillae with vascularized connective tissue covered by epithelium
- Papillomas differ from infective warts (hypertrophic papillae with viral inclusions)
- Papillomas unlike warts occur gradually and in groups

Eyelid Papillomas

- An eyelid papilloma is any lesion on the eyelid that is papillomatous, that is, of smooth, rounded, or pedunculated elevation
- Squamous papilloma is a benign tumor of epithelial origin
- Seen most frequently in patients older than 30 years (Obese, Diabetics – higher risk)
- No race or sex predilection.
- Ask the patient if any similar lesions have occurred before (ask about any malignacies)

Eyelid Papillomas

- Benign epithelial lesion (flat or pedunc.)
- Lobular projection on 99%
- Resemble mulberries / cauliflower growth
DDX

- Should be distinguished from nevi, fibroma epithelioma, actinic keratosis, and seborrheic keratosis

Treatment

- Eyelid margin papillomas for which complete excision was cosmetically unacceptable. Try cautery but lid alteration may develop.
- Surgical excision usually is a simple procedure for these benign skin lesions.

Skin Tags / Eyelids & Peri-Ocular Lesions

- Human papillomavirus (HPV) has been implicated because HPV (DNA) were found in a high percentage (88%) of skin tag biopsies obtained from 49 patients.
- Skin tags are known to develop in areas of frequent skin friction, leading to disruption of skin which might serve as a route of entry for the virus.
- Polyps: larger skin tags, with broad tips, variable stalks or bases; polypoid surface
Skin Tags / Eyelids & Peri-Ocular Lesions

- Skin tags (Acrochordons)
- Typical locations: axillae, neck, eyelids
- Non-cancerous skin tumors that hang off the skin by a connecting stalk.
- 60% of the population get skin tags by age 65, (M>F), painless unless rubbed a lot
- Some medical conditions such as obesity, diabetes, insulin resistance and atherosclerosis are associated more frequently with skin tags

Skin Findings

- Skin tag is skin colored or brown 1-5 mm papule
- Skin tags persist indefinitely or fall off
- Acute changes cause patients to seek care
- Thrombosed skin tags appear black or hemorrhagic
- Not a big diagnostic dilemma

Treatment Skin tags

- Removal because of cosmetic or tenderness
- Best treated with scissor excision with or without anesthesia
- Electrocautery and cryosurgery also used
- Most dermatologist feel histologic conformation is not necessary
Malignant Eyelid Lesions

- 5 to 10% of all skin cancers occur in the eyelid “Noli-me-tangere” (Touch me not)
- BCC and SCC account for 95%
- Other 5%:
  - Sebaceous Gland Carcinoma (1-5%)
  - MM (1% or <)
  - Merkel Cell Carcinoma
  - Kaposi Sarcoma

Basal Cell Carcinoma BCC: Key Facts

- New BCC develops in 400-700K persons/year (incidence doubles for each 3°48’ decline in latitude)
- Risk Factors: outdoor occupation, light skinned, prone to sunburn (M>W)
- BCC more aggressive in younger age groups (W>M)
- BCC can affect children / young adults (immune status genetic background, sun exposure)
- Disease Risk Factors: AIDS, arsenic exposure, radiation exposure, thermal burns, and scars

Pathophysiology/Histology

- The patched/hedgehog intracellular signaling pathway plays a role in both sporadic BCCs and nevoid BCC syndrome (Gorlin syndrome).
- The hedgehog gene encodes an extracellular protein that binds to a cell membrane receptor complex to start a cascade of cellular events leading to cell proliferation.
- When SHH is present, it binds to PTCH, which then releases and activates SMO. SMO signaling is transduced to the nucleus via Gli.

* SHH: sonic hedgehog protein
**PTCH: patched protein
***SMO: smoothened protein
****Gli: downstream genes
Pathophysiology / Histology

- BCC most commonly develops on sun-exposed areas. Zhang et al reported that ultraviolet (UV)-specific nucleotide changes in PTCH, as well as the tumor suppressor gene TP53, are implicated in the development of early-onset BCC.
- UV-induced mutations in the TP53 tumor suppressor gene, which resides on band 17p13.1, have been found in some cases of BCC. A germline single-nucleotide polymorphism (SNP) in the TP53 gene, rs78378222, has also been associated with susceptibility to BCC.

BASAL CELL CARCINOMA (BCC)

- Background
  - Most common skin cancer in humans (3.3 million Americans treated yearly in the US) (M > F)
  - >90% of malignant eyelid cancers
  - Slowly growing, non-resolving
  - Areas of chronic sun exposure
  - 3.3 Million/yr. (2018)
  - **Fair skinned adults**
    - 50 to 80 years old

BCC develop from Basal Cells of the Epidermis
90% occur on face and neck (#1 site is nose)
- Eyelids: 65% LL, 15% UL, 15% MC, 5% LC
- Close inspection: Loss of cilia over area
- Typical patient: extensive UV-B exposure (with 20-50 yr latency!), Anglo-Saxon, red or blond hair, skin that burns rather than tans (not necessarily geriatric)
- Other causes: arsenic exposure, X-rays,

History of BCC (in the family or the patient)
- Metastasis very unlikely: BCC grows by direct extension rather than by blood or lymphatic spread
- BCC does not have any precursor lesion in older patients

BCC Types
- Nodular 65%
- Infiltrating 15%
- Superficial 10%
- Micronodular 6%
- Sclerosing 4%
- Cystic <1%
- Pigmented <1%
- Linear <1%
• **Characteristics:**
  – Nodular type most common (80%)
  – Starts as sessile or dome shaped lesion
  – Translucent, waxy, gray-white papule
  – Telangiectasias, haphazard on surface

  – Loss of fine skin lines
  – Borders are hard, often rolled, "pearly"
  – Initially smooth surfaced, but later with umbilication and ulceration (bleeding, scabbing)

**Clinical Differential is Difficult**

<table>
<thead>
<tr>
<th>Squamous cell carcinoma</th>
<th>Basal cell carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Squamous cell carcinoma" /></td>
<td><img src="image2.png" alt="Basal cell carcinoma" /></td>
</tr>
</tbody>
</table>
**Nevoid Basal Cell Carcinoma Syndrome**

- Also called Grolin-Goltz Syndrome (AD)
- 0.7% of patients with BCC have this syndrome
- Patients have only a few to thousands of BCCs
- There is a predilection of the BCCs to occur on the face and eyelids
- Lesions are red, brown and vary from 1 to 10 mm in size

---

**Work-Up**

- Biopsy (Punch vs Shave)
- CT / MRI of the regional nodes
- Dye test for node involvement
- PET Scan
Topical Treatments for BCC

1. **Topical 5-FU (5%)** Small, superficial BCC treatment
2. **Imiquimod (5%)** (FDA approved for non-facial BCC)
3. **Tazarotene (0.1%)**: small low risk BCCs

Surgical and Non-Surgical Tx for BCC

1. Radiation Tx (advanced and extended lesions)
2. Photodynamic Tx (50% for superficial and 83% for nodular)
3. Oral Retinoids (long term toxicity not good)
4. Hedgehog pathway Inhibitors (Vismodegib/Sonidegib)
5. ED&C, Excisional, Moh’s and Cryotherapy.

Moh’s Procedure
The following is a list of treatments and their 5-year recurrence rates for primary BCCs:

- Surgical excision - 10.1%
- Radiation therapy - 8.7%
- Curettage and electrodesiccation - 7.7%
- Cryotherapy - 7.5%
- All non-Mohs modalities - 8.7%
- Mohs micrographic surgery - 1.0%

Squamous Cell Carcinoma (SCC) Key Facts

- Second most common in caucosoids (US) about 150K per year.
- Most cases: chronic sun exposure and skin damage elderly people with fair complexion who tan poorly. (SCC is uncommon in patients with black African phenotype (tumor appears in association with a scar)
- Latitude plays a factor: Northeast Australia (600 new cases M/ 300 W vs Minneapolis 40 new cases M/ 13 W)

SQUAMOUS CELL CARCINOMA (SCC)

- Etiologic Factors
  - Second most frequent skin cancer after BCC (about 150K per year) (age>55) (2M>F) (ranges 7 to 11%)
  - Lifetime risk of SCC (5 to 15%) Sun exposure critical
  - 12/100,000 white males, 7/100,000 white females, 1/100,000 blacks
  - Occur on sun-damaged skin (occupational or recreational), but also on scar tissue, burns, chronically draining or infected sinuses, tar from cigarettes
  - Frequent on face, head, neck, and hands (M:90% / W:80%)
  - Occurs more often on the upper eyelid than BCC but most frequently on lower eye lid
- Fair-skinned patients most vulnerable (Irish or Scottish) (Hx: never or rarely tans) Often arise from pre-cancerous conditions
  - Actinic Keratosis (AK)
  - Arsenic, tar
  - Chronic scarring
  - Bowen’s Disease
  - Keratoacanthoma
  - Much less common on eyelids than BCC
  - Frequently ulcerates centrally
  - Look for nearby AK

Histopathology
- DNA damage from (UVB) inactivates p53 suppressor gene. Regulates normal cell growth and proliferation. (Guardian of the Genome)
- Activated proteins know as ras : belong to proteins called small GTPase. When switched on overacting ras signaling to other cells ultimately lead to cancer
- Anomalous ras activation promotes carcinogenesis via mitogenesis, resistance to apoptosis and angiogenesis (promote tumor development)

Characteristics SCC
- Usually brought to the attention of the doc by the patient- “concern” or noted on routine exam
- Age: later than BCC (70 yo average)
- Lesion asympt. (bleeding, weeping, pain, tender)
- Starts as small, firm, erythematous nodule or a flat (macular) erythematous patch
- Enlarges, with variable surface scale
- Advanced Dz: pain, numbness, blepharoptosis, diplopia, and proptosis
- When deriving from actinic keratosis, surface scale is typically heavy, with a possible cutaneous horn
Axial magnetic resonance image (MRI) of a large squamous cell carcinoma of the left lower eyelid with invasion of the anterior orbit.

- When deriving from actinically damaged skin, surface scale is lighter than when deriving from actinic keratosis
- Ulceration, crusting, bleeding, infection
- Bowen’s Disease:
  - Erythematous, crusted,
  - Keratotic lesions in sun exposed areas
- Radiation blepharopathy
SCC’s have no typical appearance and are often confused with other lesions
- Actinic Keratosis (AK)
- BCC with crusting and bleeding
- Keratoacanthoma (Increasing belief that Keratoacanthoma is a variant of SCC)

- Inverted follicular keratosis (clinically very similar to keratoacanthoma, but different histologically)
- Sebaceous gland tumor (meibomian gland carcinoma)
- Seborrheic keratosis (DDx)

Variable risk of metastasis
- Eyelid SCC: etiology, tumor size, and depth
- Patients with more advanced DZ: MRI / CT of orbit
- Metastasis rare when arising from Actinic Keratoses (less than 5% risk)
- Metastasis higher when arising from scarred, damaged, or chronically draining areas (over 40%)
- Lower lip (Highest) at 10-20% metastatic Dz.
Work – Up for SCC

- Review the A,B,C,D,E’s
- History of lesions removed, burned off without biopsy
- Laboratory Testing (CBC, Liver function)
- CT/MRI with gadolinium Scanning (tumor, nodes, full body)
- PET scan (helps with CT)
- Biopsy – incisional/excisional (Gold Standard)

Risk Factors for Metastatic Dz.

- Tumor larger than 2 cm or deeper than 0.4 cm
- Immunocompromised host
- Lip or ear location has 10-20% chance of metastatic transformation
- Tumors arising from scar tissue have metastatic rate of 30%
- Decreased degree of tumor cell differentiation.

Treatment of SCC

- If suspected, must refer for excisional biopsy
- Early referral is critical since clinical diagnoses are only 50% correct at best
Overview of Non-surgical Management

1. Topical Chemotherapy (5 FU)
2. Topical Immune response Modifiers (Imiquimod)
3. PDT (Photodynamic Therapy)
4. Radiotherapy (pts with peri-neural invasion)
5. Systemic therapy (gefitinib or erlotinib- TKI & cetuximab-MCA)
6. Reduction in Immunosuppression (high risk pts)
7. Cryotherapy (Liquid Nitrogen)

Surgical Intervention

1. ED&C- Less effective for recurrent lesions (small early lesions)
2. Excision – Good for Primary and recurrent tumors
3. Moh’s – Excellent for recurrent and Primary
4. Laser Surgery- added benefit of ensuring hemostasis

Future Therapeutic Directions

- Photosensitizers and laser
- Immune Therapy
- Gene Therapy
- Targeted therapy (molecular markers on the tumor)
Anterior Segment: Herpes Simplex Infection

David P Sendrowski, OD, FAAO
Chief, Ophthalmology Consultation Service
Professor/SCCO@MBKU

Disclosure Information

Epidemiology/ Background HS (2019)

- One of the most “common” infectious causes of decreased BCVA in North America.
- Despite progression in “basic science” research for a vaccine and/or virus-eliminating cure remains elusive!
- Two main goals in 2019 are suppression of recurrences and minimizing damage to BCVA!!
Description

• Herpes simplex virus is a DNA type 1 ocular infection following introduction of the virus in childhood as a subclinical or mild systemic infection. The HSV becomes latent in ganglion around the eye (trigeminal). (Back door/ front door?)
• Conjunctival inflammation precedes corneal vesicles, Superficial Punctate Keratitis (SPK), and then branching epithelial ulcer, the classic dendritic ulcer which may enlarge to a geographic form.
• Deeper corneal forms of herpes simplex virus keratitis (HSV K) may follow days/weeks later. Disciform keratitis is an immune form of HSV involving corneal endothelium leading to edema. (only 1% of initial)

Primary Infection

• Most people are infected by age 16–about 80%
• Mainly from virus-shedding carrier.
• Primary ocular infection is “uncommon”. The rash is “extensive” over conjunctiva, eyelids, and cornea---usually younger age and “naïve” individuals who are exposed to HSV type 1

Secondary Infection

• Virus after infection becomes latent in the nerve cells of the trigeminal ganglia.
• Most people have no further “eye infections”.
• Virus presents as lips, cheek and tongue presentations!
• Ocular infections (1 to 4%), show as HSV blepharitis, conjunctivitis, keratitis, iritis, or retinitis.
• Epithelial Keratitis is the “MOST” common corneal manifestation in the eye-blurred BCVA, pain, FB sensation, photophobia, redness and tearing.
Herpes Simplex Location

HSV-specific CD8+ T cells appear to play an important role in controlling recurrent infections and reactivation.

HSV-2 has a more efficient reactivation in the lumbosacral ganglia (affecting the hips, buttocks, genitalia, and lower extremities).

Physical exam

COMMONLY ASSOCIATED CONDITIONS

- Fever blisters around the mouth, nose, and eye often accompany ocular HSV.

Ocular Herpes Simplex Presentation

- Follicular Conjunctivitis
- Isolated SPK
## DIAGNOSIS

**Variable HSV Presentations**

<table>
<thead>
<tr>
<th>Classic Dendritic HSV</th>
<th>Geographic HSV</th>
<th>Disciform Type first presentation</th>
</tr>
</thead>
</table>

Obtaining a detailed history is important in differentiating patients with HSV keratitis from other conditions affecting the cornea.

- Ocular symptoms: degree of pain, redness, discharge, blurred vision, photophobia, duration of symptoms, circumstances surrounding the onset of symptoms
- Contact lens history: wearing schedule, overnight wear, type of contact lens, contact lens solution, contact lens hygiene protocol, tap-water rinse of contact lenses, swimming, using a hot tub or showering while wearing contact lenses
- Review of other ocular history, including risk factors such as previous HSV keratitis
- Review of other medical problems and systemic medications
- Current and recently used ocular medications
- Medication allergies
RISK FACTORS (History questions)
• These HSV outbreaks can be induced by various stimuli, such as trauma, ultraviolet (UV) radiation, extremes in temperature, stress, immunosuppression, surgical and laser procedures, or hormonal fluctuations, meds (prostaglandins/steroids)
• Don’t forget about HSV-2 (new genital) eruptions, patients don’t tend to say during “eye” exam.

Secondary infection--Exam
• When examining the patient—look at the lids, conjunctiva, and cornea (with NAFL and RB/LG staining!)
• What appears to an epithelial HSV defect may start as a follicular conjunctival infection as the first cause and should be considered a HSV infection and documented.

Presentation:
• Young adult or child with ocular inflammation and eye irritation (pain) often precede HSVK.
• Blurred VA when the infection is in the visual axis.
Herpes Simplex Masqueraders

- Various ocular conditions with branching lesions: Acanthamoeba, stromal dystrophy, Fabry’s, tyrosinemia, HZO, corneal abrasion
- Corneal drug toxicity
- KEY Reminder: HSV is the “ONLY” Ulcerative corneal lesion while the others are not.

Examination

- External Examination
- Slit-Lamp Biomicroscopy
  - Eyelid margins
  - Conjunctiva (RPS Adeno test)
  - Cornea:
    - Endothelium (rule/out MFKP, stellate type KPs )
    - AC
    - IOP

PHYSICAL EXAM

Slit-lamp examination (cornea & conjunctiva) is critical to diagnose ocular HSV. Vital dyes such as fluorescein, Lissamine Green, or Rose Bengal are very helpful. PA node is helpful.

<table>
<thead>
<tr>
<th>Vital Dye Characteristics</th>
<th>Vital Dye</th>
<th>Color</th>
<th>Tissue</th>
<th>Slit Lamp Set-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Fluorescein</td>
<td>Yellow</td>
<td>Cornea</td>
<td>White 1/2 filter, Coated light, High Illumination</td>
<td></td>
</tr>
<tr>
<td>Rose Bengal</td>
<td>Red</td>
<td>Conjunctiva</td>
<td>White light, High Illumination</td>
<td></td>
</tr>
<tr>
<td>Lissamine Green</td>
<td>Green</td>
<td>Conjunctiva</td>
<td>White light, Low Illumination</td>
<td></td>
</tr>
</tbody>
</table>
Inflammatory Keratitis

- Auto-Immune response (attack) on the cornea
- 2 main forms: Stromal/Disciform

Disciform Endotheliitis

- If you have concern—send to OMD!!
- These cases are “serious” and need a combination of steroids, anti-viral treatment and glaucoma meds.
- IOPs are usually high around high 30’s and 40’s when you see them.

Lab

- Most often lab tests such as culture are not necessary as slit-lamp diagnosis of dendritic keratitis is very specific. With more complicated, deeper forms of HSVK, culture, PCR, or immune tests are used.
Lab Work Up

- **Giemsa stain** – (Multinucleated giant cells)
- **PAP Stain** – (Intra-nuclear inclusion bodies)
- **RPS** – adeno detection (In-Office) r/o adenovirus
- **Viral cultures**: HSV antigen detection tests, such as the enzyme-linked virus inducible system (ELVIS) (results 2 - 4 hours)
- **EIA** (Herp Chek -in-office) (1/2 days)
- **(PCR / Multiplex PCR)** using tear samples (3 to 5 days)

General Treatment

- Dendritic keratitis main goal is to heal the corneal surface as quickly as possible!!
- Longer the lesion stays on the cornea– greater the likelihood of corneal haze or scarring!!
- Topical or Oral treatment can be used
- Oral Acyclovir: 400mg 5x/day w/ punctal plug or BCL (some OMDs debride ulcer then oral AV)
- Topical: Viroptic (9x/day) or ganciclovir (4 to 5x/day)
- Ganciclovir preferred over Viroptic for reduced epithelial damage!

General Treatment

- Most Physicians agree that aggressively treating the severe herpetic reactions is the best way to minimize long-term damage!!
- A “Good Rule of Thumb” that the higher dosage of medication and frequency—the more rapidly it can be tapered!!
- Lower dosages “MUST” be tapered more slowly and need to followed over many months!!
TREATMENT
• 50% self resolve if < 4mm in size
• **Dendritic keratitis** responds well to trifluridine drops topically and third generation topical gels such as ganciclovir.
• **Oral antivirals**, acyclovir and valacyclovir are useful. (Famvir: OK-- but more expensive but generic available)
• **Steroids should be avoided** for ocular surface HSVK, but are used with antivirals for stromal HSVK, disciform, necrotizing and uveitis. Need to reduce scarring/w steroids.

HSV epithelial disease – Topical Treatment
- Viroptic drops q2h up to 9x/day
- Reduce drops to 4 to 5 times after 3 to 5 days OR...
- Zirgan eye gel (topical ganciclovir) (ave: $165)
- Topical Acyclovir (not avail. in US but comp labs will help)
- Topical Idoxuridine (Herplex/ Stoxil) D/c
  Hard to get and causes a lot of local toxicity
- Topical Vidarabine (Vira–A) ointment (Comp. lab)

Choosing an Oral treatment for HSK
• Patient physically unable to use drops
• CLW (no Rx)
• Pediatric patient refractory to topical Tx
• Patients that require lengthy treatment (>21 days)
• Patients with ocular surface disease (OSD) who are more susceptible to ocular toxicity
• Prophylactically treatment after or before ocular surgery
• Cost prohibitive to patient (alternative)
Oral Recommendations:

**ORAL DOSING FOR HERPES SIMPLEX KERATITIS**

- If an oral agent is appropriate, a prescription for herpes simplex should be administered as follows:
  - **Zovirax** (acyclovir, GlaxoSmithKline) 400mg three to five times daily for seven to 10 days
  - **Valtrex** (valacyclovir, GlaxoSmithKline) 500mg -1000mg three times daily for seven to 10 days
  - **Famvir** (famciclovir, Novartis) 250mg three times daily for seven to 10 days. (prodrug of the antiviral agent penciclovir)
  - Oral antiviral medications should be used with caution in patients with kidney or liver disease due to the internal processing

**HSV Epithelial Disease- Treatment Non-Topical**

- Corneal debridement used in adult if HSK is superficial and no prior use of steroids. (AB for epi. breakdown- be careful not to break Bowmans layer)


**HSV Epithelial Disease- Treatment Non-Topical**

- Recurrent Epithelial episodes
  - HEDS II found that **400 mg Acyclovir BID**, for 1 year significantly reduced the risk of recurrence (41%) of ocular HK (>one episode /year), stromal keratitis, and oro-facial HSV compared with placebo.
  - **Benefit** provided (HEDS II) by long term Acyclovir was seen in those with a history of stromal keratitis (51%).
  - **Resistance** is low in the immuno-competent population.
  - **There are no FDA approved vaccines** for the prevention of herpes simplex infection or recurrence. There have been relatively few clinical trials investigating the efficacy of a vaccine in the prevention of ocular HSV infections.
Summary

• Patients should be treated with antiviral therapy during episodes of acute ocular HSV infection and with steroid therapy for stromal inflammation in the absence of active epithelial inflammation.
• Patients should be given oral Tx with “Recurrent” infections without the worry about the time of the treatment.

Nutrition and Dietary Supplements

• Lysine.
  – Several studies suggest that lysine may help reduce the number of recurring outbreaks of cold sores. A few studies also suggest that lysine may help shorten the length of an outbreak.
• Propolis.
  – A resin made by bees, propolis is loaded with antioxidants that help fight infection and boost immune function
• Zinc.
  – In test tubes, zinc is effective against HSV-1 and HSV-2

ICD 10 CODES

ICD-10: B00.52(1 or 2) Herpes viral keratitis epithelial and stromal
CLINICAL PEARLS

• Always suspect possible ocular HSV in patients with an acute red eye and do a slit-lamp examination (cornea and conj.) with vital dye to avoid treating HSV with topical steroids especially in children.

Questions
Controversies in the Basic Glaucoma Evaluation
COPE #58568-GL

Robert E. Prouty, O.D., FAAO
Insight Vision Group
Parker, Colorado
RProuty@DrMyii.com

Disclosures
• Financial disclosures: The content of this COPE accredited CE activity was prepared independently by Dr. Robert E. Prouty without input from members of the ophthalmic community.
• Dr. Prouty is affiliated with the following companies as a member of their Speaker’s Bureau or as a Consultant but has no direct financial or proprietary interest in any products or services mentioned in this presentation:
  ✓ Alcon – Allergan – Optovue – Zeiss Meditec - Shire - B&L.
• The content and format of this course is presented without commercial bias and doesn’t claim superiority of any commercial product or service.

Glaucoma is an Optometric Problem

• > 2.5 million Americans are diagnosed with Glaucoma
  – 1% – 2% of those > 40 years
  – 1.6% > 40 (Framingham Eye Study)

• As many as 95,000 Americans lose some degree of sight to Glaucoma each year
  – 12,000 become blind

It is estimated that 1 million Americans with glaucoma are undiagnosed!

Glaucoma

• The most common types:
  – Angle Closure Glaucoma
    • Acute or Chronic
  – Primary Open Angle Glaucoma
  – Secondary Glaucomas
    • Pseudoxfoliation
    • Pigment Dispersion
    • Uveitic
    • Angle Recession

Prevalence of POAG and CACG

<table>
<thead>
<tr>
<th>Group</th>
<th>Angle-Closure (million)</th>
<th>Open-Angle (million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>22.5</td>
<td>7.4</td>
</tr>
<tr>
<td>India</td>
<td>5.6</td>
<td>5.6</td>
</tr>
<tr>
<td>South Asia</td>
<td>4.2</td>
<td>4.2</td>
</tr>
<tr>
<td>Europe</td>
<td>0.6</td>
<td>6.9</td>
</tr>
<tr>
<td>Africa</td>
<td>0.05</td>
<td>7.0</td>
</tr>
<tr>
<td>Latin America</td>
<td>0.5</td>
<td>1.3</td>
</tr>
<tr>
<td>Near East</td>
<td>0.3</td>
<td>0.7</td>
</tr>
<tr>
<td>Total</td>
<td>33.5</td>
<td>33.1</td>
</tr>
</tbody>
</table>

POAG = primary open-angle glaucoma
CACG = chronic angle-closure glaucoma

Angle Closure Glaucoma

• < 10% of diagnosed cases of glaucoma
• Estimated that 2%-8% of the population have angles that are narrow enough to close
  – 5% will progress to ACG
Angle Closure Glaucoma

Risk Factors

• Race:
  – Acute ACG is thought to be very rare in Blacks
  – ACG prevalence in Whites = 8%-16% of POAG rates
  – ACG in Asians is 4X greater than in N. Americans

• FHx:
  – 3-6X greater risk with 1st degree relative

• Age:
  – Incidence increases with age with peak 60’s

Angle Closure Glaucoma

Management:

– LPI?????

  • Zhongshan: “Angle width of treated eyes increased markedly after LPI, remained stable for 6 months, and then decreased significantly by 18 months after LPI.”

• CLE/CE

  • Eagle: “Clear-lens extraction showed greater efficacy and was more cost-effective than laser peripheral iridotomy (LPI), and should be considered as an option for first-line treatment.”

Primary Open Angle Glaucoma

• ~2.5 million Americans have POAG
  – About 1/3 of the POAG is undiagnosed
  – 25% of all cases of POAG are African Americans

Risk Factors for Glaucoma

In general, patients are at risk of glaucoma if they have the following:

• High IOP
• Family history of glaucoma
• African ancestry
• Severe myopia (nearsightedness)
• Cardiovascular risk
• Age
• Other
  – used steroids or cortisones for a long time
  – had a previous eye injury

Prevalence of Glaucoma Increases With IOP
A Cross-Sectional Population Study

Followup Month
Mean Change in VFD Score

The importance of Low IOP (AGIS)

Group A  100%
Group B  75-99%
Group C  50-74%
Group D  <50%

<18 mm Hg
Avg. IOP
20.2
16.9
14.7
12.3

Goals in Therapy
• Reduction in mean IOP to <18 mm
• Control diurnal IOP fluctuations throughout the day

Primary Open Angle Glaucoma Risk Factors
• Age:
  – 4-10 X increase with age (>40)
    • ONH damage is uncommon before age 50 in Whites
    • ONH damage is uncommon before age 40 in Blacks

Prevalence of POAG in European, African, and Asian People by Age

Clinical Workup Controversies
• Are there other high incidence ethnicities?
Risk Factors

- Race: African Americans ~5X > whites
  Comparison of prevalence of Glaucoma in LALES Latinos and African-Americans and Whites in the Baltimore Eye Study

![Graph showing prevalence of Glaucoma by age and race](image)

Projected # of Latinos with Open angle Glaucoma

![Graph showing projected increase in Latinos with Glaucoma](image)

Projected Increase in the # of Latinos with Glaucoma

- 66% increase from 2000 to 2010
- 184% increase from 2000 to 2020
- 280% increase from 2000 to 2030

Primary Open Angle Glaucoma

- Race:
  - African Americans:
    - Don’t respond as well to Tx
    - More likely to need surgery
    - Have a greater prevalence of blindness from glaucoma
    - Age adjusted prevalence:
      - 4.3 X greater for Blacks than Whites

Secondary Glaucomas

- **Pseudoexfoliation Syndrome (PEX):**
  - 1.6%-2.3% of population > 50 yo in US
  - Pseudoexfoliative Glaucoma (PEG) most commonly occurs between 60-80 yo
  - PEX is 2-3X more common in women
  - PEX is reported unilateral in 50%-70% of cases on initial diagnosis

- **Pigment Dispersion Syndrome (PDS):**
  - ~2.5% of whites in the US
  - 20%-60% of PDS OHTN
  - 25%-50% of PDS PDG

Secondary Glaucomas

- **Uveitic**
  - Estimated to be 7.6% to 23% among patients with uveitis
  - Surgery is required in children > adults*
    - 59% of children and in 35% of adults

- **Angle Recession**
  - Of those eyes with angle recession, very few (~ 0-20%) develop glaucoma
  - In those that do develop glaucoma, the onset is extremely variable

  *Ocular Immunology & Inflammation, Volume 17, Issue 4, August 2009, pages 243 – 248
General Risk Factors of Glaucoma

• Elevated IOP
• Larger diurnal IOP flux
• Compromised ocular hemodynamics
  – Vascular dysregulation
    • The more complex the regulatory system, the more susceptible it is for dysregulation and the more dramatic the potential damage

Grieshaber M, Mozaffarich M, Flammer J. What is the Link Between Vascular Dysregulation and Glaucoma. Survey Optik #92, Supp #1, Nov 2007

When to pull the trigger

• It is my observation that many ODs question themselves as to “when to pull the trigger”
  – To soon = mistake and meds cost $$$
  – To late = increases professional liability (malpractice) exposure
• How many ODs have been sued for starting a patient on meds too soon?
  None, Nada, Zero, Zilch, The big Goose Egg!

General Risk Factors of Glaucoma

• Patient characteristics:
  – Large C/Ds
  – Increased age
  – Race
  – FHx
  – Systemic conditions: HTN – Diabetes
  – Myopia
  – Corneal thickness
  – Sleep Apnea

NTG in Patients With Obstructive Sleep Apnea/Hypopnea Syndrome

• 209 patients were OSAHS and 38 normals underwent polysomnographic exams to diagnose obstructive sleep apnea/hypopnea syndrome (OSAHS) to determine the prevalence of normal tension glaucoma (NTG) and further investigate whether the severity of OSAHS would increase the risk of glaucoma.
• NTG was found in 12 patients with a prevalence of 5.7%, which was higher than that in the normal group.
• The prevalence of NTG in moderate/severe OSAHS patients was 7.1%, significantly higher than that in normal/mild OSAHS patients.
• Clinicians need to consider the possibility of glaucoma in patients with moderate and severe OSAHS.


Sleep Apnea Syndrome Represents A Risk for Glaucoma in a Veterans’ Affairs Population

• A total of 70,960 unique records were included for analysis. Of the 2,725 patients with a diagnosis of sleep apnea, 228 (8.37%) also had a diagnosis of glaucoma.
• Conclusions. Results of this investigation suggest that SAS may represent a significant risk factor for glaucoma and this should be considered when managing patients who report that diagnosis.


Glaucoma Clinical Workup

• History:
  – PMHx
    • HTN – Diabetes
    • Head injuries
  – POHx
    • Ocular injuries
  – FHx
    • POAG vs ACG vs secondary glaucomas
**Glaucoma Clinical Workup**

- **IOP**:
  - Poor sensitivity & specificity
  - Sensitivity 79%
  - Specificity 64%


**Clinical Workup Controversies**

- If IOP is poorly sensitive & specific for glaucoma, does it need to be done?
- Are there differences between the tonometers?
- Is NCT dependable enough to follow glaucoma?
- Do I need to upgrade to a Pascal?

**Early detection is important!**

“Ophthalmologists fail to diagnose more than 50% of glaucoma cases…measuring the IOP, examining the optic disc and performing visual field tests are not identifying these patients.”

(Ophthalmology Times, January 2004)

Harry Quigley, MD, Wilmer Eye Institute, Johns Hopkins University

**Physiological Factors influencing measured IOP**

- Supine vs Upright position
- Diurnal variation

**Peak IOP Outside Office Hours for 2/3 of Eyes (10:00p-7:00a)**

![Graph showing peak IOP outside office hours](image)
IOP is Higher at Night

Habitual IOP of untreated glaucomatous eyes

Clock Time

1:30 PM
11:30 AM
9:30 AM
7:30 AM
5:30 AM
3:30 AM
1:30 AM
11:30 PM
9:30 PM
7:30 PM
5:30 PM
3:30 PM
1:30 PM

22
26
25
24
23
22
21
20
19
18
17
14
15

IOP (mm Hg)

Glaucma Clinical Workup

• IOP:
  – Screening:
  – Diagnostic:
  – Serial tonometry vs Home monitoring??
  • Every 2 hrs during a day

ARTICLE IN PRESS

Diurnal Intraocular Pressure Patterns are Not Repeatable in the Short Term in Healthy Individuals

Toni Roaka, MD; Robert N. Whitehill, MD; Stephen B. Wineman, MD

Purpose: To evaluate the short-term repeatability of diurnal intraocular pressure (IOP) patterns in eyes of normal-tension glaucoma.

Design: Observational cohort study.

Participants: Forty healthy subjects without glaucoma.

Methods: Subjects underwent 12-hour diurnal IOP assessment sessions from 8:00 a.m. to 8:00 p.m. for 3 days. Subjects were allocated to either two sessions at each clock time or four sessions at clock times with a 6-hour interval. A computerized program was developed to record 1-minute IOP readings with a digital tonometer (Tono-Pen, Konan Medical, Japan). The correlation coefficient ICC was used to assess the agreement of IOP value at each time point between eyes and the difference between eyes for each clock time.

Results: The mean IOP value at each clock time was generally higher in eyes with IOP readings ranging from 0.9 to 3.1 mm Hg. The ICC for IOP change across time ranged from 0.56 to 0.88 for eyes, with ICCs ranging from 0.65 to 1.00 for eyes.

Conclusions: Eyes of healthy individuals do not maintain a constant and reproducible diurnal IOP pattern when measured by Goldman tonometry, a single-day assessment of IOP reproducibility in normal-tension glaucoma.

Physiological Factors influencing measured IOP

• Supine vs Upright position
• Diurnal variation
• Corneal dynamics
Physiological Factors influencing measured IOP

• Supine vs Upright position
• Diurnal variation
• Arterial (pulse) pressure
• Blood Flow
• Exercise
• Accommodation
• CCT
• Etc...

Clinical Workup Controversies

• Is this the new standard of care?
  – Must Pachymetry be done for all glaucoma patients?

POAG Endpoints by Central Corneal Thickness and Baseline IOP (mmHg) in Observation Group

Central Corneal Thickness and IOP

• Ehlers et al (manometric study):
  – Applanation tonometry accurate at CCT=520 µm
  – Systematic error in T_{app} proportional to the true IOP and the CCT
  – Corneas 70 µm thinner: IOP 5 mmHg lower
  – Corneas 70 µm thicker: IOP 5 mmHg higher


Central Corneal Thickness and IOP

• Medeiros, et al, AJO 2003:
  – Thinner CCT was predictive in developing VF loss
    • Mean CCT was 558 microns +/- 37 microns
    • <545 microns had >2X risk of converting to abnormal VF
    • <555 microns gave 3X risk of developing glaucoma
    • 40 micron thinner corneas than 558 microns gave 60% increase risk in developing VF changes
  – “It has been consistently demonstrated that patients with normal tension glaucoma have thinner corneas than patients with high tension glaucoma or normal subjects.”

Clinical Workup Controversies

• Should IOP always be adjusted based on nomograms for a corrected value?
Clinical Workup Controversies

• Adjusting IOP for CCT does **not** improve prediction models for POAG.
• **Conclusions**: The calculation of individual risk for developing POAG in ocular hypertensive individuals is simpler and equally accurate using IOP and CCT as measured, rather than applying an adjustment formula to correct IOP for CCT.


Central Corneal Thickness (CCT)

• However, although CCT is helpful, its diagnostic precision is relatively poor
  – Patients with > 600um CCT may have glaucoma
  – Patients with < 500um CCT may not have glaucoma

• So, the question arises:
  – Do corneal properties beyond central thickness provide better diagnostic/prognostic precision than CCT?

What is Corneal Hysteresis (CH) ?

• Research to date indicates that ORA-derived biomechanical properties provide unique insight into glaucoma…….

….. And it may have great potential to improve risk analysis, decision-making and outcomes in glaucoma

Clinical Workup Controversies

• Should IOP always be adjusted based on nomograms for a corrected value?
• Doesn’t CCT predict risk?
  – Yes, of conversion from OHT to glaucoma in the OHTS
  – In fact, thin CCT was a “powerful risk factor”


What is corneal hysteresis (CH) ?

• Corneal hysteresis (CH) is a measure of:
  – Corneal damping capacity
  – Visco-elasticity
  – Energy absorption capability of cornea

CH is **NOT** a measure of ocular rigidity/stiffness

Clinical Workup Controversies

• Is Gonioscopy required on all glaucoma patients?
  • It is the only clinical procedure that allows a differential assessment of the various glaucomas
• Does it need to be done more than once?
  – “I only get paid once in their lifetime!”
Glaucoma Clinical Workup

- AAO Preferred Practice Pattern Guidelines:
  - Perform gonioscopy periodically (e.g., 1-5 years).
- AOA Clinical Practice Guidelines:
  - To rule out the development of an angle closure component in the glaucoma, gonioscopy should be repeated periodically.

Glaucoma Clinical Workup

- Optic Nerve Evaluation:
  - Slit lamp lenses:
    - 90D/78D/60D Volks
    - BIO
  - Stereo Fundus photos

Clinical Workup Controversies

- Is fundus photography still the standard of care?

RNFL defects are the earliest sign of glaucoma

- RNFL defects precede visual field loss
  - 60% OHT converts had RNFL defects 6 years prior to VF defect
- RNFL defects precede ONH changes
  - 50% OHT converts had RNFL defects that progressed
  - 20% OHT converts had ONH defects that progressed

1Hoyt and Newman, Lancet. 1972; 1:692

~ A Video Atlas ~

Wallace L.M. Alward
Frederick C. Blodi Chair in Ophthalmology
Director, Glaucoma Service
University of Iowa Carver College of Medicine

http://gonioscopy.org/
RNFL defects precede ONH changes

Five Rules for Assessment of the Optic Disc in Glaucoma

1. Observe the scleral ring to identify the limits of the optic disc and its size

Optic Disc Size

Measurement of optic disc size with direct ophthalmoscope

Small aperture (5 degree) of Welch-Allen direct ophthalmoscope

Size of light spot ~ size of average optic disc

Optic Disc Size

Size of cup varies with size of disc
Large discs have large cups in healthy eyes

Small

Average

Large

Small discs: avg vertical diameter < 1.5 mm
(1.1 X 1.3 = 1.43)

Large discs: avg vertical diameter > 2.2 mm
(1.7 X 1.3 = 2.21)

Five Rules for Assessment of the Optic Disc in Glaucoma

1. Observe the scleral ring
2. Identify the size of the rim

“ISNT” Rule

Rim width
Distance between border of disc and position of blood vessel bending

ISNT rule
Inferior > Superior > Nasal > Temporal
“ISNT” Rule

- Original “ISNT” research:
    - “It was broadest in the inferior optic disc region (P < 0.001), followed by the superior, nasal and temporal (P < 0.001) regions.”
    - “The ISNT rule is useful in differentiating normal from glaucomatous optic nerves and is unaffected by race.”

- More recent “ISNT” research:
    - “The ISNT rule was applicable in 71% of normal eyes and 68% of early glaucoma eyes.”
    - “Violation of the ISNT rule occurs with greater frequency in the pediatric population with large optic disc cups of non-glaucomatous origin, compared with the pediatric population with normal optic discs.”
    - “The ISNT rule has limited utility in the diagnosis of open-angle glaucoma.”
  - Law SK, Kornmann HL, et al, Evaluation of the “IS” Rule to Differentiate Glaucomatous Eyes From Normal, J Glaucoma. May ’14
    - “…we agree with the conclusion of Morgan et al, that the ISNT rule has only limited utility in the diagnosis of glaucomatous optic neuropathy…”
    - “We demonstrated that a diagnostic test that combines the different features of the optic disc (increase of CDR and ISNT or IS rule) may improve the diagnostic accuracy of glaucoma based on optic disc evaluation.”

Glaucoma Clinical Workup

- Optic Nerve Evaluation:
  - Slit lamp lenses:
    - 90D/78D/60D Volks
  - BIO
  - Stereo Fundus photos
  - Scanning instruments:
Glaucoma Clinical Controversies

- Do I need to have a NFL analyzer?
- What is the current standard of care for retina/ONH monitoring?

Glaucoma Clinical Workup

- Optic Nerve Evaluation:
  - Slit lamp lenses:
    - 90D/78D/60D Volks
    - BIO
  - Stereo Fundus photos
  - Scanning instruments:
    - HRT
    - OCT

3 Imaging technologies were shown to be effective in detecting and managing ocular pathologies

- Scanning Laser Polarimetry (SLP)
- Confocal Scanning Laser Ophthalmoscopy (CSLO)
- Optical Coherence Tomography (OCT)

Glaucoma Clinical Workup

Digital Tomography Deficiencies

- 2D measurement are stacked to achieve a 3D assessment
- An inferred estimate of the RNFL height is based on a depth of 50 microns
- All estimates of glaucoma status are based on a multivariate analysis
  - This regression analysis (Moorfields regression analysis) also compensates for age and identifies glaucomatous eyes with a relatively high level of sensitivity and specificity


Tomography - CSLO

GDx Basic Principles

The amount of retardation from the RNFL is directly proportional to the RNFL thickness

GDx Basic Shortcomings

- The crystalline lens and cornea have significant birefringence which is highly variable. As such, the macula was used as a reference to variably compensate in the interpretation of the reflected RNFL birefringence (GDx VCC).
- It measures NFL thickness but only inferentially measures loss based on normative database.
- 540 healthy eyes with 271 glaucomatous eyes
  - 18-82 yo in healthy with 25-89 yo glaucoma

1

Ocular movement such as nystagmus can render GDx measurements meaningless.

Older patients, high myopia, or lightly pigmented fundus eyes, are subject to increased birefringence with an abnormal s/n ratio which can provide erroneous readings.

PPA can be a confounding factor if it falls within the measurement circle.
- The circle can be enlarged to avoid scanning the PPA region and increase the reliability of measurements yet that adds variability

Fast Optic Disc (Monocular) - Utilizes a 6 line starburst scan (4mm) through the ONH at each 12 clock hours. Each individual scan can be reviewed.

Fast RNFL (Monocular) - Three circular scans with a 3.4mm diameter are used to image the peripapillary region of the ONH to create a TSNIT image.

Fast Macula (Monocular) - The Stratus uses a 6 line radial pattern to image the macula (6mm).

Acquisition times are slow so movement artifact affects accuracy
- Database is VERY limited in patients >80yo
- Database is VERY limited in patients outside -12.00 or +8.00
- Highly myopic eyes have a wide range of “normal” RNFL thickness
- Moderately myopic individuals may have thinner peri-papillary RNFL at the superior and inferior poles when measured by OCT.
- Interpreting a myopic glaucoma suspect’s RNFL status needs to take into account these limitations.

RNFL Thickness Average Analysis

Fourier/Spectral Domain OCT Advantage

- Faster speed also allows for greater density of sampling points and reduces artifacts from eye-movements
  - RTVue FD OCT has 26,000 A scans/sec vs Stratus TD OCT with 400 A scans/sec
Fourier/Spectral Domain OCT Advantage

- FD OCT has twice the depth resolution as TD OCT
  - 5 microns vs 10 microns
- Allows imaging and segmentation of ganglion cell layers
  - Cornea
  - Angular structures
  - Macular Ganglion cell layer

Ganglion Cell Loss in the Macula

- Histologic studies have shown ganglion cell loss in the macula
- Desatnik et al., found macular ganglion cells are lost in early glaucoma
- Yucel et al., showed loss of cells in the parvocellular layers of the LGN implicating central ganglion cell loss

- Desatnik H, Quigley HA, Glovinsky Y. J Glaucoma. 1996; 5: 46-53

Glaucoma Clinical Controversies

- Do I have to upgrade to the new generation OCTs?
RNFL Thickness Average Analysis

- Black line is patient's RNFL thickness

Macular Ganglion cell density

- 50% of ganglion cells located in central 4.5mm (16°)
- Peak ganglion cell density is 15,000 cells/mm² in macula (white region left)
- Area represents only 7.3% of total retinal area
- RTVue Ganglion cell complex map covers central 6mm area

Macula thinning in Glaucoma

- Greenfield et al, showed thinning of the macula in glaucoma patients using Time Domain (TD) OCT (Stratus)
- Guedes et al, also found significant macula thinning in glaucoma patients compared to normals with TD OCT

Diagnostic Accuracy with TD OCT: Macula vs RNFL

- Medeiros et al, found the diagnostic accuracy of peripapillary RNFL thickness was significantly more accurate than macula thickness
- Wollstein et al, found similar results where RNFL thickness was significantly more accurate for detecting glaucoma than macula thickness

Progression: Macula vs RNFL

- Using TD OCT, Medeiros et al, compared the accuracy for detecting progression using RNFL versus macula thickness and found the RNFL was significantly more sensitive and specific than macula thickness

References:
TD OCT Study Limitations

- Major disadvantage in these studies is that TD OCT typically measures full retinal thickness only (does not isolate ganglion cells).
- TD OCT does not have enough depth resolution to image and segment the ganglion cells accurately and reliably.

Retinal Ganglion Cells extend through three retinal layers

GCC is:
- Nerve Fiber Layer – Ganglion cell axons
- Ganglion cell layer – Cell bodies
- Inner-Plexiform Layer – Dendrites

GCC Thinning in Glaucoma

Normal

Glucoma with thinner GCC

Overlay of the RNFL and GCC

Revisiting the Macula

- Can imaging the ganglion cells in the macula with FD OCT improve glaucoma detection?
Diagnostic Accuracy:
GCC vs FD/SD OCT RNFL
- Rao et al, found GCC had similar accuracy levels as FD/SD RNFL
- Seong et al, found similar results
- Kim et al, found values were higher for RNFL vs GCC in a group of advanced glaucoma patients, but GCC values were higher than RNFL in a group of early glaucoma patients

GCC Summary
- GCC thickness correlates well with VF
- More reproducible and more accurate for detecting glaucoma than macula thickness with TD OCT
- Similar accuracy for detecting glaucoma as FD/SD OCT RNFL thickness
- Best in early glaucoma

Glaucoma Clinical Controversies
- Do I need to have a NFL analyzer?
- What is the current standard of care for retina/ONH monitoring?

Visual field & OCT results show poor correlation in advanced RNFL loss
- A retrospective study of patients with early to advanced glaucoma showed a wide variation in mean deviation in patients with advanced retinal nerve fiber layer loss when comparing visual field sensitivity with retinal nerve fiber layer thickness.
- Jessica Neuville, OD, presented at AAOpt 2010, a study that suggests the OCT is moderately correlated to visual function in early loss, but is a poor predictor of visual function at advanced levels of RNFL loss.
Glaucoma Clinical Workup

- Visual Fields:

Glaucoma Clinical Controversies

- Is the FDT/Matrix = to SAP?
- Must SWAP be done on all patients?
- Is SAP the standard of care?

Visual Fields: Poor Sensitivity

- A large number of RGCs often are lost prior to detectable visual field abnormalities
- As many as 50% optic nerve fibers can be lost prior to a standard perimetric defect
- By the time there is a 5 dB VF loss, there is a corresponding 25% loss of RGCs

Visual Fields: Highly Variable OHTS

- 86% of visual field abnormalities not replicated on retesting

Visual Field Progression

- Visual Function (MD)
- Rate of Progression
- Level of visual disability

Identifying Progression - VF

- Changing points
- Repeateable change
- GPA™ confirms repeatable, consistent change at five points in the field
Glacon Diser Analysis (GPA)
- Multiple exams
- Baseline
- Rate-of-progression plot

SWAP in Early Detection
- Longitudinal studies
- Correlates with optic disc
- Abnormal in suspects
- 8% - 30% abnormal in OHT
- Larger defects in Glaucomatous Optic Neuropathy
- Once a SWAP defect is detected, it tends to be repeatable whereas only 45% of initial WOW defects are repeatable*

* Demirel S, Johnson C. AJO June 2001

Limitations of SWAP
- Difficult and prolonged testing
  - SITA SWAP now available
- Vulnerable to lens effects
- Higher threshold variability

Frequency Doubling Illusion
- Actual Stimulus
- Perceived Stimulus
- Nonlinear Response

FDT in Glaucoma Detection
- Correlates well with SAP
  - 95% sensitive and specific
- Frequently abnormal in suspects
- Predicts SAP defects

Summary of Functional Tests
<table>
<thead>
<tr>
<th>Advantages</th>
<th>SITA SAP</th>
<th>SITA SWAP</th>
<th>FDT Matrix</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Gold Standard</em></td>
<td>As fast as SITA SAP</td>
<td>More portable</td>
<td></td>
</tr>
<tr>
<td>Possibly more sensitive</td>
<td>Possibly more sensitive</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disadvantages</th>
<th>SITA SAP</th>
<th>SITA SWAP</th>
<th>FDT Matrix</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not sensitive enough to detect early glaucoma</td>
<td>Limited clinical evaluation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited clinical evaluation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Variability</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cataract effects</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Best use</th>
<th>SITA SAP</th>
<th>SITA SWAP</th>
<th>FDT Matrix</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline VF and following progression in advanced disease</td>
<td>Early diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Younger patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Controversies in Treatment

• Is ALT/SLT a better option as primary treatment than medication?

Interpreting the GLT Results

• Initial treatment with ALT is at least as effective as initial treatment topical medication in patients with POAG in terms of control of IOP, optic disc and visual field.
• Ultimately, ALT will need to be supplemented with other modes of intervention.
• What about SLT????

SLT as an alternative to PGAs

• SLT vs. latanoprost for IOP control in OHT and POAG
• 12-month study
• 90°, 180°, 360° SLT
• Success criterion
  – 20% - 30% IOP reduction from baseline


SLT as an alternative to PGAs

• Results
  – More 360° SLTs (60%) achieved success criterion (> 30% IOP reduction) than did 90° or 180°
  – Latanoprost-treated eyes achieved success criterion in more cases than 90° or 180° and did as well as 360° in maintaining diurnal IOP reduction


Controversies in Treatment

• Do all patients need to be treated?
• If the eye is NLP, what are the treatment goals?

MJ & Glaucoma

• So for glaucoma.....
  – There are far better management regimens now available
    • 3-4 hr efficacy ≠ good control
    • Constant intoxication ≠ good citizens
    • Health concerns ≠ future safety profile
  – Colorado ODs can be certified for DEA Schedules 3 narcotic – 5
  • Marijuana is still Schedule 1
Medicinal Management

- Prostaglandin Derivatives
- Topical CAI's
- Adrenergics
- Beta-Blockers
- Combos
- RhoKinase Inhibitors
- Cholinergics/Anticholinesterases
- Oral CAI’s

Prostaglandin analogues

- **Zioptan™**
  - Tafloprost 0.0015%
  - The only preservative free PGA!!
  - ~30% - 35% IOP decr
  - QHs use
    - Vials often hold > 4 drops

Combinations

- **Cosopt®**
  - Timolol 1/2% & dorzolamide
    - As effective as separate dosing (?)
    - Still stings!!
  - 32%-38% IOP decr
    - bid use
- **Cosopt PF®** (was Merck but now is Akorn)
  - Preservative Free!!
- **Simbrinza™** (Alcon)
  - Brinzolamide 1% & Brimonidine 0.2%
  - As effective as separate dosing
  - Better convenience & compliance
    - Less sting!!
    - 21%-35% IOP decr
    - tid use
    - Used bid in Europe

CAI’s

- Sulfonamide sensitivity
  - Topical CAI cross-sensitivity is being re-thought
  - So the use of topical CAIs may be safely used with sulfonamide allergy depending on severity of allergic response
    - Hives, swelling of throat, etc. is probably NOT safe!
    - General atopy is probably LESS safe
Nitric Oxide Donation

• In the past, nitric oxide (NO) was considered “toxic” as one of several environmental pollutants (i.e. cigarette smoke & smog)
  – ≠ nitrous oxide (N₂O) “Laughing Gas”
• By late ’90s, it was determined that NO is a fundamental player in general body physiology as a messenger molecule
  – Essential to daily functions ranging from BP regulation & digestion to antimicrobial defense

NO-Prostaglandins

• Vyzulta®
  – Latanoprostene bunod
    • Nitric Oxide-Donating PGF₂α
    • OHS administration
• Dual Mechanism:
  – PGF₂α: enhanced uveoscleral outflow
  – NO: affects outflow through relaxation of TM
  • ?? Analogous to ROCK I’s

RhoKinase Inhibitors

• Mechanism:
  – Rhokinase is a serine/threonine kinase that serves as an important downstream effector of Rho GTPase
  – It plays a critical role in regulating the contractile tone of smooth muscle tissues in a calcium-independent manner
  – ROCK inhibitors reduce IOP by enhancing aqueous humor drainage through the trabecular meshwork
    • ROCK inhibitors also appear to lower the episcleral venous pressure, which contributes approximately half of IOP in healthy subjects

Rho Kinase Inhibitors

• Rhopressa Phase 3 Trial (Rocket 1)
  – Missed Primary Endpoint
    • All end points of subjects Tapp < 26 were met but not > 26+
    • FDA allowed modification of study endpoints

NEWEST Rho Kinase Inhibitor

• Roclatan™:
  – Essentially = Rhopressa™ + Xalatan®
    • Netarsudil 0.02% + Latanoprost 0.005%
Things we already know…

- Third party insurers have greatly changed the medical care environment
- Nationwide, nearly 65% of the average ODs gross income is coming from a third party insurer
- Older adults make up >1:6 patients and >1:7 practice revenue dollars
- Glaucoma can be “owned” by Optometry
Pot & Glaucoma Updates: What We All Should Know
COPE #52520-GL
Robert E. Prouty, O.D., FAAO
Insight Vision Group
Parker, Colorado
RProuty@DrMyii.com

Disclosures
• Financial disclosures: The content of this COPE accredited CE activity was prepared independently by Dr. Robert E. Prouty without input from members of the ophthalmic community.
• Dr. Prouty is affiliated with the following companies as a member of their Speaker’s Bureau or as a Consultant but has no direct financial or proprietary interest in any products or services mentioned in this presentation:
  ✓ Alcon – Allergan – Optovue – B&L – Glaukos – Shire
• The content and format of this course is presented without commercial bias and doesn’t claim superiority of any commercial product or service.

Cannabis and Glaucoma
• The smoking of MJ was first reported to lower IOP in 1971
  – 11 participants that did not have glaucoma
  – “Compassionate Investigational New Drug Program”
    ✓ In 1978, Robert Randall was the first person to receive cannabis from the Feds to Tx his glaucoma

Hepner RS, Frank IR, Marihuana smoking and intraocular pressure, JAMA 1971, Sept 6:217(10): 1392

History of MJ use
• In January 1997, the director of the white house Office of National Drug Control Policy (ONDCP) asked the Institute of Medicine (IOM) to review the evidence for the potential benefits and risks associated with the use of marijuana
  – The IOM is a non-governmental, apolitical, non-profit organization of scientists

History of MJ use
• NIH held a scientific meeting in Feb 1997 to review the scientific data concerning the potential uses of marijuana and the need for & feasibility of additional research
History of MJ use

• The report of the 18-month IOM study was released to both the ONDCP and the public in March ’99
  - There was remarkable consensus about the potential of cannabinoid drugs for medical use
  - There was far less convincing data about proven medical benefits

History of MJ use

• Review of the science behind marijuana and cannabinoids suggests that the debate has been misunderstood
• Medical use of potent, controlled psychoactive drugs has not led to abuse
• Rather than focusing on drug control policy, the medical marijuana debate should really be about the promise of future drug development

MJ Use in the USA

• There has been a significant change in the attitude of acceptance of use of marijuana in the U.S.
  - 33 states & DC now have laws broadly legalizing MJ use in some form
    • 23 Medical
    • 10 Recreational

Cannabinoid Consequences

• I found only one large-scale study that sought to determine the frequency with which MJ smokers develop cancer
  - No association was found between MJ use and any other type of cancer, including cancers normally linked to tobacco smoking
  - The study was limited by how many of its participants were younger than the average ages when many cancers appear as well as by the short duration of their MJ use

States where marijuana is legal

- Legalized recreational and medical marijuana
- Legalized medical marijuana

Cannabinoid Consequences

• Taken as a whole, these findings indicate that smoking MJ could have dangerous consequences for patients with compromised immune systems (including people with AIDS & cancer) particularly those who are receiving immunosuppressive chemotherapy as well as organ transplant recipients
Cannabinoid Consequences

• Exposure to cannabinoids can also affect the cardiovascular system
  – Both smoked MJ and synthetic THC have been shown to raise heart rate
    • from 20%–100% above normal in some cases
  – THC can also exaggerate the drop in BP that occurs when a person rises to standing after lying down causing syncope
  – People at risk for cardiovascular disease would be wise to avoid MJ and THC

Cannabinoid Consequences

• MJ – IOP – BP Hypothesis:
  – 18 patients with glaucoma
  – The BP lowering effect of MJ mediates the reduction in IOP
  – The concern is that this may also reduce the perfusion at the optic nerve
    • IOP reduced = BP reduced = OBF reduced
  – Did not follow longitudinally!!!


Cannabinoid Consequences

• 9 patients followed 9 months:
  – Their glaucoma was poorly controlled by other treatments
    • Initial decrease in IOP
    • IOP decrease was not sustained over time
  – Marijuana was in the form of capsules
  – Measured weekly, time of day constant until IOP was stable
  – Followed up to 9 months, some less


Cannabinoid Consequences

• All participants elected to discontinue use!!

  Comment of an intern involved in the IOP research:
  “At the point the IOP reduced, the patients were so high they were falling off the chair.”


Cannabinoid Consequences

• Fertility research on MJ users has yielded conflicting results
  • The few studies that have been conducted to assess THC’s effects on human reproduction have produced results that are consistent with those of the animal studies
  • In a study of Jamaican women (they prepared it as a tea to relieve morning sickness), no neurobiological or behavioral differences were detected between newborn babies of those who used MJ and those who did not

Risks of MJ use

• Fertility:
  – Decreased sperm count?
  – Chromosome breakage?
  – Testosterone levels?
  – Size & shape of sperm?
Risks of MJ use
• Cardiovascular:
  - ’14 report of the J of Am. Heart Assoc. of the French Adictovigilance Network
  - Over 5 yr period, there were 35 of 1979 cannabis related reports of serious adverse events (1.8%)
  - Most (63%) of the events were cardiac (22) with 25.6% resulting in death

Chronic use & RGC’s
• Association Between Regular Cannabis Use and Ganglion Cell Dysfunction
  - 52 participants (18-35 yo)
    - 28 regular cannabis users (24 male/4 female)
      - At least 7 consumptions per week over the last 30 days
      - (+) THC on urine analysis
      - Also + tobacco users
    - 24 controls (20 male/4 female)
      - No history of THC, (-) THC on urine and (-) tobacco user

Chronic use & RGC’s
• Association Between Regular Cannabis Use and Ganglion Cell Dysfunction
  - Findings:
    - There was a significant increase in the N95 implicit time (latency) of the pattern ERG (pERG) in cannabis users with a median of 8.4 milliseconds difference between controls and users
    - It is unclear if this increase in latency (delay in processing) is permanent or disappears after withdrawal from use

Chronic use & RGC’s
• Association Between Regular Cannabis Use and Ganglion Cell Dysfunction
  - Conclusion: Our results demonstrate a delay in transmission of action potentials by the ganglion cells in regular cannabis users, which could support alterations in vision. Our findings may be important from a public health perspective since they could highlight the neurotoxic effects of cannabis use on the CNS as a result of how it affects retinal processing.

Cannabinoid Consequences
• Memory
  - One study involving over a 1,000 individuals found that chronic cannabis use is associated with cognitive decline
    - Greater deterioration being observed in those individuals with more persistent use
  - Among the various cognitive domains studied, memory is one of the most frequently identified as being negatively affected by cannabis
**Cannabinoid Consequences**

- In summary, there are many reasons to worry that for people who might choose to use MJ as medicine (and especially those who smoke it) the drug could actually add to their health problems.

**Most Current Report:**

“The Health Effects of Cannabis and Cannabinoids”

- From the National Academies of Sciences, Engineering, and Medicine (NASEM):
  - Possibly the most comprehensive review of existing scientific evidence related to the health effects and potential therapeutic benefits of cannabis
  - Provides a research agenda as well as summarizes and prioritizes pressing research needs.

**NASEM: Health Effects of Cannabis and Cannabinoids**

- There is limited evidence that cannabis or cannabinoids are ineffective for:
  - Improving symptoms associated with dementia (cannabinoids) (4-13)
  - Improving intraocular pressure associated with glaucoma (cannabinoids) (4-14)
  - Reducing depressive symptoms in individuals with chronic pain or multiple sclerosis (nabiximols, dronabinol, and nabilone)

**Cannabis and Glaucoma**

- A theoretical mechanism has been proposed for the IOP lowering effect of Δ9-THC being from action on the ciliary body cannabinoid receptors causing decreased aqueous production.

- MJ has been shown to lower IOP by approximately 25% in 60%-65% of both glaucoma and non-glaucoma patients.

---


Cannabinoids vs Cannabidiol

- The psychotropic cannabinoids (notably ∆9-THC) does show IOP reduction when administered IV or inhaled
  - No IOP lowering effect has been shown with topical administration
- The non-psychotropic cannabidiol (CBD) does not show IOP reduction
  - High dosages may increase IOP

Cannabinoids: THC and CBD

- 6 participants with glaucoma
  - 5 mg ∆9-THC Lowered IOP
  - 20 mg CBD No effect
  - 40 mg CBD Transient Incr IOP
  - Placebo No effect
- While effect of THC often cited, rarely hear the concerns with higher doses of CBD

Cannabinoids vs Cannabidiol

- MS: Cannabis plant extracts containing 2.5-120 mg of a THC-CBD combination is taken by mouth daily for 2-15 weeks
- Schizophrenia: 40-1,280 mgs of CBD is taken by mouth daily for up to four weeks

Medical Use of MJ for Glaucoma

- Alaska
- Arizona
- Arkansas
- California (Doc specific)
- Colorado
- Connecticut
- District of Columbia
- Delaware
- Florida
- Hawaii
- Illinois
- Louisiana
- Maine
- Maryland
- Massachusetts
- Michigan
- Minnesota
- Montana
- Missouri
- Nevada
- New Hampshire
- New Jersey (If topical med fail)
- New Mexico
- New York (Glas: NOT specified)
- North Dakota (Not yet active)
- Ohio
- Oklahoma (Doc specific)
- Oregon
- Pennsylvania
- Rhode Island
- Utah (Not yet active)
- Vermont
- Washington
- West Virginia (Doc specific)
Methods:
There are twenty-eight states that allow for the use of medicinal plant cannabis. The states typically have a list of approved conditions and the conditions may differ by state. The conditions are primarily to medicinal vaping systems and oral tinctures. Smoking plant materials, edibles such as candy and brownies are not allowed. There are a few other states that allow for all of the products (CBD & ∆9-THC).

Results:
An estimated 4,416 patients are using cannabis/marijuana related to glaucoma. This was found in twenty-two states with glaucoma as a disease to be treated with marijuana. Of these, there were data from eleven states. Of the twenty-two states, four states had new programs not yet being followed in a manner optimum for vision health. Data collection in cases where an eye condition exists is difficult. Differences in the states may be related to education and also taxation. The low prevalence rate in Minnesota may have been influenced by greater use of other means to treat glaucoma. Of note; Israel, considered to be on the forefront in cannabis medicine, recently dropped glaucoma as an approved disease for marijuana/cannabis use.

Increased Awareness

Increased Diagnosis

Glaucoma Percentage of State Glaucoma

<table>
<thead>
<tr>
<th>State</th>
<th># of Certifications</th>
<th>Glaucoma Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arizona</td>
<td>7855/50,879</td>
<td>1.50%</td>
</tr>
<tr>
<td>Colorado</td>
<td>1,183/35,620</td>
<td>3.30%</td>
</tr>
<tr>
<td>Hawaii</td>
<td>302/16,064</td>
<td>1.90%</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>277/98,583</td>
<td>0.28%</td>
</tr>
<tr>
<td>Minnesota</td>
<td>482/14,287</td>
<td>0.33%</td>
</tr>
<tr>
<td>Montana</td>
<td>281/8,461</td>
<td>1.21%</td>
</tr>
<tr>
<td>Nevada</td>
<td>408/24,465</td>
<td>1.67%</td>
</tr>
<tr>
<td>New Hampshire</td>
<td>225/17,522</td>
<td>1.30%</td>
</tr>
<tr>
<td>New Mexico</td>
<td>43/42,873</td>
<td>0.10%</td>
</tr>
<tr>
<td>Oregon</td>
<td>919/63,120</td>
<td>1.46%</td>
</tr>
<tr>
<td>Rhode Island</td>
<td>21/8,716</td>
<td>0.22%</td>
</tr>
</tbody>
</table>

Previous year data of glaucoma rate in each state from: https://www.preventblindness.org/glaucoma/download/9364091.

**IMMAD**

Medical Marijuana and Glaucoma: The United States Experience
Denise A. Valenti, OD, FAAO

Lack of Education

Results in Increased Use Medical Marijuana

- Study in Washington, D.C.
- 204 patients with glaucoma
- Intent to use marijuana as a treatment associated with false perceptions about marijuana and glaucoma
- Also associated with cost of glaucoma medications
- As well as impression of legal access


**A paper from Johns Hopkins (JAMA, June ’15, pg 2491) showed high variability in label accuracy in edible medical cannabis products (CBD & ∆9-THC)
- 75 products purchased in 3 regions
  - San Francisco, Los Angeles, Seattle
- THC
  - 17% were accurately labeled
  - 25% were underlabeled (most in LA)
  - 60% were overlabeled (most in Seattle)
Israel: Glaucoma and Marijuana

• Israel has strong history of cannabis related research.

• Israel has dropped glaucoma as an approved disease for which cannabis can be used as treatment.

Societal Trends

• Federal regulations and enforcement continue to be potentially problematic!
  – Started with the Obama administration but seems to be continuing with the Trump administration.....
  – So Federal policies have not changed with the last 2 administrations despite changed legislation within the states

Societal Trends

• A FDA Advisory Panel unanimously recommended approval of an epilepsy medication made of CBD.

• On June 25, 2018, the FDA approved the CBD oral solution for the treatment of seizures associated with two rare and severe forms of epilepsy, Lennox-Gastaut syndrome and Dravet syndrome, in patients two years of age and older.

Societal Trends

• So the question became:
  – How can the DEA schedule Cannabis as Schedule 1 (“No currently accepted medical use and a high potential for abuse”) if Epidiolex® is FDA approved?
  – The FDA scheduled Epidiolex® as Schedule V and other non-FDA approved CBD preparations remained in Schedule I!!
  – NOT different from all other cannabis preps!!

Societal Trends

• But CBD is experiencing a proliferation in use:
  – Beauty and wellness companies are using it in everything:
    • Kush mascara (by Milk Makeup) – now vegan!
    • Vertly CBD infused balms & lotions
    • Lord Jones body lotion & confections
    • Ambika Herbals: CBD bath salts
    • CBD For Life: Eye serum
    • From Ever Since: Face Serum

Societal Trends

• Healthy Kids Colorado Survey
Societal Trends

• Revenue trending:

<p>| Marijuana Taxes, License, and Fee Revenue |
|-------------------------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Calendar Year</th>
<th>Total Revenue</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>$567,594.22</td>
</tr>
<tr>
<td>2015</td>
<td>$138,411.17</td>
</tr>
<tr>
<td>2016</td>
<td>$195,634.81</td>
</tr>
<tr>
<td>2017</td>
<td>$247,368.47</td>
</tr>
<tr>
<td>2018 (Jan - Mar)</td>
<td>$363,658.12</td>
</tr>
</tbody>
</table>

Updated April 2018

Health Topic of the Month January 2017

Should You Trust That Latest Marijuana Study?

Marijuana is a controversial issue, with both its proponents and opponents having strong views. As research continues, always be aware of new information. That’s all it took to focus on marijuana. Here’s how to navigate the information you read online and in social media, and how to discern what you believe. They can make us or take us on a high road or lead down a steep path. It’s up to us and our ability to discern the information we are receiving and determine if it’s trustworthy. So, how do you deal?

Let’s take the website FoxNews as an example. It’s a news outlet that provides news stories and information on various topics, including marijuana. However, it’s important to critically evaluate the information presented on this site. How do you evaluate all these media to determine what you believe in and what you shouldn’t?