

Interactive Anterior Segment Grand Rounds

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Disclosures:

- Sun Pharmaceuticals: speakers bureau,
- Dompe: advisory board,
- RVL Pharmaceuticals: advisory board
- Thea Pharmaceuticals: advisory board

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30 YR WM

- Patient calls from his PCP office asking if we can see him today because he has had red/painful eyes for over a week and has not resolved
- Medical history:
 - Past week has been experiencing painful urination and discharge
 - New sexual partner approx 10 days ago, who also had developed a red eye
 - Chlamydia and gonorrhea testing were negative
 - Has tested positive for HSV2 but no current flare up



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30 YO WM

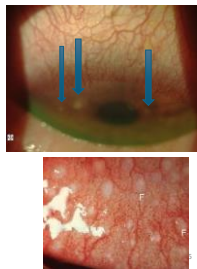
- Medications:
 - In the past week patient:
 - 2 courses of azithromycin (1 gram each)
 - Injection of rocephin
 - Injection of penicillin G
 - Currently taking doxycycline 100 mg bid
 - Valtrex 1 gram 3 times per day for 7 days (d/c 1 day ago)
 - Was on Vigamox qid for 7 days (d/c 1 day ago)
- VA: 6/7.5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



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30 YO WM

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



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30 YO WM

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



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30 YO WM

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



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30 YO WM

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

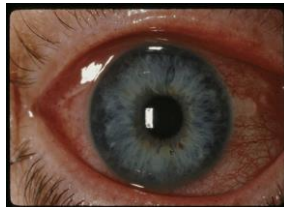
What did we learn from this?



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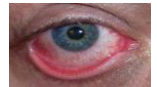
Viral Conjunctivitis

- Most common infectious keratitis presenting on emergent basis
- 62% caused by adenovirus
- **Two major types:**
 - Pharyngoconjunctival fever (PCF)
 - Epidemic keratoconjunctivitis (EKC)



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Viral Conjunctivitis



- PCF: **history of recent/current upper respiratory infection**
 - **classic triad of fever, pharyngitis, and acute follicular conjunctivitis**
 - occurs more commonly in children, is caused by serotypes 3 and 7, and is spread by respiratory secretions.
 - tearing and foreign body sensation that is initially unilateral.



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Viral Conjunctivitis



- PCF:
 - **corneal involvement is not a key feature, there is occasionally a punctate keratitis;**
 - SEIs are rare.
 - **self-limiting condition that varies in severity and may last from 4 days to 2 weeks**
 - Treatment if symptomatic though topical steroids are rarely needed.



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Viral Conjunctivitis: EKC (Epidemic Keratoconjunctivitis)

- EKC initially manifests as a flu-like syndrome consisting of fever, malaise, and myalgias followed by the appearance of ocular signs and symptoms, including a red eye, eyelid edema, excessive tearing, irritation, foreign body sensation, and photophobia.
- EKC frequently begins as a unilateral condition but, in 70% of cases, will become bilateral within the first week of symptoms as a result of hand-to-eye transmission
 - **Adenovirus 8 common variant leading to "rule of 8's"**
 - First 8 days red eye with fine SPK
 - Next 8 days deeper focal epithelial lesions
 - Following 8 potential development of infiltrates
 - Resolution

<https://www.aaao.org/feyenet/article/epidemic-keratoconjunctivitis-prevention-strategie>

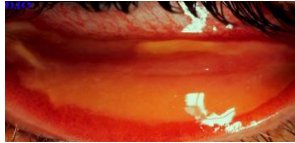


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Viral Conjunctivitis: Signs and Symptoms

- Gritty sensation
- Watery discharge
- Sticky in mornings
- **Follicular response**
- Chemosis
- Injection
- SPK
- Infiltrates possible
- **Positive lymph nodes**

- **Pseudomembranes in severe cases**
- Subconjunctival hemes



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Management

- **Considering the use of anti-inflammatory treatment to relieve patient symptoms and improve comfort**
 - E.g. Lotemax® QID OU
- EKC patients are typically very uncomfortable and would benefit from anti-inflammatory treatment
 - especially if infiltrates or pseudomembrane present
- studies have shown that steroids are effective in reducing inflammation during the acute phase of EKC and decreasing the likelihood of development of corneal subepithelial infiltrates.
- However, the studies also showed that their use increased viral replication and titers and prolonged the mean duration of viral shedding
- routine corticosteroid use is generally not indicated for EKC
 - when managing a severe EKC inflammation, you should carefully weigh the risks and benefits of steroids

<https://www.aao.org/eyenet/article/epidemic-keratoconjunctivitis-prevention-strategy>



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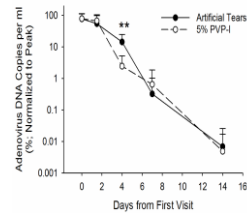
Management

- Betadine (Melton-Thomas Protocol):
 - Proparacaine
 - 4-5 drops of Betadine 5%
 - Get patient to close eye and gently roll them around
 - After one minute, lavage the eye
 - Lotemax 4 times a day for 4 days
- Alternative: Betadine swabsticks.
 - 5% Betadine solution only comes in 30 ml bottles cost \$14.00.
 - Case of 200 Betadine swabsticks approx. 45 dollars.



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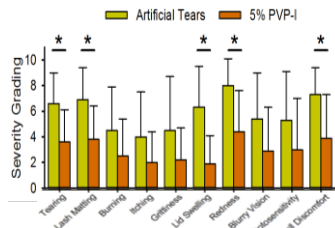
Reducing Adenoviral Patient-Infected Days (RAPID) Study
Effect of 5% PVP-I on qPCR-Derived Viral Titers



Andrew Hartwick, Tammy Than, Bojana Rodic-Polic, Spencer Johnson, Mary Migneco, Ellen Shorter, Jennifer S Harthan, Christina Morettin, Meredith Whiteside, Alison Olson, Matthew Margolis, Julia Huecker, Gregory Storch, Mae O Gordon; Reducing Adenoviral Patient-Infected Days (RAPID) Study: A Randomized Trial Assessing One-Time, In-Office Application of 5% Povidone-Iodine in Treatment of Adenoviral Conjunctivitis. Invest. Ophthalmol. Vis. Sci. 2019;60(9):6257. doi: <https://doi.org/10.1167/19.9.6257>

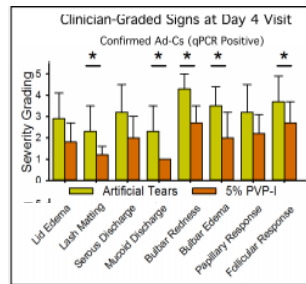
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Day 4: qPCR + Participant-Reported Symptoms



Andrew Hartwick, Tammy Than, Bojana Rodic-Polic, Spencer Johnson, Mary Migneco, Ellen Shorter, Jennifer S Harthan, Christina Morettin, Meredith Whiteside, Alison Olson, Matthew Margolis, Julia Huecker, Gregory Storch, Mae O Gordon; Reducing Adenoviral Patient-Infected Days (RAPID) Study: A Randomized Trial Assessing One-Time, In-Office Application of 5% Povidone-Iodine in Treatment of Adenoviral Conjunctivitis. Invest. Ophthalmol. Vis. Sci. 2019;60(9):6257. doi: <https://doi.org/10.1167/19.9.6257>

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Management

- Antivirals used in HSV keratitis have traditionally thought to be ineffective in treatment of viral conjunctivitis
- Ganciclovir: In a double-masked, controlled, and randomized study it was found to shorten the mean time of recovery from 18.5 days to 7.7 days in patients who were treated vs. those who just received artificial tears.
 - Tabbara K, Jarade E. Ganciclovir effects in adenoviral keratoconjunctivitis. 2001; ARVO abstract 3111 (suppl); S579
- In clinical trial Avenova[®]: proposed end date November 2020
 - The investigators propose a study to evaluate the role of Avenova[®] (0.01% hypochlorous acid) in the treatment of common ocular viral infections.
- Important to stress limited contact with others, frequent hand washing, not sharing of towels, etc



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Efficacy of Hospital Germicides against Adenovirus 8, a Common Cause of Epidemic Keratoconjunctivitis in Health Care Facilities. ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2006, p. 1419-1424

An important finding from our study was that of the four disinfectants recommended by the CDC and Association for Professionals in Infection Control and Epidemiology for elimination of adenovirus type 8 from ophthalmic instruments, two (70% isopropyl alcohol and 3% hydrogen peroxide) were found to be ineffective. Based on these data, 3% hydrogen peroxide and 70% isopropyl alcohol are not effective against adenovirus that is capable of causing epidemic keratoconjunctivitis and similar viruses and should no longer be used for disinfecting applanation tonometers.



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EKC Disinfection

- Commercial grade disinfectants that include compounds such as:
 - peracetic acid,
 - aldehydes [glutaraldehyde and ortho-phthalaldehyde],
 - chlorine-based products [1,900 to 6,000 ppm available free chlorine],
 - ethanol mixed with quaternary ammonium compounds)
- E.g. Cidex, DisCide



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Case

- A 68-year-old woman with a history of poorly controlled diabetes presents with poor vision of the left eye for about 2 months.
- She notes an episode of left eye pain 2 months ago that lasted for a week



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Case Presentation



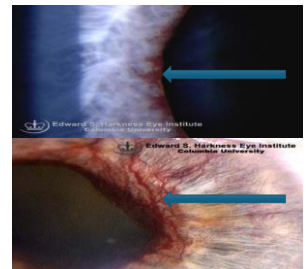
	OD	OS
VA	20/40	20/800
Pupils	No APD	Mild APD
SLE	Cornea clear No NVI Angle Open 2+ NS	Extensive NVI with angle synechiae 20% hyphema 4+ NS
IOP	18 mm Hg	44 mm Hg
Fundus	PDR with NVD and NVE Focal area of subhyaloid hemorrhage	PDR with NVD and NVE Focal area of subhyaloid hemorrhage
C/D	0.4	0.7



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Iris Neovascularization

- New vessel growth usually begins at the pupil margin
- enlarge, and grow in an irregular pattern along the iris surface

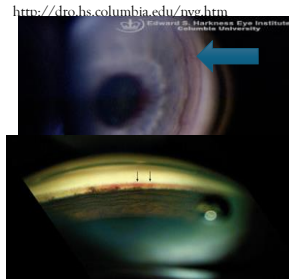


<http://dro.hs.columbia.edu/nvg.htm>

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Angle Neovascularization

- New vessels grow to anterior chamber angle
- new blood vessel growth brings along fibrovascular tissue
- causes a reduction of aqueous humor outflow



<http://www.reviewofophthalmology.com/article/another-role-for-avastin-neovascular-glaucoma>

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Peripheral Anterior Synecchia (PAS)

- If the membrane contracts it pulls the peripheral iris into the TM leading to the formation of PAS

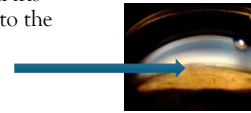
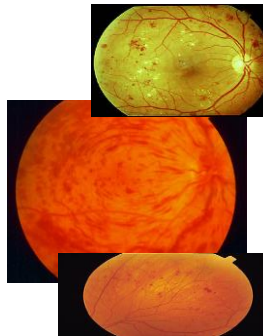


Image courtesy: John McSoley, OD

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NVG: Etiology

- Ocular ischemic disorders account for 97% of cases with NVG
- The most common disorders leading to NVG are:
 - diabetes mellitus,
 - CRVO, and
 - ocular ischemic syndrome.



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NVG and VEGF

- There is adequate evidence supporting the role of VEGF-A in the pathogenesis of ocular neovascularization,
 - studies have confirmed the increased levels of VEGF-A in glaucoma and NVG in particular
 - experimental elevation of VEGF-A levels induces typical neovascularization



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NVG: Management

- Treatment of the underlying disease and control of IOP.
- The key to NVG management lies in elimination of the angiogenic stimulus
- Effective treatments for retinal ischemia include:
 - Panretinal photocoagulation (PRP),
 - cryotherapy, and
 - endolaser treatment combined with vitrectomy.
- Despite the reduction of retinal ischemia and additional antiglaucoma medication
 - NVG frequently exhibits irreversible intraocular pressure (IOP) elevation.



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NVG: Medical Management

- Medical therapy is beneficial in lowering the IOP and include:
 - topical β -blockers,
 - α -2 agonists, and
 - topical or oral carbonic inhibitors
- Miotics (pilocarpine) and epinephrine drugs are contraindicated:
 - they may increase inflammation (increase permeability of the blood-aqueous barrier),
 - cause miosis, and
 - worsen synechial angle closure



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NVG: Medical Management

- Topical prostaglandins are generally not used because they too can exacerbate inflammation
- **intraocular inflammation NEEDS to be controlled:**
 - topical atropine 1% to decrease ocular congestion and topical steroids (eg, prednisolone acetate) to decrease inflammation



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NVG: Anti-VEGF

- Treatment includes the use of anti-VEGF
 - several studies have shown that specific inhibition of VEGF-A inhibits pathologic neovascularization in the iris, choroid, cornea, and retina
- Olmos, et. al (March 2016):
 - **role of bevacizumab in NVG is that of a temporizing rather than a definitive treatment, and eyes with NVG should uniformly receive PRP to treat ischemia, regardless of prior intravitreal bevacizumab injection(s)**
- Anti-VEGF should be combined with PRP



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NVG: Glaucoma Surgery

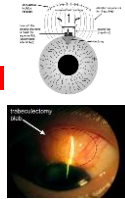
- **Glaucoma filtering surgery is now considered standard for the treatment of the elevated IOP in NVG patients**
- Glaucoma surgery is indicated to optimally control IOP if medical therapy has proven to be inadequate. Includes procedures such as:
 - aqueous tube shunt surgery,
 - cyclodestruction, or
 - antimetabolite-enhanced filtration surgery



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Trabeculectomy

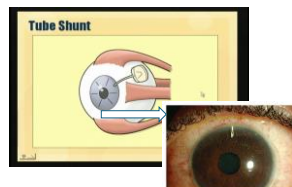
- Trabeculectomy:
 - Channel made from TM to bleb
- **Trabeculectomy for NVG has been considered to be a difficult treatment with low success rates**
 - intraoperative or early postoperative bleeding and inflammation caused by neovascularization adversely affects the scarring process of the filtering bleb.



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Glaucoma Drainage Implant

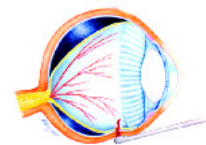
- implantation of a tube shunt
- **most common treatment for glaucoma when medications have proven to be insufficient**



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Cyclodestructive Procedures

- Ablating a portion of the ciliary body
 - IOP is lowered by decreasing aqueous humor production
- Destruction of the ciliary body by:
 - transcleral application of cryotherapy or
 - transcleral or endoscopic delivery of diode, krypton or Nd:YAG laser.



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NVG: End Stage

- For blind painful eyes with uncontrollable IOP, options include:
 - continued medical therapy,
 - cyclodestruction,
 - retrobulbar alcohol injection, or
 - enucleation.

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

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

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- Not all patients are symptomatic
- Most common symptom is mild FB sensation which is worse in dry weather, wind and air conditioning
- Blurred vision from irregular astigmatism or rapid TBUT
- Pain is usually secondary to a RCE (recurrent corneal erosion) in approx 10%

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

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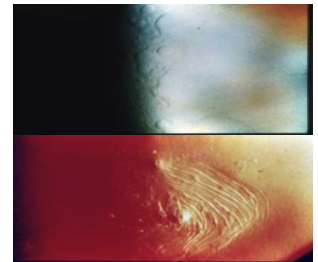


- Most common findings are:
 - chalky patches,
 - intraepithelial microcysts, and
 - fine lines (or any combination) in the central 2/3rd of cornea



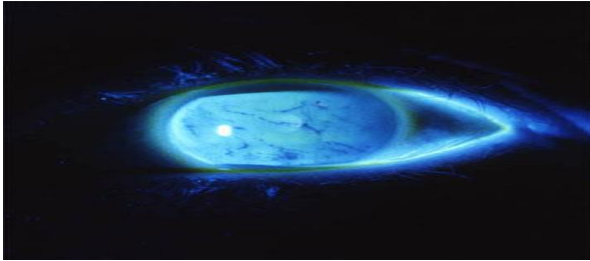
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- Often referred to as:
 - maps,
 - dots or
 - fingerprints

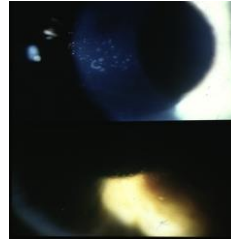


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EBMD-Negative Staining

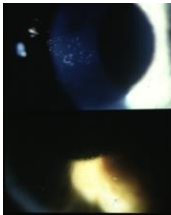


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- Typically directed towards preventing RCE
- If RCE's develop:
 - awake with painful eye that improves as day wears on
 - chalky patches/dots in lower 2/3rd of cornea

Acute Treatment of RCE:
Dr Greenwood, MD

- use of hyperosmotic ointment at bedtime
- bandage contact lens
- Frequent lubrication
- Plugs
- Topical meds
- No ceiling fans
- Nighttime ointment
- PTK

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Recurrent Corneal Erosion: Treatment

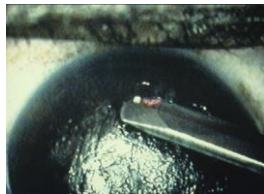
- If severe enough to cause vision loss or repeated episodes:
 - oral doxycycline with/without topical corticosteroid
 - Doxy 50 mg bid and FML tid for 4-8 weeks
 - both meds inhibit key metalloproteinases important in disease pathogenesis
 - debridement,
 - Debridement + diamond burr polishing
 - stromal puncture (not commonly done anymore)
 - PTK
 - Latest development: amniotic membrane transplant e.g. Prokera typically after debridement



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CORNEAL DEBRIDEMENT

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



Pictured: Kimura Platinum Spatula

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Diamond Burr Polishing

- Removes abnormal basement membrane
- Provides smooth surface for cells to grow



Vo, et al (2014): epithelial debridement with diamond burr polishing was 95% effective after single treatment in preventing recurrence for an average of 32 months follow up time



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Aussie Patient Story

- Male 59 Anglo Celtic heritage
- Asymptomatic , accidental detection by daughter following island holiday Bali and further sun exposure August 2016
- Hx : surfer and excessive sun exposure - coconut oils etc for first 2 decades of life.



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Aussie Patient Story

- Initial dermatologist opinion – BCC (basal cell carcinoma)
- **BUT** biopsy confirmed aggressive malignant melanoma, 2.2 mm thick , 5 mm cell growth rate



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Aussie Patient Story

- Initial excision September 14 2016 .
 - Found to have invaded sentinel axillary node –
- further surgery October 6 - complete axillary dissection right underarm - pathology clear.
- Final dx - stage 3 malignant melanoma.



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Pre-Malignant Eyelid Lesions: Keratoacanthoma

- Appears as a solitary, rapidly growing nodule on sun exposed areas of middle-aged and older individuals
- **Nodule is usually umbilicated with a distinctive crater filled with keratin**
- Lesion develops over weeks and undergoes spontaneous involution within 6 mo to leave an atrophic scar
- **Complete excision is recommended as there are invasive variants**



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Pre-Malignant Eyelid Lesions: Actinic Keratosis

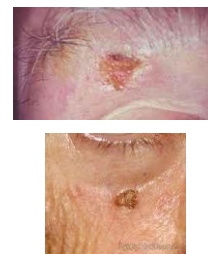
- Also known as solar or senile keratosis
- **Most common pre-malignant skin lesion**
- **Develops on sun-exposed areas and commonly affect the face, hands and scalp (less commonly the eyelids)**
 - Predominately white males



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Pre-Malignant Eyelid Lesions: Actinic Keratosis

- Appear as multiple, flat-topped papules with an adherent white scale.
- **Development of SCC in untreated lesions as high as 20%**
- Management is surgical excision or cryotherapy (following biopsy)



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Malignant Eyelid Lesions: Basal Cell Carcinoma (BCC)

- Most common malignant lesion of the lids (85-90% of all malignant eyelid tumors)
- 50-60% of BCC affect the lower lid followed by medial canthus 25-30% and upper lid 15%
- Metastases is rare but local invasion is common and can be very destructive



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Malignant Eyelid Lesions: Basal Cell Carcinoma

- Diagnosis is initially made from its clinical appearance, especially with the noduloulcerative type with its raised pearly borders and central ulcerated crater
- categorized into two basic types: noduloulcerative and morpheiform
- The morpheiform variant is typically diffuse, relatively flat with indistinct borders. This variant is more aggressive and can be invasive despite showing less obvious features.



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Malignant Eyelid Lesions: Basal Cell Carcinoma

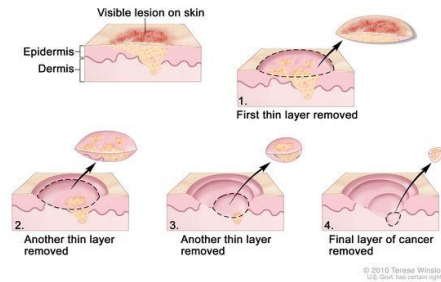
- Definitive diagnosis made on histopathological examination of biopsy specimens
- loss of adjacent cilia, is strongly suggestive of malignancy and occurs commonly with basal cell carcinoma of the eyelid
- Surgery is generally accepted as treatment of choice
 - Mohs' surgery technique



<https://entokey.com/tumors-of-the-eyelids/>

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Mohs Surgery



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Malignant Eyelid Lesions: Squamous Cell Carcinoma (SCC)

- Much less common than BCC on the eyelid but has much higher potential for metastatic spread
- Typically affects elderly, fair-skinned and usually found on the lower lid



<https://www.aao.org/oculoplastics-centers/squamous-cell-carcinoma-of-eyelid>

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Malignant Eyelid Lesions: Squamous Cell Carcinoma (SCC)

- Presents as an erythematous, indurated, hyperkeratotic plaque or nodule with irregular margins
- Lesions have a high tendency towards ulceration and tend to affect lid margin and medial canthus



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Malignant Eyelid Lesions: Sebaceous Gland Carcinoma

- Highly malignant neoplasm that arises from the meibomian glands, Zeis and the sebaceous glands of the caruncle and eyebrow
- Aggressive tumor with a high recurrence rate, significant metastatic potential and notable mortality rate
 - rates of misdiagnosis have been reported as high as 50%



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Malignant Eyelid Lesions: Sebaceous Gland Carcinoma

- Relatively rare, 3rd most common eyelid malignancy
- Uncommon in the Caucasian population and represents only 3% of eyelid malignancies
 - most common eyelid malignancy in Asian Indian population, where it represents approximately 40% or more of eyelid malignancies



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Malignant Melanoma (MM)

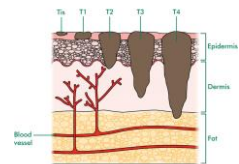
- MM of the eyelid accounts for about 1% of all eyelid malignancies (leading cause of death due to skin disease)
- Incidence been increasing and it causes about 2/3 of all tumor related deaths from cutaneous cancers
- Incidence increases with age
- Eyelid cutaneous melanoma arises most frequently in the lower eyelid and can appear de novo or grow from a preexisting pigmented lesion that increases in size and changes in shape and color.
- Eyelid melanoma can often involve the eyelid margins.



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Malignant Melanoma

- Tumor thickness is the single most important prognostic factor.
- Ten-year survival rates—related to thickness in millimeters—are as follows:
 - less than 1 mm, 95%;
 - 1–2 mm, 80%;
 - 2–4 mm, 55%; and
 - greater than 4 mm, 30%.
- With lymph node involvement, the 5-year survival rate is 62%; with distant metastases, it is 16%.



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Melanoma

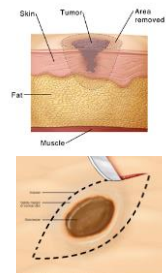
- Risk factors include congenital and dysplastic nevi, changing cutaneous moles, excessive sun exposure and sun sensitivity, family history, age greater than 20 and fair skinned.
- History of a changing mole is the single most important historical reason for a closer inspection or referral
- History of severe sunburns rather than cumulative actinic exposure thought to be a major risk factor



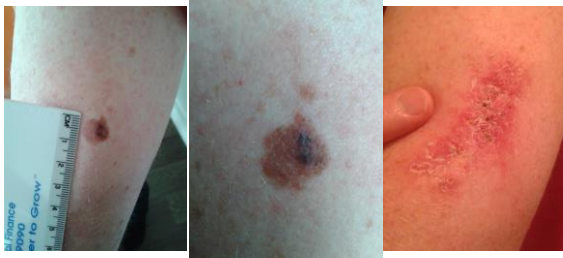
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Melanoma

- Prognosis and metastatic potential are linked to the depth of invasion and thickness of the tumor
- Treatment is wide surgical excision confirmed with histological monitoring

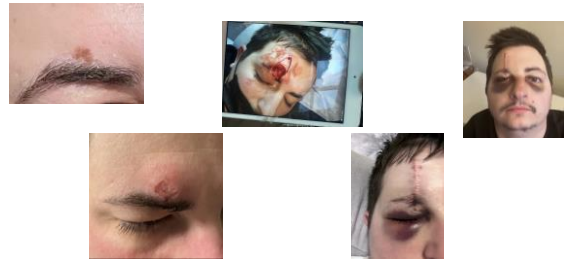


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Recent Patient



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Malignant Eyelid Lesions: Malignant Melanoma

The ABCDEs of Detecting Melanoma					
	A	B	C	D	E
	Asymmetry	Border	Color	Diameter	Evolving
NORMAL					
	Symmetrical	Borders Are Even	One Color	Smaller Than 1/4 Inch	Ordinary Mole
MELANOMA					
	Asymmetrical	Borders Are Uneven	Multiple Colors	Larger Than 1/4 Inch	Changing in Size, Shape and Color

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Case

- 50 YR WM
- POHx: had cataract surgery in his left eye at age 25 secondary to trauma to the eye,
 - Has a mid-dilated pupil post trauma
- PMHx: no known health problems and no medications
- VA: 6/6 (20/20) OD, OS

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Health Assessment

- SLE:
 - OD unremarkable
 - OS: mid-dilated pupil with sluggish response to light
 - PCIOL well centered and no haze
- IOP: OD 12 and OS 26 mm Hg (TAG)
 - NCT OS (31 and 23)
 - Second visit: OD: 13 and OS: 27

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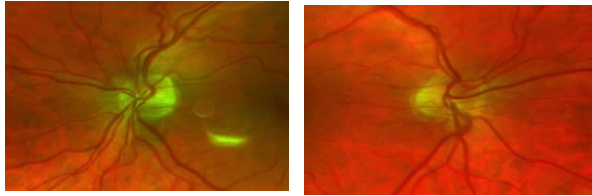
Health Assessment

- Gonioscopy:
 - OD: unremarkable
 - OS: see photo



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Optic Nerves

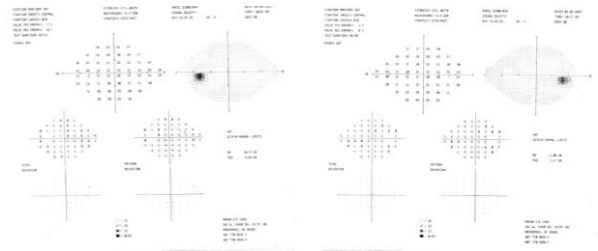


OS

OD

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Visual Fields

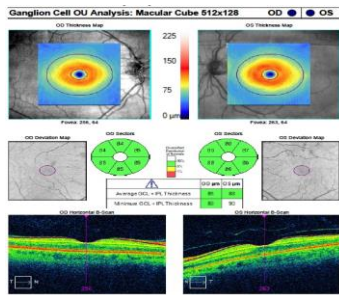


OS

OD

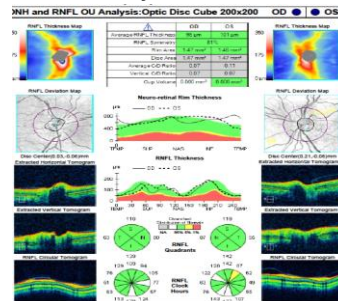
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Ganglion Cell Analysis



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RNFL and ONH Analysis



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Patient Update

- Patient was seen a year later
- Latanoprost qhs (remembers 5 days out of week)
- IOP's: OD: 14 and OS: 13 mm Hg
- No change in OCT

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Angle Recession Glaucoma

- Although recession of the iridocorneal angle is common after blunt trauma,
 - only 6% to 7% of these eyes will eventually develop glaucoma
- There appear to be two peak incidences of glaucoma after angle recession.
 - the first peak occurs within the first few weeks to years after the trauma, and
 - the second peak occurs 10 or more years after the injury

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Angle Recession Glaucoma

- There is an association between the extent of angle recession and the development of glaucoma
- It appears that those eyes with less than 180 degrees of recession are unlikely to develop glaucoma
- whereas most investigators agree that patients with 180 to 360 degrees of angle recession will have a greater risk of developing late-occurring glaucoma



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Angle Recession Glaucoma

- In eyes that do develop angle recession glaucoma:
 - the contralateral non-traumatized eye has been reported to have a 50% chance of developing open-angle glaucoma, sometimes years after the pressure rise was noted in the traumatized eye.



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Angle Recession Diagnosis

- The diagnosis of angle recession is made by patient history and clinical examination.
 - In cases of unilateral glaucoma or traumatic hyphema or after blunt trauma, angle recession should always be considered
- With milder injuries
 - the examiner may have to compare the gonioscopic appearance of two parts of the angle of 1 eye to identify subtle changes in the injured angle.



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Thank you!!

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