

SYSTEMIC MEDICATIONS WITH OCULAR COMPLICATIONS

Dave Trujillo 13 May 2021

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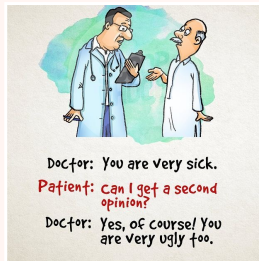
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> NONE

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SIDE EFFECT VS ADVERSE REACTION

- > SE: Documented therapeutic effect that occurs when treatment goes beyond desired effect, or a problem occurs in addition to the desired therapeutic effect
- > AR: Undocumented therapeutic event that is unforeseen or a dangerous reaction. Completely unpredictable



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COMMON COMPLAINTS

- > Abnormal/uncomfortable vision
- > Color perception
- > Red eye
- > Blurry vision
- > Pain



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RESOURCES

[Pill ID](#)

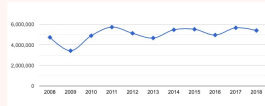
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PLAQUENIL (HYDROXYCHLOROQUINE)

- > What is it used for?
 - > Treat or prevent malaria
 - > Treat auto-immune diseases: most commonly lupus and rheumatoid arthritis



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- Disease modifying anti-rheumatic drug (DMARD)
- Regulates the immune system
- Modifies the underlying disease process rather than treating the symptoms

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- > Malaria
 - > 400 mg/week for prevention
 - > 800 mg day one/400mg/day for 3 days
- > Auto-immune
 - > 200-400mg daily

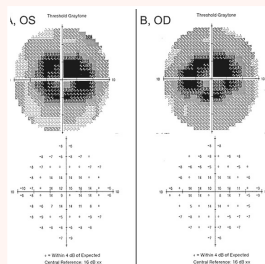


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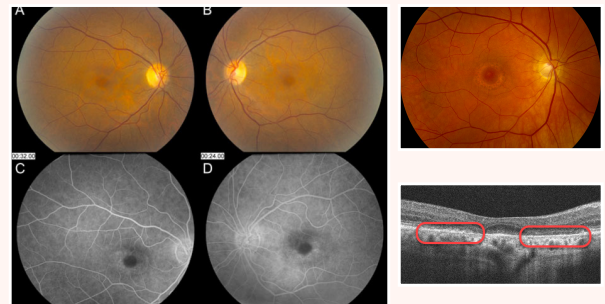
- Vortex Keratopathy
- Whorl-like deposits at the base of the epithelium
- Retinal Toxicity - Binds to melanin in RPE causing damage and atrophy
- Pigmentary retinopathy - (depigmentation and usually bilateral)
- Early retinal findings are often asymptomatic
- Progression reveals parafoveal depigmentation (bull's eye) and atrophy with scotoma

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- Daily dosage
- Cumulative dosage
- Renal or liver disease
- Retinal disease



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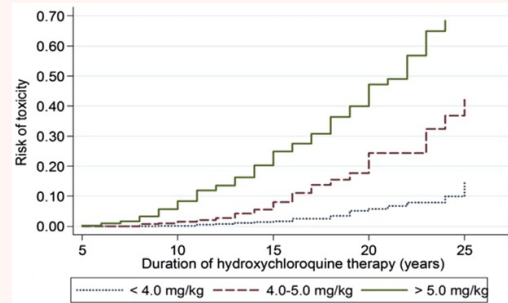


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WHO'S AT RISK?

- Risk depends on length of treatment and cumulative dosage
- At 5 years risk of toxicity is <1%
- 2% after 10 years
- Close to 20% at 20 years
- Recommended dose is $\leq 5\text{mg/kg}$

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LBS TO KG

"Estimate"

1. Cut weight (lbs) in half
2. Subtract 10%

Ex: 175 lbs \rightarrow ~88

88-8 \rightarrow 80 Kg

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MANAGEMENT

- Baseline examination at initiation of treatment
- Annual screenings after 5 years of treatment for low risk patients
- More frequent screening is recommended for high-risk patients
- Higher doses
- Renal or liver disease
- 10-2 visual field, OCT, fundus photo (AF)

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HYDROXYCHLOROQUINE TAKE HOME POINTS

- Binds to melanin in the RPE leading to damage and atrophy
- Risk is dose related
- Asymptomatic in early stages
- Damage even after cessation
- Recommended dose of 5mg/kg
- Communicate with Rheumatologist

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PHOSPHODIESTERASE INHIBITORS

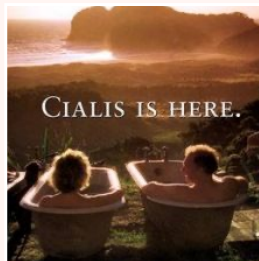
- Treatment for erectile dysfunction
 - Sildenafil citrate (Viagra) #207
 - Tadalafil (Cialis) - #253
- 4,675,935 US prescriptions/year
- Can be used in the treatment of pulmonary hypertension and benign prostatic hyperplasia



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HOW DOES IT WORK

- Phosphodiesterase 5 (PDE 5) Inhibitor
- Blocks the break down cyclic guanosine monophosphate
- Stimulating smooth muscle relaxation



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COMMON COMPLAINTS AND RISKS

- Blue tinge or haze in vision
- Light sensitivity
- Decreased color vision
- Retinal vascular occlusion
- Ischemic optic neuropathy



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MOST CONCERNING SIDE EFFECT

- Ischemic optic neuropathy
- 3% taking low doses (25 - 50mg)
- 11% in 100mg dosage
- 50% in 200 mg dosage
- By taking this medication, they have "blood flow" issues and other risk factors Predisposing to NAION, RVO, and RVA



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PHOSPHODIESTERASE INHIBITORS TAKE HOME POINTS

- Phosphodiesterase inhibitor leads to smooth muscle relaxation and increased blood flow
- Mild lowering of blood pressure may result
- At the normal dose of 50mg, has a 3% chance of increased risk of optic neuropathy
- Dx of exclusion - already have predisposing factors for NAION, RAO, & RVO
- Communicate with comanaging doctor

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AMIODARONE

- Cordarone or Pacerone
- Treatment:
 - Ventricular tachycardia
 - Ventricular fibrillation
 - Atrial fibrillation



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FACTS

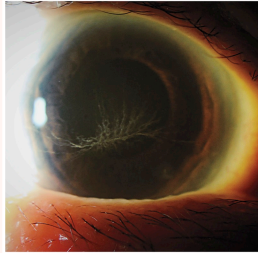
- 3,171,077 US Prescriptions
- #189 on Top Drug List
- Loading dose 800-1600mg
- Maintenance dose 400mg qd
- Tablet: 100, 200 & 400mg



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SIDE EFFECTS

- Most common (usually asymptomatic)
- Vortex Keratopathy (70-100%)
- Anterior sub-capsular opacities of the lens (50-60%)



SIDE EFFECTS

Less common but more SEVERE

- Optic neuropathy
- Similar presentation to NAION
- Patient already have NAION risk factors
- Dx of exclusion



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AMIODARONE TAKE HOME POINTS

- Gradual onset with milder degree of vision loss
- Commonly bilateral with longer duration of disc edema
- Accumulates in the lysosomes of the optic nerve - decreasing axoplasmic flow
- Half-life 58-142 days...so swelling can persist for months
- No correlation between dosage or duration
- Most patients taking amiodarone already have vascular factors increasing their risk for NAION
- Communicate with Cardiologist/Comanaging

FINGOLIMOD (GILENYA)

- First oral treatment for relapsing-remitting multiple sclerosis
- Effective in reducing the number of relapses
- Siponimod (Mayzent) & Ozanimod (Zeposia)

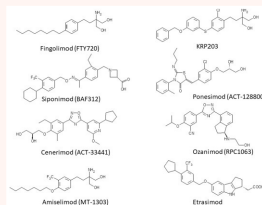


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FACTS

- Over 100,000 prescriptions since 2010
- Nearly 1 million dx in the US
- Price tag of over \$8,000 for 30 day supply
- 2019 FDA approved a generic



NOT SO FAST

- August 2020, U.S. District Court upheld the validity of the Gilenya (fingolimod) dosage regimen patent.
- Prevents generic drug makers through 2027



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HOW DOES IT WORK

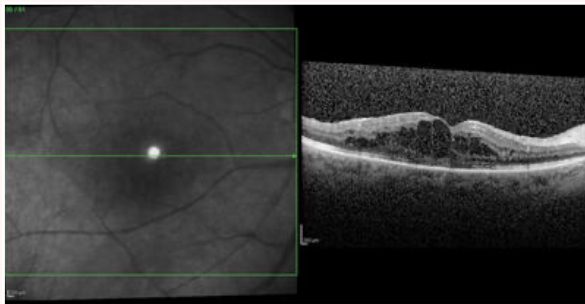
- Immunomodulating agent that binds to sphingosine-1-phosphate (S1P) receptors on lymphocytes
- Prevents release of lymphocyte from the lymph nodes
- Sparing the central nervous system from attack by the myelin-reactive lymphocytes

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OCULAR SIDE EFFECTS

- Fingolimod associated macular edema (FAME)
- Secondary effects on vascular endothelial barrier function leading to increased permeability in the blood-retina barrier
- ~1-2% incidence rate
- Within four months of starting treatment
- 25% had a history of uveitis
- Symptoms
 - Metamorphopsia
 - Blurred vision
 - 25% of FAME is bilateral
- Resolution with the discontinuation of the drug

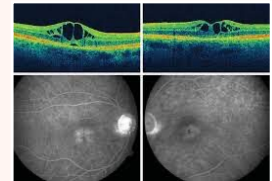
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MANAGEMENT

- Baseline (if possible)
- Amsler grid
- OCT
- DFE



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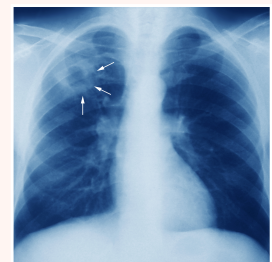
FINGOLIMOD TAKE HOME POINTS

- Effective at reducing frequency of relapses
- Fingolimod associated macular edema usually presents in the first 4 months of treatment
- Metamorphopsia and blurred vision
- Resolves with the discontinuation of treatment
- With the release of generics will we see more FAME??

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ETHAMBUTOL

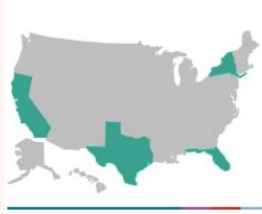
- Treatment:
 - Tuberculosis
 - Mycobacterium avium complex lung disease
- A fourth of a complex drug cocktail



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2019 TRENDS

- > 8,916 reported cases in US
- > 4 states responsible for 51 % of cases
- > 542 deaths (2018)
- > Incidence rate: Asian persons (35.3%), Hispanic persons (30.2%), Black/African American persons (19.7%), and White persons (11.4%)

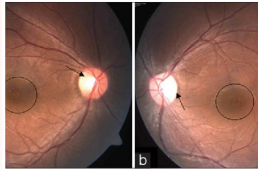


MYCOBACTERIUM TUBERCULOSIS

- > Usually attacks the lungs, but can attack kidney, spine and brain
- > Not everyone infected with TB becomes sick
- > Two TB related conditions exist
 - > Latent TB infection (LTBI)
 - > Isoniazid, rifampentine, and rifampin
 - > TB disease
 - > Isoniazid, rifampin, pyrazinamide, and ethambutol

HOW DOES IT EFFECT THE EYE

- > Optic neuropathy → optic atrophy
- > Bilateral central vision loss (>60%)
- > Color vision loss
- > Central or cecocentral scotomas



COMANAGE

- > Baseline dilated exam:
 - > Vision screening
 - > Color vision
 - > Amsler grid (+ one to take home)
 - > Visual field
 - > NFL OCT
- > Monthly F/U while on ethambutol treatment
- > 1/3 - 2/3 of patient show visual recovery if optic neuropathy is detected early

ETHAMBUTOL TAKE HOME POINTS

- > Most likely something we will never commonage
- > 4th drug in a complex cocktail in the treatment of TB
- > Optic neuropathy progressing to optic atrophy with central vision loss
- > Cessation does not reverse the damage
- > Communicate with infectious disease or comanaging doctor

DUPIXENT (DUPILUMAB)

- > Approved 2017
- > Treatment:
 - > Atopic dermatitis and eczema (6+)
 - > Asthma (12+)
- > Blocks interleukins (IL-4 and IL-13) from binding with their cell receptors - lessening inflammation and decreasing symptoms



SIDE EFFECTS

- > Studies show ~30% developed conjunctivitis, keratitis or dry eye during treatment vs placebo
- > The inhibition of IL-13 decrease concentration of epithelial goblet cells, leading to increased inflammation
- > Symptoms: burning, tearing and decrease in vision
- > Most resolve with steroid drops



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DUPIXENT TAKE HOME POINTS

- > Biologic drug approved for atopic dermatitis and asthma
- > Conjunctivitis, keratitis and dry eye are all common side effects
- > Most resolve with surface treatment
- > Can continue Dupixent
- > Do not have to stop Dupixent to get COVID-19 Vaccine

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ISOTRETINOIN (ACCU-TANE)

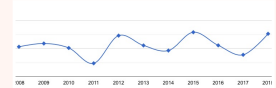
- > Naturally occurring derivative of vitamin A
- > Used in the treatment of moderate to severe cystic acne and psoriasis
- > Treatment is usually 4-6 months
- > Average dose of 40mg/day



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FACTS

- > #280 on US prescription
- > 1,531,101 prescriptions in US (2018)
- > Average age ~22
- > Decreases lipid composition, sebaceous gland size and sebum production in the skin
- > Anti-inflammatory properties



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OCULAR SIDE EFFECTS

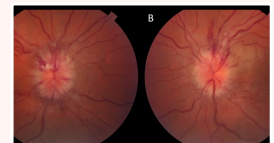
- > Meibomian gland dysfunction
- > Dry eye
- > Ocular surface irritation
- > Decreased contact lens comfort
- > Increased intracranial hypertension
- > All leading to blurred vision



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INCREASED INTRACRANIAL PRESSURE

- > Symptoms
 - > Headaches, blurred vision & tinnitus
- > Signs
 - > Bilateral optic nerve head edema
 - > Vision-threatening if left undetected



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ISOTRETINOIN TAKE HOME POINTS

- Derivative of vitamin A used in the treatment of nodular/cystic acne
- Works on inflammation but decreases oil/lipid production leading to ocular dryness
- Lasik?
- More concerning SE is papilledema

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TAMOXIFEN

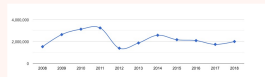
- Selective estrogen receptor modulator (SERM)
- Treatment for hormone receptor positive:
 - Advanced metastatic
 - Early stage



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FACTS

- # 244
- 2,009,016 prescriptions in US (2018)
- Nolvadex or Soltamox (brand)



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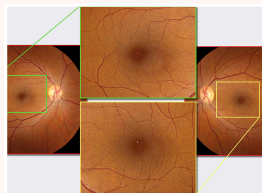
POSITIVE VS NEGATIVE

- Following a biopsy or surgery, cancer cells are tested for certain proteins
- Positive have proteins that are estrogen or progesterone receptors
- Negative are absent these receptors
- Treatment DEPENDS on this classification
- Tamoxifen is only used in the treatment of hormone receptor positive by competing for estrogen receptors in breast or tumor tissue

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RETINAL TOXICITY

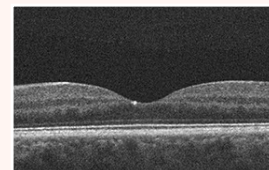
- Presents as yellow-white crystalline deposits
- Typically found in the macular or paramacular region
- Dose related (50-100mg/day) or cumulative dose (>100g)
- Studies suggest 6% developed retinal toxicity on normal dose (20mg/day)



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RETINAL TOXICITY

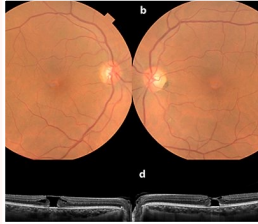
- Crystalline deposits are localized to the NFL and IPL
- Thought to represent axon degradation
- Can lead to decreased vision, decreased color vision, and macular edema
- Cessation of treatment should be considered if vision loss presents (if possible)
- Deposits remain after treatment is complete
- Anti-VEGF has been successful at treating persistent macular edema



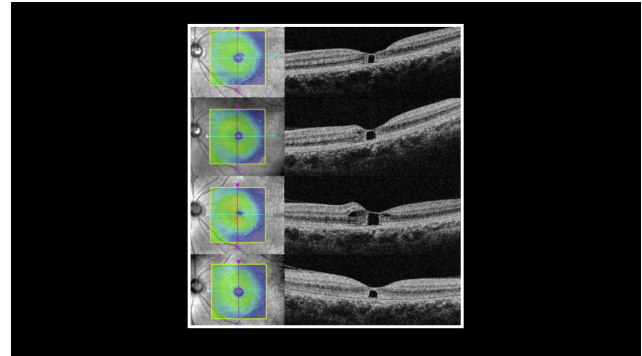
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MACULAR HOLE

- Rare side effect
- Related to low dose extended treatment?
- What's missing?
- Importance of OCT
- Macular hole may present years after completion of treatment



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TAMOXIFEN TAKE HOME POINTS

- Tamoxifen retinopathy is characterized by superficial crystalline deposits
- Vision loss and macular edema may present with increased deposits
- Toxicity is more common at higher doses but can occur at lower daily dosages of 20mg/day if it is administered over a long period of time
- Macular holes may be more frequent with the longer treatment time
- Communicate with oncologist

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TOPIRAMATE (TOPAMAX)

- Sulfa derived anti-seizure medication
- Common treatment option for migraines
- As well as epilepsy, bipolar, post-traumatic stress and obsessive compulsive disorders



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FACTS

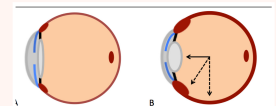
- 8,648,513 Prescriptions in US
- #89
- Qudexy XR & Topamax



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OCULAR SIDE EFFECTS

- Ciliary body effusion
- Myopic shift
- Anterior rotation of the ciliary process
- Angle closure glaucoma



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MYOPIC SHIFT & ANGLE CLOSURE

- > Side effects usually occur within the first 2 week of starting the medication or increasing dosage
- > Unknown incidence rate but it is believed to be low
- > Ultrasound and anterior segment OCT can evaluate anatomic changes
- > Glaucoma medication and cycloplegics
- > Associated ocular changes usually resolve after discontinuing the medication

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PEARLS

- > Get a good history: ROS and medication
- > Communicate
 - > Patient
 - > Comanaging physician



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THANK YOU

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