CONCURRENT MEDICATIONS/DRUG INTERACTIONS/ADVERSE REACTIONS

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What Factors Increase the Risk – Product Specific Variables

- **Amount of Drug Administered**
  - All medications have potential for toxicity if given in excessive amounts.
  - Long term use of therapeutic doses over time increase the risk of toxicity.
- **Nature of the Drug**
  - Ease of absorption into systemic circulation.
  - Ability to penetrate the blood-brain, blood-aqueous, and blood-retinal barriers.
  - Absorption by ocular tissues such as Melanin.
- **Route of Administration**
  - Highest levels of adverse effects have been seen with oral administration (over inhaled, intranasal, etc.)

What Factors Increase the Risk – Patient Specific Risks

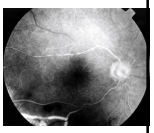
- **Pathophysiologic Variables**
  - Liver and Kidney Function
- **Age and Sex**
  - More common in the very young or the very old.
  - More adverse drug reactions are reported in women than in men.
- **History of Allergy to Drugs**
  - Adverse reactions are always more likely in a patient who has had a history of previous trouble.
- **Individual Idiosyncrasy**
  - Factors such as enzymatic differences, muscle mass, etc.
  - Altered tissue responsiveness to a medication is likely hereditary.

What Factors Increase the Risk?

- Drug Interactions
  - Incidence of ADR's is directly related to the number of drugs administered.
  - Always important to specifically ask about social habits, supplements, etc.

Amikacin: Aminoglycoside Antibiotic

- This systemically administered aminoglycoside is primarily used for Gram-negative infections.
  - However, it is the injection of this medication for the treatment of endophthalmitis that is likely to cause ocular problems
    - retinal infarcts have been reported with this agent, with perifoveal capillaries becoming occluded
  - It is still a recommended part of the treatment for endophthalmitis but only one injection will be given during treatment for fear of toxicity



Fluorescein angiogram at 31 seconds showing delayed retinal perfusion with attenuated arterioles and incomplete venous filling.
https://bjo.bmj.com/content/83/10/1194.11

Penicillin Antibiotics

- Includes amoxicillin, ampicillin, nafcillin
- Semisynthetic penicillins are primarily effective against staphylococci, streptococci, pneumococci and various other Gram positive and Gram-negative bacteria.
- There are surprisingly few ocular side effects to these medications other than potential allergic related dermatologic symptoms
- However, ampicillin and other semisynthetic penicillins may unmask or aggravate ocular signs of myasthenia gravis.

Chloramphenicol: Systemic

- particularly effective against Salmonella typhi, H. influenzae meningitis, rickettsia and the lymphogranuloma-psittacosis group and is useful in the management of cystic fibrosis.
- Ocular side effects from systemic chloramphenicol administration are uncommon in adults but may occur more frequently in children, especially if the total dose exceeds 100 g or if therapy lasts more than six weeks.
  - Optic neuritis with secondary optic atrophy is the most serious side effect.
    - These are most often of acute onset and bilateral; and optic neuritis is much more frequent than retrobulbar neuritis.
    - First sign may be sudden visual loss with cecocentral scotoma.

Chloramphenicol: Topical

- There are almost 70 cases of blood dyscrasia or aplastic anemia following topical ocular chloramphenicol that have been reported in the literature
  - the risk of developing pancytopenia or aplastic anemia after oral chloramphenicol treatment is 13 times greater than the risk of idiopathic aplastic anemia in the general population
  - It is likely that certain individuals are "genetically" more susceptible and that this is likely a rare occurrence

Ciprofloxacin

- This fluoroquinolone antibacterial agent is used primarily against most Gram-negative aerobic bacteria and many Grampositive aerobic bacteria.
- Ciprofloxacin causes relatively few and minor ocular side effects from systemic use.
- However, there are conflicting reports of rhegmatogenous retinal detachments associated with systemic use. The original reports were in 2012 but several reports since that time have not found an increased association. This issue remains unsettled at this point.

Tetracyclines

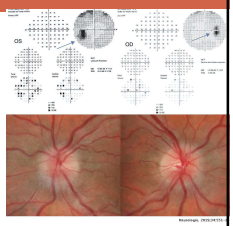
- Drug of choice for Rocky Mountain Spotted Fever, Cholera, Lyme disease, mycoplasma pneumonia, and chlamydial infections.
- Side effects include gastric discomfort, effects on calcified tissues, vestibular problems.
- **Should not be used in children under the age of 8 due to discoloration of teeth.**

Tetracyclines

- This group includes:
  - Tetracycline (250mg - 500 mg cap BID-QID) needs to be taken 1 hour before or 2 hours after a meal.
  - Minocycline (100 mg cap BID)
  - Doxycycline (20mg - 100 mg cap or tab BID)
- **Rules of Thumb with Doxy:**
  - **Do not take before lying down (>2 hours before)**
  - **Do not take with calcium and avoid antacids**
  - **Do not take with dairy**
  - **Do take with food**
  - **Do take sun precautions**

Tetracyclines: Ocular SE

- Systemic use of this group rarely causes serious SE.
- The most commonly reported SE is pseudotumor cerebri (IIH) associated primarily with tetracycline and minocycline. Minocycline has the ability to cross the blood/brain barrier.
  - Increased intracranial pressure is not dose dependent and may occur as early as 4 hours after first taking the drug or after many years of drug use.
- All tetracycline agents are photosensitizers.
  - Doxycycline may be the greatest photosensitizer in this group, with minocycline being the least.



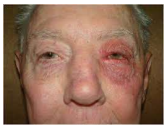
Minocycline-induced intracranial hypertension in a patient with a levonorgestrel intrauterine device

Gentamicin

- Topical ocular gentamicin may cause significant local side effects, the most common being a superficial punctate keratitis.
  - Chronic use can also cause keratinization of the lid margin and blepharitis
- Intraocular gentamicin has caused severe retinal ischemia, rubeosis, iritis, neovascular glaucoma, optic atrophy and blindness
  - Intraocular Gentamicin used to be for endophthalmitis treatment but has since been replaced with Amikacin

Neomycin

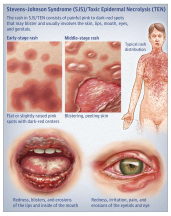
- These drugs are not used parenterally because of nephro- and ototoxicity.
- Topical ocular application of neomycin has been reported to cause allergic conjunctival or lid reactions in 4% of patients using this drug.
  - if the patient has been previously exposed to neomycin, there is a significantly higher chance of an allergic response



https://joii-journal.springeropen.com/articles/10.1186/s12348-017-0133-4

Sulfa Based Medications

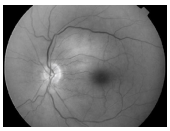
- While there are numerous reported ocular side effects from systemic sulfa medication, most are rare and reversible.
- Probably the most common ocular side effect seen in patients on systemic therapy is myopia.
  - This is transient, with or without induced astigmatism, usually bilateral and may exceed several diopters.
- anaphylactic reactions, Stevens-Johnson syndrome and exfoliative dermatitis have all been reported, although rarely from topical ocular administration of sulfa preparations



Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis JAMA Dermatol. 2017;153(12):1344. doi:10.1001/jamadermatol.2017.3957

Quinine

- Originally, quinine was prescribed to combat malaria. Currently it is effective in the management of nocturnal leg cramps, myotonia congenita, and resistant P. falciparum. It is also used in attempted abortions. Ophthalmologically it is useful in the treatment of eyelid myokymia.
- Quinine seldom causes significant ocular side effects at normal dosage
  - The recommended daily dose is less than 2 g. Signs of systemic toxicity occur with doses greater than 4 g, and the fatal oral dose is 8 g.
- In large overdose situations retinal arteriolar constriction, venous congestion, pronounced retinal and papillary edema and permanent loss of the peripheral vision field occur. Complete, irreversible loss of vision may occur, but most patients have some return of vision



Left eye of case of ocular quinine toxicity 40 h after overdose demonstrating marked arteriolar attenuation and retinal pallor.

Lamotrigine (Lamictal^{R})

- This is an antiepileptic drug believed to suppress seizures by inhibiting the release of excitatory neurotransmitters.
- In placebo-controlled clinical trials, two of its five most common side effects were ocular
  - 22% of patients having diplopia and 15% having blurred vision compared to controls
  - less than 5% had nystagmus
  - Visual hallucinations have been reported

Antimalarials

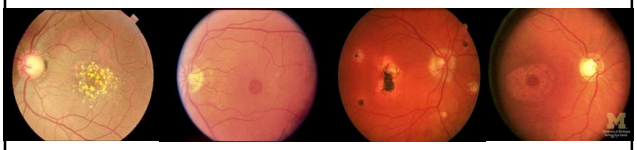
- hydroxychloroquine or Plaquenil
- Common medication used by patient's who are suffering from rheumatoid arthritis
- usual dose is 200-400 mg/d @night with onset of action after a period of 2-4 months
- Primarily used to help manage pain and increase mobility, has a mild affect on slowing down joint destruction

Antimalarial Ocular Complications

- affinity for pigmented structures such as iris, choroid and RPE
- Toxic affect on the RPE and photoreceptors leading to rod and cone loss.
- slow excretion rate out of body with toxicity and functional loss continuing to occur despite drug discontinuation.

Question

Which of the following depicts a retina undergoing hydroxychloroquine toxicity?



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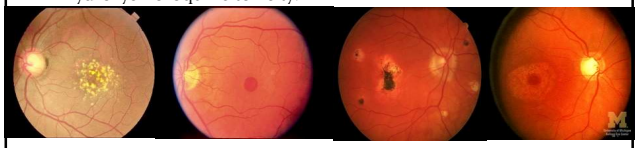
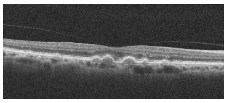
Question

Which of the following depicts a retina undergoing hydroxychloroquine toxicity?



ARMD | Macular Hole | OHS | Bull's Eye Maculopathy

Which of the following represents a patient undergoing plaquenil toxicity?



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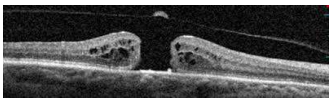

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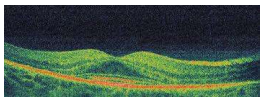

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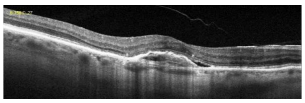

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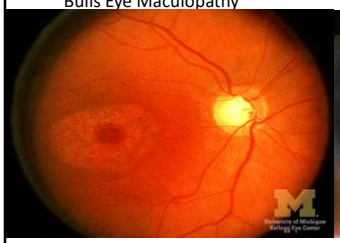
Antimalarial Ocular Complications

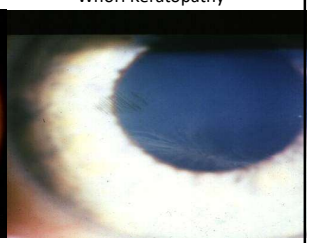
- Toxicity can lead to whorl keratopathy, "bulls eye" maculopathy, retinal vessel attenuation, and optic disc pallor.
- Early stages of maculopathy are seen as mild stippling or mottling and reversible loss of foveal light reflex
- "Classic" maculopathy is in form of a "bulls eye" and is seen in later stages of toxicity
  - this is an irreversible damage to the retina despite discontinuation of medication

Antimalarials

Bulls Eye Maculopathy



Whorl Keratopathy



Fabry Disease

- alpha-galactosidase-A deficiency.
  - insufficient breakdown of lipids, which build up to harmful levels in the eyes, kidneys, autonomic nervous system, and cardiovascular system.
- Fabry disease is one of several lipid storage disorders and the only X-linked lipid storage disease.
- Lipid storage may lead to impaired arterial circulation and increased risk of heart attack or stroke.
  - The heart may also become enlarged and the kidneys may become progressively involved.
- Other signs include decreased sweating, fever, and gastrointestinal difficulties.

Revised Recommendations on Screening for Retinopathy

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

Revised Recommendations on Screening for Retinopathy

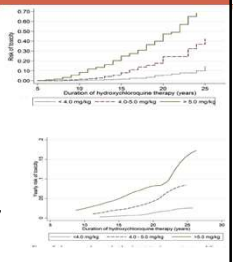
- Amsler grid testing removed as an acceptable screening technique
  - NOT equivalent to threshold VF testing
- Strongly advised that 10-2 VF screening be supplemented with sensitive objective tests such as:
  - Multifocal ERG
  - Spectral domain OCT
  - Fundus autofluorescence

"New" New Recommendations

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

2016 Recommendations

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

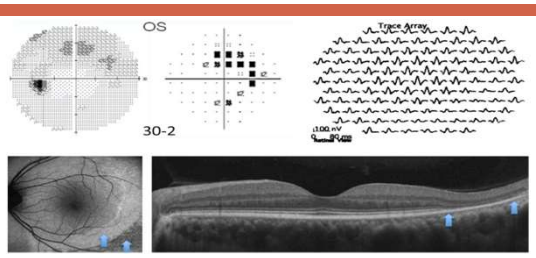


2016 Recommendations

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

2016 Recommendations

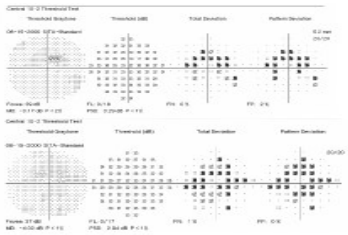
- primary screening tests are automated visual fields plus spectral-domain optical coherence tomography (SD OCT)
- most patients of Asian descent will show initial damage in a more peripheral extramacular distribution near the arcades (require a 24-2 as opposed to 10-2 and OCT scans need to be analyzed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



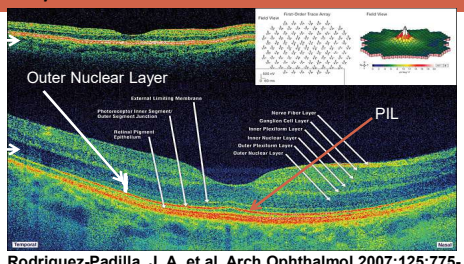
Revised Recommendations on Screening for Retinopathy

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

Paracentral Scotomas



Normal Retina: VF/OCT/ERG



Rodriguez-Padilla, J. A. et al. Arch Ophthalmol 2007;125:775-780.

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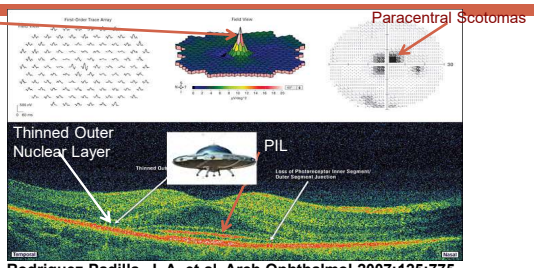
PIL=PR Integrity Line

Mild Maculopathy



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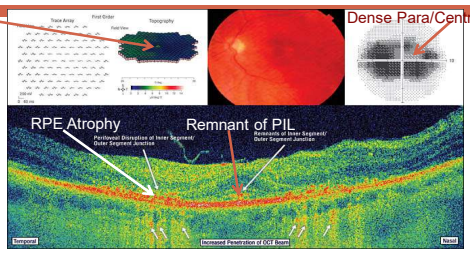
Bull's Eye Maculopathy



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Major Risk Factors

Table 1. Major Risk Factors for Toxic Retinopathy

Daily dosage	
HCQ	>5.0 mg/kg real weight
CQ	>2.3 mg/kg real weight
Duration of use	>5 Yrs, assuming no other risk factors
Renal disease	Subnormal glomerular filtration rate
Concomitant drugs	Tamoxifen use
Macular disease	May affect screening and susceptibility to HCQ/CQ

CQ = chloroquine; HCQ = hydroxychloroquine.

Screening Recommendations

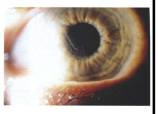
Table 2. Screening Frequency

Baseline Screening	
Fundus examination	within first year of use
Add visual fields and SD OCT	if maculopathy is present
Annual Screening	
Begin after 5 yrs of use	
Sooner in the presence of	major risk factors

SD OCT = spectral-domain optical coherence tomography.

Ibuprofen

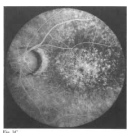
- The adverse ocular event most commonly associated with this drug is transient blurred vision.
- refractive error changes, diplopia, photophobia, dry eyes and decrease in color vision appear to be well documented.
- A typical vortex keratopathy with deposition limited to the corneal epithelium has been described
  - Once the drug is stopped this resolves within weeks.



Vortex keratopathy associated with ibuprofen therapy https://www.semanticscholar.org/paper/Vortex-keratopathy-associated-with-ibuprofen-Fitt-Dayan/2c42bef553288ad269b40a81aaf11ecc9897cb1a

Indomethacin (NSAID)

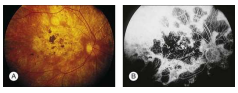
- Oral NSAIDs are considered first-line therapy for scleritis for their ease of use, cost, and relatively mild side effect profile
  - Commonly used is indomethacin 75 mg TID
- Its most serious potential side effect of indomethacin use is retinal pigmentary retinopathy, with macular atrophy and a waxy disk.
  - This is associated with depressed ERG and constricted visual fields.



Fluorescein angiography demonstrating macular pigment mottling https://bjo.bmj.com/content/bjophthalmol/72/6/434.full.pdf

Phenothiazine (e.g. Chlorpromazine)

- These phenothiazines are used in the treatment of depressive, involutional, senile or organic psychoses and various forms of schizophrenia. Some of the phenothiazines are also used as adjuncts to anesthesia, antiemetics and in the treatment of tetanus.
  - Their overall rate of side effects is estimated at only 3%. However, if patients are on phenothiazine therapy for a number of years, a 30% rate of ocular side effects has been reported. If therapy continues over 10 years, the rate of ocular side effects increases to nearly 100%

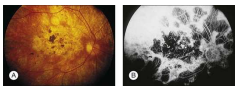


Intermediate thioridazine toxicity. Photograph (A) and fluorescein angiogram (B) show central and peripheral nummular pigmentary changes with corresponding atrophy of the choriocapillaris.

Typical chlorpromazine-induced anterior stellate lens opacities. These findings are generally not felt to be of visual significance.

Phenothiazine (e.g. Chlorpromazine)

- Blurred vision, dyschromatopsia (reddish or brownish discoloration of vision), and nyctalopia characterize acute toxicity with thioridazine.
- Retinal toxicity from thioridazine is dependent more on the total daily dose than on the cumulative amount of drug received.



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Alcohol

- Acute intoxication may result in nystagmus, a finding used by law enforcement personnel to screen for inebriated motor-vehicle operators.
- Pupil abnormalities, ptosis and strabismus are also well-known effects of inebriation.
- When chronic, alcoholism leads to malnutrition in severe cases, with resultant xerophthalmia or toxic amblyopia.
- The ocular side effects of retrobulbar alcohol injections are many, and thus the use of alcohol in cases of blind and painful eyes should be considered if evisceration or enucleation is not possible.

Cannabinoids (Marijuana)

- The cannabinols found in marijuana can lower intraocular pressure by an average of 25%, but the effect only lasts 3–4 hours.
- There is significant variation in the individual response to these agents, as well as diminished response with time.
- Most patients on this agent for glaucoma control cannot use it for prolonged periods due to lack of glaucoma control

https://www.aao.org/eye-health/tips-prevention/marijuana-glaucoma-infographic

Cannabinoids (Marijuana)

- alterations of depth perception, sensorial disconnection when talking with people, intermittent light phenomena, strobelike effects, bright spots flickering randomly in high frequency and alteration of the sensory perception of one's external environment have also been reported by individuals smoking marijuana. These changes are short term and reversible
- Cannabinoids bind to receptors on blood vessels resulting in vasodilation which results in patients eyes being red.

https://www.boerejongens.com/why-your-eyes-turn-red-after-smoking-cannabis/

Allopurinol

- This potent xanthine oxidase inhibitor is primarily used in the treatment of chronic hyperuricemia (gout).
- patients taking a cumulative dose of more than 400 g of allopurinol for longer than three years were associated with a twofold increased risk for cataract surgery
  - the gout medications as second only to steroids as a major risk factor in cataractogenesis
  - anterior and posterior capsular changes with anterior subcapsular vacuoles are noted

Methotrexate

- This folic acid antagonist is effective in the systemic treatment of certain neoplastic diseases, rheumatoid arthritis, psoriasis and uveitis. Intravitreal methotrexate is used in the management of intraocular lymphomas, both primary CNS lymphomas and non-Hodgkin lymphomas. It is also used in the management of uveitis and advanced diabetic retinopathy.
- Methotrexate-related ocular toxicities consist of:
  - peri-orbital edema,
  - ocular pain,
  - blurred vision,
  - photophobia,
  - conjunctivitis,
  - blepharitis,
  - decreased reflex tear secretion and
  - nonarteritic ischemic optic neuropathy

periorbital edema, blepharitis, conjunctival hyperemia, increased lacrimation or photophobia may occur in about 25% of patients on methotrexate

Methotrexate

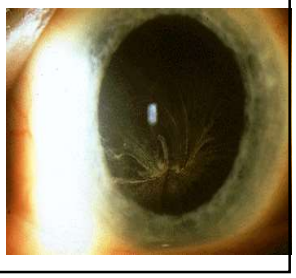
- The optic neuropathy has been linked to folate deficiency, either nutritional or genetic.
- Folate supplementation when co-administered with methotrexate, minimizes its adverse effects and may therefore prevent the development of optic neuropathy.
- when this condition is recognized, the nerve damage can be reversed if methotrexate is stopped and appropriate folate supplementation is administered promptly
- Every 6 months repeat visual acuity, screening visual field, Amsler grid, funduscopy. Central threshold visual field for suspected optic neuropathy. Repeat color vision and fundus photography periodically, as indicated. Annual comprehensive eye examination.

Antianginal: Amiodarone

- Brand names: Cordarone, Pacerone
- Antiarrhythmic agent used in the treatment of atrial and ventricular tachcardias.
- Systemic adverse SE include: interstitial pulmonary fibrosis, GI intolerance, tremor, ataxia, dizziness, liver toxicity, photosensitivity, muscle weakness etc.
- After long-term use, more than 50% of Px have to discontinue use due to toxic responses.

Antianginal: Amiodarone Ocular SE

- corneal microdeposits occur in nearly all Px who are using the drug long-term
  - epithelial whorl-like pattern similar as seen in chloroquine treatment
  - horizontal, irregular branching line near the junction of the mid to outer 1/3rd of cornea



Antianginal: Amiodarone Ocular SE

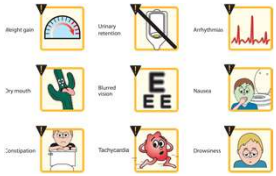
- generally visible keratopathy develops in most Px within 6 weeks after drug initiation and reach peak within 3-6 months
- minimal deposition in Px on a dose of 100-200 mg/day though 400 mg or more will have all Px show deposit
- will see regression in 3-7 months after discontinuation
- other complications include:
  - decreased VA,
  - color vision defects,
  - photosensitivity,
  - dry eyes,
  - decreased corneal sensation,
  - optic neuropathy and
  - IIH

Antidepressants

- Includes:
  - Tricyclic antidepressant (TCA): amitriptyline, nortriptyline (Elavil, Levate) (inexpensive medication)
  - Selective serotonin re-uptake inhibitors (SSRI): fluoextine (Prozac), paroxetine (Paxil), sertraline (Zoloft) (all of these are very expensive medications!)
  - monoamine oxidase (MAO): isocarboxazid (Marplan)

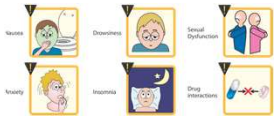
Antidepressants- TCA's

- These tertiary amine tricyclic antidepressants are used in the treatment of psychoneurotic anxiety or depressive reactions.
  - Block norepinephrine and serotonin reuptake into the presynaptic neuron
- Adverse SE's: urinary retention, constipation, epilepsy, dry mouth, sedation, orthostatic hypotension
- Ocular SE's: blurred vision, mydriasis, and increased risk of glaucoma (narrow angle, angle closure)



Antidepressants-SSRI

- Block the reuptake of serotonin, leading to increased concentrations of the neurotransmitter in the synaptic cleft
- Adverse SE: GI upset, weakness, sexual dysfunction, sleep disturbances, and potential drug interactions
- Ocular SE: mydriasis, decreased accommodation (blurred vision), and infrequently conjunctivitis, photophobia, diplopia, eye pain

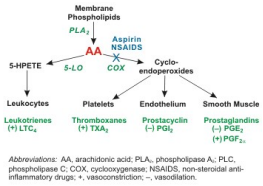


Antidepressants: Summary of Ocular Side Effects

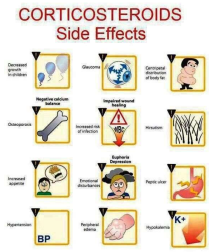
- most of the side effects are transient, reversible, and cause little clinical significance
- most common side effects is blurring of vision which is generally mild and transient (improves with sustained use of medication)
- mydriasis can be a concern in patients with NAG or narrow angles
- diplopia and nystagmus have been reported though generally in patients who are currently using other agents such as lithium or diazepam
- increased symptoms of dry eye

Corticosteroids (Glucocorticoids)

- Influence tissue regeneration and repair
  - Reduce collagen deposition, thus <u>reduce scarring</u>
  - Decrease fibroblast proliferation
  - Decrease vascular permeability



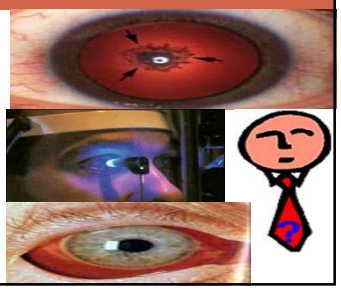
Corticosteroids- Systemic SE



- Systemic administrations can result in:
  - Osteoporosis
  - Increased appetite
  - Emotional disturbances
  - Hypertension
  - Edema
  - Peptic ulcers
  - Increased risk of infection

Corticosteroids- Ocular SE

- Systemic use can result in:
  - PSC cataracts
  - Increased IOP
  - Delayed wound healing
  - Decreased resistance to infection
  - Visual hallucinations
  - Subconjunctival/retinal hemes and edema
  - Papilledema



Corticosteroids: Ocular SE

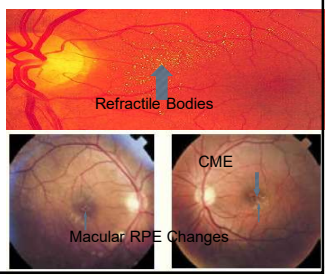
- Race is important as steroid induced glaucoma is more frequent in whites than blacks, and depigmentation from SC injection is more frequent in blacks.
- Steroid IOP responders tend to have more field loss than non-responders, more common in POAG and 1st degree relatives of POAG patients, higher risk in younger children and typically presents 4-6 weeks after initiation of steroid.
- Steroids affect all ocular structures resulting in development of steroid induced glaucoma, PSC cataracts, enhanced HSK infections, decreased wound healing, band keratopathy, etc.

Estrogen Receptor Antagonist-Tamoxifen

- Tamoxifen is used in the treatment of breast cancer (normal breast tissue stimulated to grow by estrogens, so estrogen antagonists can result in tumor regression)
- The most common adverse affects include: hot flashes, nausea, and vomiting. Menstrual irregularities and vaginal bleeding can also occur.

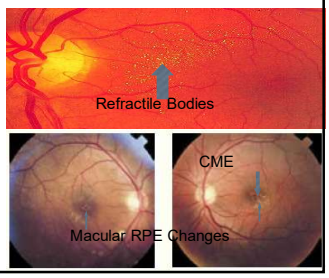
Tamoxifen- Ocular SE

- Significant visual loss can occur with tamoxifen.
  - Stopping Tx usually prevents further deterioration but may not result in visual recovery.
- Tamoxifen retinopathy characterized by presence of refractile bodies (due to axonal death).



Tamoxifen- Ocular SE

- Additional findings may include CME, macular and peripheral retinal RPE changes, parafoveal hemes and subepithelial corneal deposits.
- Patients also taking Plaquenil have to be monitored for toxicity.

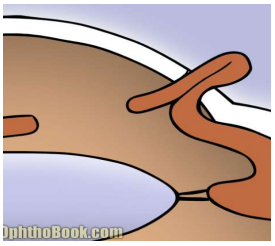


Antihistamines: Ocular SE

- Systemic use of the medications have a weak atropine action that accounts for the pupillary changes. With chronic use, anisocoria, decreased accommodation, and blurred vision can also occur.
- There has also been evidence to demonstrate a decrease in tear production making Px symptomatic for dry eyes and CL intolerance.

Tamsulosin (Flomax)

- Used to treat prostate enlargement and improve urinary flow in men (urologists are treating women with this drug).
- The well-known syndrome, intraoperative floppy iris syndrome, used to occur only in men but now has to be a concern for women who may also be taking the medication.
- Even if the drug is discontinued, the patient is at a lifetime risk of more complicated cataract surgery.

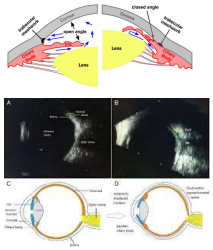


Topiramate (Topamax)

- Used for the treatment of:
  - seizures,
  - epilepsy,
  - migraine prophylaxis,
  - bipolar and post-traumatic stress disorders, and neuralgias.
- used off-label to control binging and purging, and to promote weight loss in people with eating disorders

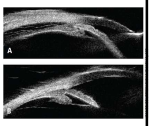
Topiramate Ocular SE

- include:
  - acute angle closure glaucoma,
  - ocular pain,
  - headache,
  - hyperemia,
  - mydriasis,
  - uveitis,
  - visual field defects,
  - acute onset myopia (up to 8.75 D!!!!)
  - suprachoroidal effusions,
  - blepharospasm,
  - retinal hemorrhage and
  - scleritis



Question? Do psychiatry doctors know the ocular side effects of topiramate when they prescribe it?

- **Topiramate-induced angle closure: Don't assume prescribers know its ocular side effects. By Cindi Yim, BA and Nisha Chadha, MD** July 1, 2017
- A total of 10 psychiatry and eight neurology residents participated in the study. Among psychiatry residents, nine out of 10 prescribed topiramate at least yearly, most commonly for depression and bipolar disorder. Five out of eight neurology residents prescribed topiramate monthly, mostly for migraine and epilepsy.
- Pretest evaluation indicated none of the psychiatry residents were familiar with the ocular side effects of topiramate and only three neurology residents were aware of this side effect. On pretest, at least half the residents did not know when TiACG most commonly occurs following initiation of topiramate, or at which dosage TiACG frequently occurs



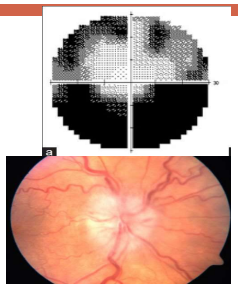
A. UBM showing shallow anterior chamber, anterior rotation of ciliary body with closed angle, and suprachoroidal effusion in the same patient with acute TiACG. B. One week after drug discontinuation, UBM with deep anterior chamber, open angle and resolution of suprachoroidal effusion.

Sildenafil citrate (Viagra) and tadalafil (Cialis)

- Prescribed for men with erectile dysfunction. These drugs divert blood flow away from the head
- They cause two problems:
  - can cause blue vision, because they interfere with neurotransmission within the retina. That is fortunately not a permanent side effect.

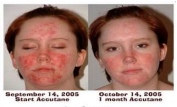
Sildenafil citrate (Viagra) and tadalafil (Cialis)

- The other possible side effect is ischemic optic neuropathy.
- The evidence that there is a cause-and-effect relationship is tenuous.



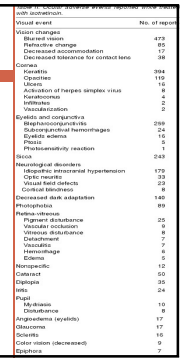
Retinoids: Isotretinoin

- Retinoids are analogues of Vitamin A used because of their ability to damage rapidly dividing cells.
  - Isotretinoin (Sotret, Claravis, Amnesteem, Generics, Formerly known as Accutane) is the most commonly prescribed Retinoid used in the control of severe acne or various keratinizing dermatoses.
  - It was originally developed as a chemotherapy agent.
- MOA: Temporarily suppresses the sebaceous gland activity, altering the surface lipid composition on the skin, and inhibiting keratinization.



Isotretinoin

- Very frequent cause of ocular side effects.
- Complications generally begin within 4 weeks of starting the medication, and will resolve approximately 4 weeks following discontinuation.
- Symptoms are dose related.



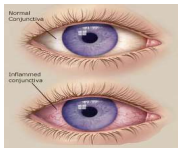
Visual event	No. of reports
Vision changes	
Blurred vision	473
Refractive change	65
Decreased accommodation	17
Decreased tolerance for contact lens	38
Cornea	
Keratitis	394
Opacities	110
Ulcers	16
Activation of herpes simplex virus	8
Keratoconus	4
Infiltrates	2
Vascularization	2
Eyelids and conjunctiva	
Blepharoconjunctivitis	269
Conjunctival hemorrhages	34
Eyelids edema	16
Ptosis	5
Photosensitivity reaction	1
Sicca	243
Neurological disorders	
Idiopathic intracranial hypertension	179
Optic neuritis	33
Visual field defects	23
Cortical blindness	8
Decreased dark adaptation	140
Photophobia	89
Retina-vitreous	
Pigment disturbance	25
Vascular occlusion	9
Vitreous disturbance	8
Detachment	7
Vasculitis	7
Hemorrhage	6
Edema	5
Nonspecific	12
Cataract	10
Diplopia	35
Iritis	24
Pupil	
Mydriasis	10
Disturbance	8
Angioedema (eyelids)	17
Glaucoma	17
Scleritis	16
Color vision (decreased)	9
Epiphora	7

Isotretinoin

- Major Ocular Side Effect: Alteration of Meibomian Gland Secretions
  - Gland atrophy frequently develops which is beneficial for the treatment of acne, but harmful for the ocular surface.
  - Decreased Volume with Increased Thickness
  - Results in:
    - High levels of tear evaporation
    - Increased Tear Film Osmolarity
    - Ocular Discomfort
- Most Common Ocular Finding in 20-50%:
  - Blepharoconjunctivitis

Isotretinoin and Blepharoconjunctivitis

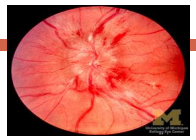
- Severity can vary, but may lead to corneal involvement and blurry vision.
- Nearly all patients will experience difficulty with Contact Lenses.
  - Need to reduce wearing time.
- Treatment is Artificial Tear Supplementation:
  - Which type would you recommend?

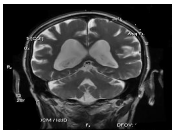


Isotretinoin

- Most commonly affects the anterior segment, but also known as a "certain" cause of nyctalopia.
  - It is believed that the drug becomes incorporated into the rod photoreceptors, thus causing dark adaptation to become reduced.
- Recommend following patients with VF testing, dark adaptometry, and ERG.

Retinoids/Isotretinoin

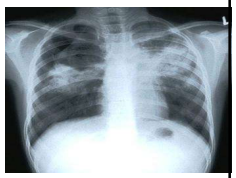




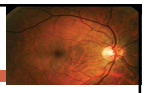
- Intracranial HTN (Pseudotumor Cerebri)
  - Can be caused by Vitamin A itself or the derivatives such as Isotretinoin.
  - Retinoids are one of the two main categories of drugs that result in increased intracranial pressure.
    - Second major drug class is the tetracycline derivatives, especially minocycline.
    - Risk increases if tetracyclines are used in combination with retinoids.

Ethambutol

- Bacteriostatic, antimycobacterial medication used in the treatment of tuberculosis.
- Recommended to be given in combination with first line treatment Isoniazid, Rifampin, and Pyridoxine until drug susceptibility has been determined.



Ethambutol



- Primary Ocular Manifestation: Retrobulbar Neuritis
  - Two forms resulting from toxicity:
    - Most Common: Central with loss of VA and color vision
    - Less Common: Peripherally with contraction of VF
- Also, can have retinal findings such as ONH swelling, hemes, and macular edema = RARE.
- MOA: Damage to the amacrine and bipolar cells (Not fully understood)
- Earliest finding is often loss of contrast sensitivity, followed by color vision.
  - Isoniazid is also known to cause optic neuritis, but in much less frequent numbers.

Ethambutol

- Deterioration will continue even if ethambutol is discontinued.
- Largely affected by dosage:
  - Recommended levels should not exceed 15 mg/kg daily.
    - Can tolerate higher levels for no longer than 2 months to prevent optic nerve damage.