Course description: This course presents current information about common oral prescription medications and their ocular complications and manifestations. The use of case examples and series culled from the literature highlight and reinforce the instructional objectives.

Learning Objectives/Outcomes: At the conclusion of this lecture, the attendee will be able to:

- Recognize the ocular and non-ocular complications associated with oral amiodarone.
- Recognize the ocular and non-ocular complications associated with oral hydrochloroquine.
- Recognize the ocular and non-ocular complications associated with oral benztropine.
- Recognize the ocular and non-ocular complications associated with oral sildenafil.
- Recognize the ocular and non-ocular complications associated with oral tamsulosin.
- Recognize the ocular and non-ocular complications associated with oral topiramate.

Common Drugs with Ocular Complications
- Alendronate
- Amiodarone
- Benztropine
- Diphenhydramine
- Hydroxychloroquine
- Sildenafil
- Tamsulosin
- Tetracycline
- Topiramate
- Warfarin
• **AMIODARONE**
  – Trade: Cordarone®, Pacerone®, numerous generics
  – Drug class: anti-arrhythmic agent (Class III)
  – Indication: for life-threatening cardiac arrhythmias
    ▪ hemodynamically unstable ventricular tachycardia
    ▪ shock-resistant, recurrent ventricular fibrillation
  – Typical dosage: 200-400 mg/day
  – Ocular Complications
    ▪ Corneal Verticillata
    ▪ i.e. “vortex keratopathy”, “hurricane keratopathy”
      • Generally asymptomatic
      • Rarely may cause haloes or slight decrease in VA
      • Seen in ~90% of patients on amiodarone >6 mos, especially those taking >400 mg/day.
      • No management required; Self-limiting & reversible
      • WARNING: Vortex keratopathy can also be associated with FABRY’S DISEASE
        ♦ Hereditary enzyme deficiency
        ♦ α-Galactosidase A
        ♦ located on the X-chromosome
        ♦ Leads to intracellular accumulation of neutral glycosphingolipids in various organs, e.g. skin, eyes, nervous tissue, kidney and heart
        ♦ Findings: angiookeratomas, pain in the hands & feet, lesions of the mouth and multiple ocular signs
      ▪ Pseudotumor cerebri or Idiopathic intracranial hypertension
  – Other Manifestations
    ▪ “Blue skin”, “blue man syndrome”
    ▪ Long-term use; more commonly seen with lighter skin tones

• **TOPIRAMATE**
  – Trade: Topamax®
  – Drug class: anticonvulsant
  – Indication(s):
    ▪ Primary: treatment of epilepsy and other seizure disorders
    ▪ Secondary: prevention of migraine headaches in adults
    ▪ Off-label: treatment of bipolar disorder, obsessive-compulsive disorder, alcoholism, smoking cessation, cocaine dependence, eating disorders, and neuropathic pain.
  – Typical dosage: (adults) 100 – 400 mg daily
– Ocular Complications
  • Acute myopic shift
  • Acute angle-closure glaucoma
  • Pathological Mechanism
    • Appears to be a sulfa-allergic response
    • Swelling/congestion and forward rotation of the ciliary body
    • Ciliochoroidal effusion with forward shifting of lens-iris diaphragm
    • Induces extreme anterior chamber shallowing and angle-closure
    • Congestion of ciliary body allows lens zonules to go slack
      • Results in lens thickening; this, in addition to the forward rotation of the lens-iris diaphragm induces a myopic shift
      • Lens thickening generally does not contribute to angle closure
  • Cyclocongestive glaucoma
    • Normal open angle
    • Cyclocongestive angle closure
– Other Manifestations
  • Dysgeusia (taste perversion)
  • Parasthesias (numbness & tingling)
  • Fatigue
  • Difficulty with concentration, attention and memory
  • Weight loss

• TAMSULOSIN
  – Trade: Flomax
  – Drug class: alpha-adrenergic antagonist
  – Indication(s):
    • Primary: signs and symptoms of benign prostatic hyperplasia (BPH)
    • Off label: urinary retention in women and those with multiple sclerosis; facilitated passage of kidney stones
  – Typical dosage: 0.4 mg once daily
  – Mechanism: works by relaxing smooth muscle at the distal portion of the urethra
  – Ocular Complications
    • IFIS - Intra-operative Floppy Iris Syndrome
    • Clinical manifestations:
      • Poor preoperative dilation
      • Iris billowing and prolapse
      • Progressive intraoperative miosis
Management:
- Identify patients at risk and discontinue medication if possible
- Use of stronger dilating agents, e.g. epinephrine and/or atropine
- Use of Malyugin or Morcher ring

Other Manifestations
- Sulfa Allergy
- Pustular, erythematous skin eruptions with urticaria
- Can affect any part of the body
- May progress to Stevens-Johnson syndrome in severe cases
- Fever, chills, body aches, or flu symptoms
- Light headedness, dizziness, weakness, drowsiness
- Headache
- Nausea, diarrhea
- Runny nose
- Diminished ejaculate
- Decreased sex drive, which leads us to...

SILDENAFIL
- Trade: Viagra®
- Similar medications: tadalafil (Cialis®), vardenafil (Levitra®, Staxyn®)
- Drug class: phosphodiesterase enzyme inhibitor (PDEI)
- Originally studied as an anti-angina medication!
- Indication(s):
  - Primary: treatment of erectile dysfunction
  - Secondary: symptoms of benign prostatic hyperplasia
  - Off-label: pulmonary hypertension, Raynaud’s phenomenon (Revatio®)
- Typical dosage: 50 mg (not to exceed 100 mg)

Mechanism of action (warning: GRAPHIC)
- Ocular Manifestations
  - Cyanopsia (“blue vision”)
    - By affecting PDE6 in the retina, sildenafil can lead to altered color vision perception (usually a blue or green “tinge” to vision).
    - 4 out of 5 men without vascular risk factors reported this problem after taking sildenafil.
  - Nonarteritic anterior ischemic optic neuropathy
Other Manifestations
  - Headache
  - Stuffy nose
  - Facial flushing

Other Manifestations

HYDROXYCHLOROQUINE
  - Trade: Plaquenil®, numerous generic
  - Drug class: aminoquinoline
    - anti-malarial drug
    - DMARD
  - Indication(s):
    - treatment of malaria
    - treatment of discoid and systemic lupus erythematosus, and rheumatoid arthritis
  - Typical dosage: 400-800 mg/day (malaria); 200-400 mg/day (lupus & RA)
  - Ocular Manifestations
    - Corneal deposits
    - “Bulls-eye” maculopathy
      - 66 visual fields from patients with HCQ retinal toxicity.
      - HVF changes preceded fundus changes in 60% of patients.
      - Abnormalities were more obvious on pattern deviation than the gray scale.
      - Authors recommend white stimulus 10-2 fields (vs. red-stimulus), as per AAO guidelines.
    - OCT: The New Standard
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    - Focal thinning and loss of parafoveal PIL (photoreceptor integrity line)
  - ERG: The Emerging Standard
  - Risk factors for maculopathy
    - Maintenance dose greater than 6.5 mg/kg/d
    - 120 lb. woman: >400 mg/d
    - 200 lb. man: >600 mg/d
    - Duration of treatment: >10 years
- Evidence of renal insufficiency or hepatic disease
- Obesity
- Advanced age
- Presence of macular degeneration or dystrophy

- Other Manifestations
  - Vertigo, tinnitus, headache
  - Skin rashes and dermatitis
  - GI disturbances
  - Muscle weakness

- BENZTROPINE
  - Trade: Cogentin® (discontinued in US); numerous generics
  - Drug class: anti-parkinsonian medication
  - Possesses both anticholinergic and antihistaminic effects
  - Indication(s):
    - As an adjunct in the therapy of all forms of Parkinsonism
    - For control of medication-induced movement disorders due to antipsychotic agents, e.g. chlorpromazine (Thorazine®), haloperidol (Haldol®), risperidone (Risperdal®), olanzapine (Zyprexa®), quetiapine (Seroquel®)
  - Typical dosage: 1-2 mg/day
  - Ocular Manifestations
    - Anticholinergic effects (think atropine!):
      - Mydriasis
      - Cycloplegia
      - Impaired accommodation
      - Transient refractive shift
    - Dry eyes
    - Esotropia / diplopia
      - Proposed mechanism: The ratio of convergence to accommodation may increase with anticholinergics due to partial block of accommodation. To see a near target in the setting of blocked accommodation, children would increase accommodative effort, resulting in increased convergence. Too much convergence may cause esotropia.
  - Other Manifestations
    - MORE anticholinergic effects

- CONCLUSIONS:
  - Optometric PHYSICIANS must realize that the eye is impacted by numerous systemic diseases and drugs.
  - A working knowledge of pharmacology and common drugs is essential (especially when dealing with an adult or geriatric population).
  - Even if you don’t (or can’t) prescribe them, you have the responsibility to recognize the potential ocular impact of commonly prescribed medications.