1. Objectives: The objectives of the lecture are reviewed
   a. Age-related macular degeneration (AMD) Landscape
   b. Current management of AMD patients and the unmet medical need
   c. Abnormal dark adaptation is an indicator of early and subclinical AMD
   d. How to integrate dark adaptation testing into the practice
2. AMD Landscape: Large Unmet Need
   a. Review the prevalence of AMD, diabetic retinopathy, and glaucoma
   b. AMD is three times more prevalent than glaucoma
   c. 9.2 million Americans are estimated to have AMD compared with 4.9 million people with diabetic retinopathy, and 2.7 million people with glaucoma.
   d. 1 out of 8 adults over 60 years old are estimated to have AMD.
3. AMD is underdiagnosed
   a. Up to 78% of AMD patients present with irreversible vision loss at first diagnosis.
   b. About 40% are legally blind in one eye when first diagnosed
   c. AMD is not adequately detected by current methods of slit lamp biomicroscopy performed during a routine eye examination
   d. Retina specialists see too many AMD patients who were diagnosed too late
4. Treatments for early to intermediate AMD
   a. Treatments are available to slow the progression of the disease and preserve vision
   b. AREDS & AREDS2 supplements lower risk of progression to late AMD by 25%
   c. Behavior modification lowers risk of progression. For example, cessation of smoking
   d. Anti-VEGF therapy preserves vision. Prompt therapy can save an additional 5 or more lines of visual acuity compared with deferred treatment.
5. AMD pathogenesis
   a. Cholesterol accumulation leads to panmacular deposits of cholesterol located between the RPE cells and Bruchs’ membrane and within Bruchs’ membrane.
   b. Initially, the accumulation is invisible to clinical imaging techniques. With sufficient accumulation, the peaks of basal laminar deposits become visible as drusen upon clinical examination and imaging.
   c. These cholesterol deposits negatively affect photoreceptor health. The deposits cause inflammation and oxidative stress. These pathways predispose the eye to progress to choroidal neovascularization or geographic atrophy
   d. These deposits also serve as a barrier to transport of nutrients into the eye, including vitamin A which is necessary for night vision
   e. In effect, AMD causes a localized deficiency of vitamin A in the eye. The classic method to detect localized vitamin A deficiency is dark adaptation
6. Dark adaptation defined
   a. Dark adaptation is the process of adjusting from day vision to night vision
   b. It is a good proxy measurement of overall night vision function
7. Dark adaptation impairment is the first symptom of AMD
a. Dark adaptation impairment has been shown in AMD patients in over 20 peer-reviewed clinical studies conducted by multiple investigators around the world.
b. AMD patients often give up driving at night and self-report difficulty with mobility in low illumination
c. Studies have shown that night vision deficits proceed day vision deficits
d. Night vision deteriorates with aging. Thus, it is difficult to know whether night vision complaints are due to aging or disease based upon interviewing the patient. Night vision should be measured.

8. An overview of dark adaptometers is provided
   a. Currently there are only two dark adaptometers on the market

9. Goldmann-Weekers Dark Adaptometer
   a. Gold standard device for the measurement of dark adaptation.
   b. World War II era technology used for the detection of vitamin A deficiency to triage vitamin A supplements which at the time were very expensive.
   c. Discontinued over 20 years ago, but still used at some academic centers

10. LKC Technologies SST-1
    a. A portable dark adaptometer
    b. Manually operated – operator had to write down thresholds
    c. Discontinued about 8 years ago

11. Roland Consult DarkAdaptometer
    a. An automated dark adaptometer
    b. Primarily sold in Europe, not widely marketed
    c. Only one published paper describing its use

12. MacuLogix AdaptDx
    a. An automated dark adaptometer
    b. Unlike ERGs, or scotopic microperimetry, no prior dark adaptation is required before testing.
    c. Low patient burden, most patients self-report that it is an easier exam than perimetry
    d. The device calculates dark adaptation speed and provides a metric for interpretation
    e. Dark adaptation testing is reimbursable
    f. The AdaptDx has been cleared by the FDA

13. How to measure dark adaptation
    a. Technician operates the dark adaptometer in a fashion similar to operating a perimeter
       i. Enters patient data
       ii. Aligns patient to optics
       iii. Starts the test
       iv. Monitors testing
    b. The patient is presented with a moderately intense camera flash, similar to a cell phone camera flash. The flash is local and nonirritating because it is outside the fovea
    c. After the camera flash, a stimulus randomly appears. The patient pushes a response button when the stimulus is detected.
    d. Recovery of light sensitivity is tracked
    e. Once, the substantial dark adaptation recovery occurs, the test stops

14. A typical normal dark adaptation curve is described
a. Rod and cone function is identified  
b. The rod intercept is defined.

15. Representative dark adaptation curves for AMD patients are described  
a. Early AMD case has 20/20 vision but requires almost three times longer than a normal adult to dark adapt.  
b. Intermediate AMD case requires more time to dark adapt than an early AMD case.  
c. Late AMD case has almost no rod-mediated recovery in the first 20 minutes of testing.  
d. This is a profound effect.

16. Validation Study  
a. A multisite validation study was conducted at three academic institutions  
b. Sample was 127 AMD patients and 21 normal old adults  
c. Disease severity classified by gold standard method of fundus photograph grading system

17. Validation study results  
a. Patients were classified as having AMD if the rod intercept was > 6.5 minutes  
   i. This was a pre-specified cut point  
b. Using the cut point, dark adaptation status correctly identified 90.6% of the AMD cases  
c. Dark adaptation status correctly identified 90.5% of normal cases  
d. Thus the test exhibited a high sensitivity and specificity and a 90% overall accuracy

18. 90% accuracy put into context  
a. Visual field testing used for the detection of glaucoma at best is 83% sensitive and 95% specific  
b. Retina specialists using slit lamps to detect AMD are 82% sensitive and 91% specific

19. Dark adaptation compared to other visual function tests  
a. Dark adaptation is much more sensitive than contrast sensitivity, visual fields, and visual acuity

20. Dark adaptation is being studied at over 20 academic institutions

21. Typical output from a dark adaptometer is described

22. Case Study #1  
a. This case is a typical intermediate AMD patient  
b. This patient presents with large confluent soft drusen  
c. Drusen appear on OCT image and color fundus image  
d. Patient exhibits dark adaptation impairment worse than expected.  
e. Should this patient be monitored more closely?

23. Case Study #2  
a. This case is a typical subclinical AMD patient  
b. This patient has hard to detect small and intermediate drusen  
c. No appearance of drusen on OCT  
d. Dark adaptation is impaired  
e. How should this patient be managed?  
   i. Education, modify at-risk behaviors  
   ii. The doctor placed patient on nutritional supplementation

24. Dark adaptation reveals the disease and is not simply a risk factor

25. How to interpret a positive dark adaptation test
a. Differential diagnosis is explained to determine whether a patient has AMD or subclinical AMD

26. AMD patient treatment standard of care is described
   a. Examination – annual, semi-annual, or more frequent based upon disease severity
   b. Testing – diagnostic modalities used to follow patient
   c. Management – role of supplementation, light protection, counseling, and Amsler grid
   d. Referral – The appropriate time to refer patient to retina specialist

27. Subclinical patient treatment protocol
   a. Examination – monitor as appropriate depending on risk factors
   b. Testing – diagnostic modalities used to follow patient
   c. Management – role of supplementation, light protection, and counseling

28. Practice integration models
   a. Type of practice
   b. Medical reimbursement or wellness screenings
   c. Primarily tests only known AMD patients to benchmark impairment
   d. Tests night vision to differentiate between cataract and AMD

29. Impact of AMD on your practice
   a. Good for patients – prevent vision loss
   b. Good for practice – ROI similar to glaucoma

30. ICD-9 codes matched to testing model

31. Key Takeaways
   a. AMD is highly prevalent
   b. Proactive detection and management of early subclinical AMD can provide better patient outcomes
   c. Dark adaptation testing can help preserve vision