There’s Nothing Dry About Dry AMD: New Perspectives on an Old Problem

Abstract: Astonishing new observations about the anatomy and physiology of age related macular degeneration have critical implications for management of the millions of affected individuals. These new observations are of particular importance for management of non-exudative age related macular degeneration, the prevalence of which increases sharply among the oldest adults. This symposium will review the results of improved imaging techniques and new understandings of photoreceptor functioning at various light levels, with discussion of implications for assessment of new pharmaceutical treatments and for clinical practice, from early detection through end stage management.

Introduction to the Symposium
Dawn DeCarlo, OD, MSPH, University of Alabama at Birmingham, School of Medicine

Drusen and the Oil Spill in Aging Bruch’s Membrane
Christine A. Curcio, PhD, University of Alabama at Birmingham, School of Medicine

I. Basal Linear Deposit, Soft drusen: 2 forms of one lesion
   a. Cholesterol is abundant in drusen and Bruch’s membrane
   b. Largest single druse component is lipid (esterified cholesterol, phospholipid)
   c. No consistent relationship of AMD with any measure of plasma cholesterol or lipoproteins
   d. AMD is associated with cholesterol processing genes (Chen et al, Neale et al 2010)

II. Lipoprotein particles form an oil spill
   a. Lipoprotein particles accumulate with age in Bruch’s, especially in the macula
   b. Particles fill in towards RPE, form a layer on Bruch’s membrane inner surface (Oil Spill).
   c. Fusion and pooling of lipoproteins form basal linear deposit
   d. Soft drusen (found only in the macula) are made of the same material as basal linear deposits.
   e. RPE secreted lipoproteins provide cholesterol to Bruch’s membrane and drusen Fatty acid profile suggests that DIET is the source (High in linoleate 18:2n6 – like plasma lipoproteins and LOW in DHA 22:6n3 – unlike outer segments)
   f. Source of cholesterol is unknown (endogenous synthesis, plasma lipoprotein uptake, outer segments)

III. Functional consequences of the Oil Spill
   a. Esterified cholesterol correlates with high hydraulic resistivity and poor transport across Bruch’s membrane
   b. Lipoprotein constituents interact with free-radicals, generate pro-inflammatory/pro-angiogenic compounds
c. Biomechanically unstable basal linear deposits are a cleavage plane for ingrowing neovessels

IV. Treatment implications of the Oil Spill
a. Imagine treatment strategies based on cleaning up or preventing an Oil Spill
   i. Skimmers and dispersants to refurbish Bruch’s membrane
      1. Biormediation agents (detergents, surfactants, encapsulated lipases, apoliprotein mimetics)
      2. Model systems (human Bruch’s membrane explants, ApoE-/- mouse)
   ii. Top Kill – limit Apo-B particles from RPE
   iii. Bottom Kill – Diet (modulate source of fatty acids available to lipidate apoB; Omega-3 fatty acids improve activity of RPE lipases)

V. Imaging insights from druse lipid composition
a. The future is to see the Oil Spill as well as the Tar Balls
b. Magnetic resonance spectroscopy gives a signal for esterified cholesterol (used by cardiologists to view atherosclerotic plaques similar in composition to drusen)
c. Multispectral interferometry used by geologists to compute surface area and thickness from aerial photographs.

Reticular Macular Disease
R. Theodore Smith, MD, PhD, New York University, School of Medicine

I. Introduction
a. Yellow reticular pattern in the macula of patients with AMD observed with blue light described for the first time in 1990
b. Advancements in scanning laser ophthalmoscopy and spectral domain optical coherence tomography localized reticular lesions above the RPE with a predilection for the superior temporal macular area
b. Histopathological studies show that reticular lesions are similar to drusen in their composition
d. Historically, names for the lesions have included: reticular soft drusen, reticular pseudodrusen, reticular macular disease, subretinal drusenoid deposits, reticular drusen, but no standardized nomenclature exists
e. 2 models proposed to explain the development of reticular lesions:
   i. Defect in the lipid vector between the REP and Inner Segment ellipsoid (ISce) band
   ii. Choroidal/vascular alteration leading to the accumulation of subretinal drusenoid deposits

II. Imaging
a. Infra Red – group of hyporeflectant lesions against background of mild hyperreflectance; one of the most sensitive (~95%) but least specific imaging techniques to detect reticular lesions
b. Spectral Domain OCT – lesions appear as granular hyperreflective deposits between the ISce band and the RPE layer (sensitivity 95%, specificity 98%)
c. Other techniques useful for confirming diagnosis: fundus autofluorescence, near infrared fundus autofluorescence, confocal blue reflectance, indocyanine green angiography
d. At least 2 methods recommended to detect and confirm diagnosis

III. Differences between soft drusen and reticular lesions
a. Soft drusen associated with both early and late stage AMD, whereas reticular lesions highly prevalent in late AMD
b. Drusen localized under the RPE in the cone-rich foveal area, whereas reticular lesions more common in rod-rich perifoveal area (especially superior-temporal)
c. Patients with soft drusen tend to be younger with an equal gender ratio, whereas patients with reticular lesions tend to be older and are more likely to be female
d. Drusen are associated with pigmentary changes, reticular lesions are not

IV. Association with advanced AMD
a. Risk factor for progression to advanced AMD in Beaver Dam Eye Study
b. Pumariega et al found that being female and having reticular lesions doubled the risk of developing late AMD
c. Reticular lesions nearly universally present in multilobular geographic atrophy

V. Effects of reticular lesions
a. Decreased macular sensitivity on microperimetry paralleling localization of reticular lesions
b. Choroidal thickness decreased in eyes with reticular lesions with sparing of the superior foveal area due to fibrotic changes
c. Accumulation of subretinal drusenoid deposits may decrease the demand for oxygen and nutrients by the photoreceptors, thus leading to choroidal atrophy and fibrosis

VI. Recommendation: Patients with reticular lesions are at risk for development or rapid progression to late AMD and should be monitored closely for early detection and management

Dark Adaptation and Early AMD
Gregory R. Jackson, PhD, Maculogix, Hummelstown, PA

I. Introduction to Dark Adaptation
a. Classic dark adaptation
b. Dark adaptation & retinoid cycle

II. Innovations in Dark Adaptometry
a. Fast dark adaptation protocol
b. Rod intercept speed measurement

III. Dark Adaptation Impairment in AMD
a. Sensitivity & specificity of dark adaptation for detection of AMD
b. Mechanisms underlying dark adaptation deficit
c. Monitoring progression of AMD

Low Vision Rehabilitation for the Patient with Dry AMD
Dawn K. DeCarlo, OD, MSPH, University of Alabama at Birmingham
I. Overview of quality of life issues as measured by the NEI VFQ
II. Evaluation of functional complaints
   a. Scotoma detection and measurement
      i. Amsler grid
      ii. Standard perimetry
      iii. Microperimetry
   b. Contrast sensitivity
   c. Reading acuity and speed
III. Magnification
   a. Pearls for determining amount of magnification
   b. Microscopes
   c. Hand held and stand magnifiers
IV. Illumination
V. Case examples

Panel Discussion