Age-related Macular Degeneration Update

AMD: The Burden of Disease
Carlo J. Pelino, OD, FAAO
cpelino@salus.edu
Joseph J. Pizzimenti, OD, FAAO
pizzimen@nova.edu

Course Goals
- Statement of the problem
- Epidemiology
- Natural history
- Functional anatomy review
- Clinical features
- Examination and diagnostic work-up
- Interactive!

The Problem
- The AMD “Epidemic”
- AMD is the principle cause of registered legal blindness for those aged over 65 in the USA, Canada, Western Europe, Australia and Japan.

Survey of Ophthalmology, June 2003
Adamis et al

Prevalence of Ocular Diseases
- Glaucoma: 4 Million
- Diabetic Retinopathy: 5 Million
- Intermediate AMD: 8 Million
What is AMD?
- Continuum of Normal Aging and Disease
- Degenerative changes are observed in maculae of most elderly persons to some degree.

What is AMD?
- Cell Death and Functional Loss *
  - Only in some individuals do age-related changes progress to this stage
  - Transition From “Normal Aging” to Disease ?
    - Loss of Visual Acuity
    - Funduscopic Appearance
    - Measurable Loss of Functional Vision *

About AMD
Leading cause of irreversible visual impairment and blindness among the elderly

Age Related Eye Disease Study estimated a prevalence of more than 8 million individuals in the US with at least “intermediate” AMD in one eye who are at risk for “advanced” AMD

AMD has a genetic component but the disease is “multifactorial”

Environmental, dietary, medical and lifestyle factors are influential

About AMD

Latest Terminology:
- Age Related Maculopathy – age related changes in the retina
- Example - drusen
- Age Related Macular Degeneration – retinal status when vision deteriorates

About AMD

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AMD

“Dry”
Drusen, RPE clumping, RPE atrophy

“Wet”
CNVM

“Dry” ARMD = 90% of all cases
“Wet” ARMD = 10% of all cases (but 90% of all cases of severe vision loss)
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**AMD by the Numbers**

- AMD accounts for 16,000 cases or 14% of new legal blindness yearly.
- The prevalence of AMD increases with age, and approximately 20-30% of persons over age 75 are affected.
- AMD cases in USA rose 25% from 2002 to present
- "Vision Problems in the U.S." Study
  - www.preventblindness.org

**Beaver Dam Eye Study**

- 5 yr. results: 3,583 whites, 43-84 y/o
  - Used Wisc. AMD Grading System (photos)
- >75 y/o
  - 30% had early signs of AMD
  - Another 23% within 5 yrs
  - Incidence was 2.2X more likely in women
  - Soft drusen, RPE abnormalities increase risk of GA or CNVM.

**Blindness from AMD: A Growing Problem**

<table>
<thead>
<tr>
<th></th>
<th>2003</th>
<th>Projected 2030</th>
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</thead>
<tbody>
<tr>
<td>Number of Legally blind</td>
<td>1.2 Million</td>
<td>6.3 Million</td>
</tr>
<tr>
<td>New Cases Annually</td>
<td>200,000</td>
<td>500,000</td>
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**Why?**

**The Aging Population is Growing**

- Projections for U.S. population over age 65
  - 2000: 35 Million
  - 2010: 40 Million
  - 2020: 54 Million
  - 2030: 71 Million
- In just the next 15 years, the number of people over age 65 is expected to increase by 20 Million
  - U.S. Census Bureau, 2004

**Vision Impairment and Aging**

- The world’s population is aging.
  - Increase in life expectancy
- The rate of vision impairment increase with age.
- The combination of these factors will result in a predictable, dramatic growth in vision impairment worldwide.
- Therefore, improved prevention, detection, treatment, and rehabilitation of eye conditions in older persons must be a global priority!
**The AMD “Epidemic”**

- Age-related macular degeneration (AMD) is the principle cause of registered legal blindness for those aged over 65 in the USA, Europe, Australia and Japan.

*Survey of Ophthalmology, June 2003*  
*Adamis et al*

**Prevalence of AMD**

- 2 million Americans have advanced AMD
- 8 million Americans have intermediate AMD
- Approximate % of patients with AMD
  - 48% of patients over age 75
  - 9% of patients over age 52

*Add Preferred Practice Pattern; AAO Clinical Practice Guidelines*

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**The AMD “Epidemic”**

*How should we as optometrists respond?*

- Early Diagnosis
- Early Intervention
- Improved Visual Outcomes

**Projected Prevalence of Advanced AMD* in the United States**

![Graph showing projected prevalence of advanced AMD* in the United States from 2000 to 2020.](source)


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**Advanced AMD starts out like this:**

![Advanced AMD image](source)

**Advanced AMD**

- Defined as either:
  - Geographic atrophy (GA)
  - GA of the RPE and/or photoreceptors, CC
  - "End-stage" non-exudative (dry) AMD
  - Choroidal neovascularization (CNV)
  - Exudative "wet"

- Approximately 80-90% of advanced AMD cases are due to CNV.
Early detection and treatment of CNV could be one of the most important factors contributing to the reduction of blindness from AMD over the next several years.
– Neil Bressler MD, Wilmer Eye Institute, Johns Hopkins

Of bilateral dry AMD patients, 18% will progress to wet AMD within 5 years
Of monocular AMD patients, 50% will lose sight in their remaining eye within 5 years

AMDS Report No. 8 Arch Ophthalmology 2001

How do these dramatic changes and projections impact your practice?

The size of the AMD patient population in need of frequent monitoring has no equal in primary eye care
The primary focus for the eye care professional managing AMD is monitoring patients for change in disease status
In managing AMD, frequent monitoring of patients has a significant effect on the final outcome
AMD management creates a valuable patient revenue source for your practice

1.5 million affected in the United States
Distribution (age)
- 55–64: 17%
- 65–74: 26%
- >75: 42%

Beaver Dam Eye Study

- 5 yr. results: 3,583 whites, 43-84 y/o
- Used Wis. AMD Grading System (photos)
- >75 y/o
- 30% had early signs of AMD
- Another 23% within 5 yrs
- Incidence was 2.2X more likely in women
- Soft drusen, RPE abnormalities increase risk of GA or CNVM.
- Smoking ID as a RF

Identifying Retinal Signs of Disease

- Signs of vascular disease
- Signs of degenerative disease
- Signs of other disease
  - Infectious
  - Inflammatory
  - Neoplastic
  - Retina/Optic Neuropathy

Functional Anatomy

A Brief Review

Functional Anatomy of Posterior Segment

Peripheral vs Central Retina

Approx 6 Disc Diameters

Central Retina
Peripheral vs Central Retina

Posterior Pole

"Mid-Periphery"

Exit Site of Ampulla

Clinical Landmark - Equator

Functional Anatomy: The Retina

- RPE
- Neurosensory
- 6 million Cones
  - Detailed vision
  - Color vision
- 120 million Rods
  - Peripheral retinal receptors
  - Great sensitivity to light

- Detailed vision
- Color vision

Retinal layers

Schematic drawing of the nine layers of the neurosensory retina, retinal pigment epithelium, Bruch's membrane, choroid, and sclera.

Identification of Retinal Layers

Cross-sectional image of live tissue; a “virtual biopsy”
Retinal Pigment Epithelium
- 120 million cells in monolayer
- T-junctions
- Outer blood-retina barrier
- Functions of RPE
  - Phagocytosis of renewable discs of PRs
  - O2 diffusion to PRs
  - Provision of nutrients to PRs

Photoreceptors
- Macula
  - “sacred ground” or “belt”
  - Centered on fovea
  - X in NFL absorbs blue WL, “macula lutea”
  - Supplied by lobular pattern of CC
- Fovea
  - Shallow depression in middle of macula, 1.5 DD
  - Retinal cells displaced exposing only the PR
  - Has the highest concentration of cones
- Capillary free zone 500 microns (FAZ)

Note yellow macular pigment
**Fovea**

Schematic drawing of the fovea. The normal foveal depression results from displacement of the inner retinal layers including the nerve fiber layer, ganglion cell layer, inner plexiform layer, and inner nuclear layers.

**Retinal Arterial Supply**

- **Arterial**
  - CRA
  - SPCA
  - LPCA
  - ACAs

**Retinal Vasculature**

- 2 main sources of blood supply:
  - Choroidal BV
    - Supplies outer retinal layers, including PRs
  - CRA
    - 4 branches nourish inner retina
    - Run radially toward fovea
Retinal Capillaries
- Capillary Network
- Pericytes surround each endothelial cell and provide support
- Tight junctions between endothelial cells
- Pericytes + tight junctions form inner lining
- Pericytes marked by ng2 staining (blue) and endothelial cells are marked by PECAM (red).

Retinal Venous Supply
- Venous
  - CRV
  - Anterior ciliary veins
  - Vortex veins

Venous System
- Central Retinal Vein
- Retinal veins join at disc to form CRV
- Drains into superior ophthalmic v.
- Retinal blood flow is under autoregulation
- Most O2 extracted before blood enters CRV

The Choroid
- Located between the sclera and the RPE
- Extends from ora serrata to optic nerve
- Pigmented/vascular tissue - 75mm thick
- Nourishes the RPE
- Choriocapillaris designed to leak
- Absorbs light that passes through retina

The Choroid
- Loose connective tissue
- Melanocytes
- Choriocapillaris
  - Fenestrated endothelium allows diffusion of proteins
  - Regulation
  - High blood flow
  - Very little O2 extracted, so high venous O2

- Choroid 80% of blood supply = Sympathetic Control
- Retina 5% of blood supply = Autoregulate
- Iris / Ciliary Body 15%
Retina Quiz

- The earliest clinically detectable feature of Dry Age-related Macular Degeneration (AMD) is:
  a. Geographic atrophy
  b. Drusen
  c. Choroidal Neovascular Membrane
  d. Fibrovascular scar

Questions?

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Bruch’s Membrane

- Basal lamina of RPE
- Anterior collagenous layer
- Elastic layer
- Posterior collagenous layer
- Basal lamina of CC endothelium

Contamination of Bruch’s can result in d________.
CNVM

Choroidal Vasculature

- SPCAs provide blood flow to choroid posterior to equator
- ACA and LPCA supply anterior choroid
- Vortex veins drain choroidal veins
- V.V. drain into sup, inf ophthalmic vein

The choroid is a rich vascular network supplying oxygen and nutrition to the retinal pigment epithelium and outer retina. It is arranged in a zonular pattern.

Examination of the Posterior Segment

- Biomicroscopy
  - View anterior vitreous
- Funduscopy
  - Direct Ophthalmoscopy
  - Binocular Indirect Ophthalmoscopy
  - Fundus Biomicroscopy
- Direct Ophthalmoscopy
  - Until invention of direct ophthalmoscope by von Helmholtz in 1851, the living retina was not visible.
**Binocular Indirect Ophthalmoscopy**
- Stereoscopic view of central, peripheral fundus
- Real, upside down, inverted image
- View fundus in 30 degree increments
- Scleral indentation may allow viewing out to pars plana
- View fundus in p________
- Consider 14 D condensing lenses for post pole

**Fundus Biomicroscopy**
- Adjunct to BIO
- Further study of retinal structures
- Macular edema
- CNV
- Breaks/holes/tears
- Non-contact lenses
- Real, inverted image
- 60D, 90D
- Contact fundus lenses
- Goldmann 3-mirror
- Plano-concave "pancake" lens
- Image is virtual, direct

**Fundus Biomicroscopy**

**Examination of the AMD Patient**
- VA w/PH
- Contrast Sensitivity
- Amsler Grid
- Photostress Recovery Test
- DFE w/60 or 90 D, Pancake Lens
- Photos: Stability vs. Progression
- Imaging: FA, ICG
- B-scan Ultrasonography if VH obscures view *

**Signs of Degenerative Disease**
- Macula and posterior pole
  - Pigment
  - Hyper/hypopigmentation
  - Drusen
  - Hard
  - globular deposits of hyaline
  - Soft
  - extracellular deposits of lipid, protein, cellular debris
  - Elevation (CNV)
  - Vitreo-retinal interface signs

**Stages of AMD**

1. Early AMD
2. Intermed. AMD
3. Advanced AMD

- CNV
- GA
Degenerative Changes: Pigment and Drusen

- Areas of hard drusen, focal RPE hyperpigmentation and RPE atrophy
- Soft confluent drusen indicates diffuse disease of Bruch’s, more likely to lead to Geographic Atrophy, CNV

Soft Drusen

- Histopathology
  - Amorphous material between inner and outer Bruch’s
  - Soft, confluent more inclined to lead to ___________ AMD *
- Ophthalmoscopic Appearance *
  - Large, ill-defined
  - May become confluent

Geographic Atrophy (GA)

- GA w/ dystrophic calcification of drusen which appears as glistening, bright yellow specks.

Clinical Features of Exudative (Wet) AMD

- 
  - 
  - 
  - 
  - 
  - 

Degenerative Changes: Elevation
Serous RPE Detachments

- Dome-shaped elevation
- Blood within detachment implies CNVM

RPE Detachments-Hemorrhagic

- Hemorrhagic detachment of RPE/sensory retina
- Confluent drusenoid RPED associated with soft drusen

Wet AMD Pathology

- Characterized by abnormal growth of blood vessels (Choroidal Neovascularization – “CNV”) into the subretinal space
- Poorly formed vessels leak to fill subretinal space and distort macula
- Causes injury to the retina, promotes scarring of the fovea and loss of central vision

Fluorescein Angiography (FA)

- FA answers the question: is the blood-retinal barrier intact?

FA

- The “gold standard” for the evaluation of new onset choroidal neovascularization (CNV) in AMD patients.
Fluorescein Angiography

- Indications
  - Unexplained decrease in VA
  - PHP shows significant defect
  - OCT results c/w CNV
  - Amsler changes
  - Significant visual function changes such as decreased foveal threshold, increased photostress time
  - Intermediate AMD baseline, esp. soft confluent drusen
    - Replaced by OCT
    - RPE break or detachment
    - Suspect CNVM: FA within 72 hrs**

The Fluorescein Angiogram

- Stages
  - Choroidal phase (10 sec post-injection)
    - Free dye in CC produces "choroidal flush" just before retinal arteries start filling.
  - Arterial phase
  - Laminar venous phase
  - Venous phase
  - Recirculatory phase
  - Late phase

The Fluorescein Angiogram

- Arterial phase (12-14 sec)
  - Retinal arteries prominent
- Laminar venous phase (14-20 sec)
  - Dye begins to fill retinal vein

The Fluorescein Angiogram

- Venous phase (20-30 sec)
  - Complete filling of veins
  - Recirculatory phase (2-4 min)
    - A & V equal in brightness
  - Late phase (5 min+)
    - Elimination of dye from vasculature
    - Hyperfluorescence in abnormalities (CNV)

Obstacles in FA Evaluation

- Thick b___________
- Pigment
- Fibrous tissue
- RPE Detachment
- FA may fail to identify a well-defined area of leakage. Successful therapy depends on Tx. of entire CNVM.
Forms of Subfoveal Wet AMD

- Predominantly classic: 18%–24%
- Minimally classic: 0%–19%
- Occult with no classic: 60%–75%


Indocyanine Green Imaging

- ICG dye absorbs & emits fluorescence in the near-IR WL
- Fluorescence is only partially absorbed by RPE, therefore choroidal vasculature seen
- Better able to penetrate heme, melanin, fluid
- Occult CNVM detection
- SLO for ICG imaging
- Well-defined CNVMs, small retinal BVs (Tx. landmarks) better visualized with FA

Indocyanine Green Imaging

- A: Red-free
  - Photo of classic CNV.
- B: Early-phase (1-2 sec)
  - Rapid filling of choroidal BVs, retinal arteries.
  - ICG hyperfluorescence of the CNVM.
- C: Mid-phase (3-15 min)
  - Fading of choroidal, retinal vessels.
  - Staining of CNV.
- D: Late-phase (15 min+)
  - Hypofluorescence of choroidal vasculature
  - Retinal BVs not visible
  - Late staining of the hyperfluorescent CNV.

http://www.retinalphysician.com

CNVM/FA/ICG Imaging

Indocyanine Green Angiography

- Clinical CNVM Case

Summary

- Age-related eye disease is on the rise.
- In order to truly understand macular disease processes, one must have a firm grasp of:
  - Functional anatomy
  - Post segment examination
  - Signs of retinal degenerative disease
- Optometry can contribute mightily in the war against AMD.
See you...

After a break!

Carlo & Joe

Cpelino@salus.edu  pizzimen@nova.edu