# Age Related Macular Degeneration (AMD)

## **Background**

- 1. Definition:
  - Breakdown of light-sensitive cells of the macula leading to progressive loss of central vision, sparing of peripheral vision
- 2. Leading cause of vision loss & legal blindness in adults over 60 y/o
- 3. Patients rarely complain of symptoms until disease (Dz) advanced
- 4. Dz responds to early detection/ prevention

### **Pathophysiology**

- 1. Theories
  - o Build-up of waste products (environmental & dietary)
  - o Family hx
  - o Breakdown of retinal circulation
  - o HTN, smoking
- 2. Two forms
  - Wet AMD (exudative)
    - 10% of initial presentations
    - 80% of legal blindness or severe visual loss
    - Abnormal blood vessel growth with fluid leakage behind macula
    - Rapid vision loss months to years
  - o Dry AMD (Atrophic)
    - 90% of pts at onset
    - 13%-18% progress to Wet AMD at three years
    - Slow breakdown of macular cells will see drusen deposits & chorioretinal atrophy
- 3. Prevalence: Dz affects 25-30 million people worldwide
- 4. Incidence rate in US based on study involving 4000 peopled followed over 15 years incidence of early and late AMD was 14.3 and 3.1 percent respectively.
  - o Incidence expected to triple by 2025 secondary to aging Baby Boomers
- 5. Risk factors
  - >50 y/o, family hx, fair skin, blue eyes, farsighted vision, h/o: smoking,
    Htn, diabetes, CVD, exposure to UV light, obesity, cataract surgery, diet
- 6. Depression common secondary to vision loss

## **Diagnostics**

- 1. History
  - Normal changes as eye ages
    - Difficulty adjusting to changes in light
    - Changes in color perception
    - Loss of contrast
    - Floaters
    - Dry, burning, or sandy feeling in eyes
  - o Phantom visions (Charles Bonnet Syndrome)

- Symptoms of possible AMD:
  - Inability to find personal article in familiar environment
  - Difficulty recognizing faces
  - Print appears faded, colors washed out
  - Water spots in center of pages
  - Difficulty distinguishing colors
  - Spilling reaching across table
  - Problems with depth perception
- Wet AMD: early symptom → distortion of straight lines, i.e. poles, appear wavy
- o Dry AMD: early symptom → gradual blurring of central vision
- 2. Physical exam
  - o Dx made primarily by symptoms
  - Full ophthalmologic exam indicated if suspected
    - Neovascularization
    - Drusen: lipid and calcium deposits under retina
      - Small numbers normal as eye ages
      - Large amount associated with AMD
- 3. Differential Diagnosis
  - o R/o other causes of vision loss: diabetic retinopathy, chronic Htn, CVD

#### **Therapeutics**

- 1. Diet & nutritional supplements
  - Antioxidants
    - No more effective than placebo in prevention of age-related macular degeneration
  - Antioxidants in combination with zinc
    - Modest benefit in reducing progression to advanced macular degeneration
- 2. Treatment for Wet AMD
  - Laser surgery
    - Only effective in small percentage of pts
    - Greater risk than benefit
  - Photodynamic therapy
    - Verteporfin injected IV; activated by retinal illumination
    - Slows progression of dz, does not restore vision
  - o Referral to low vision specialist to maintain lifestyle despite vision loss
  - o Glucocorticoids uncontrolled trails –shows benefits, requires randomized trials. <sup>2,3,4</sup>
  - o VEGF (Vascular endothelial growth factor) Inhibitors
    - Ranibizumab for those with acute and later lesions of fovia and no preserved vision in second eye. Also for large or well defined extrafoveal lesions (Grade 1B)<sup>2</sup>
    - Bevacizumab –same as ranibizumab (antibody fragment of bevacizumab with modification) (Grade 1B)<sup>3</sup>

 Pegaptanib –more side effects than benefits as compared to ranibizumab and bevacizumab<sup>4,5</sup>

#### Prevention

- 1. Early detection & prevention critical due to poor prognosis of advanced disease
- 2. Prevention/delay
  - Diet high in Lutein rich foods (dark-green leafy veg, yellow/red peppers, squash, pumpkin, kale)
  - o Annual eye exams after 55 y/o
  - No clear evidence to benefits of prevention; however, in wet AMD, supplementation with vit D, E, zinc, copper, beta carotene delays progression<sup>6,7</sup>
  - Smokers should be supplemented with only zinc, as beta-carotene linked to increase risk of lung cancer and coronary disease<sup>8</sup>
  - Decrease omega-6 fatty acids (vegetable oils), incr. omega 3 (cold-water fish...sardines, herring, salmon and tuna)
  - o Eliminate trans. fats (burgers, fries, high cooking heat)
  - o Regular exercise
  - o Maintain normal BP and normal lipids for age and comorbidities
  - o Sunglasses to block UV (need to say UV blocking)
  - o Avoid tobacco, in any form, but smoking worst

## **Prognosis**

- 1. Prognosis worsens with degree of disease
- 2. Can lead to complete vision loss
- 3. Early detection via careful hx critical to implement treatment and prevent progression

## **Evidence-Based Inquiry**

- 1. What is the role of antioxidants in age-related macular degeneration?
- 2. What is the role of antioxidants in macular degeneration?

#### References

- 1. Klein R, Klein BE, Knudtson MD, Meuer SM, Swift M, Gangnon RE. Fifteen year cumulative incidence of age related macular degeneration: The Beaver Dam Eye Study. Ophthalmology. 2007;114(2):253.
- 2. Rosenfeld PJ, Brown DM, Heier JS, Boyer DS, Kaiser PK, Chung CY, Kim RY, MARINA Study Group Ranibizumab for neovascular age-related macular degeneration. N Engl J Med. 2006;355(14):1419.
- 3. Steinbrook R. The price of sight--ranibizumab, bevacizumab, and the treatment of macular degeneration. N Engl J Med 2006; 355:1409.
- 4. Gragoudas ES, Adamis AP, Cunningham ET Jr, Feinsod M, Guyer DR, VEGF Inhibition Study in Ocular Neovascularization Clinical Trial Group. Pegaptanib for neovascular age-related macular degeneration. N Engl J Med. 2004;351(27):2805.

- 5. Steffensmeier AC, Azar AE, Fuller JJ, Muller BA, Russell SR. Vitreous injections of pegaptanib sodium triggering allergic reactions. Am J Ophthalmol. 2007;143(3):512.
- 6. Wang JJ, Klein R, Smith W, Klein BE, Tomany S, Mitchell P. Cataract surgery and the 5-year incidence of late-stage age-related maculopathy: pooled findings from the Beaver Dam and Blue Mountains eye studies. Ophthalmology. 2003;110(10):1960.
- 7. Age-Related Eye Disease Study Research Group. A randomized, placebocontrolled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. Arch Ophthalmol. 2001;119(10):1417.
- 8. Virtamo J, Pietinen P, Huttunen JK, Korhonen P, Malila N, Virtanen MJ, Albanes D, Taylor PR, Albert P, ATBC Study Group. Incidence of cancer and mortality following alpha-tocopherol and beta-carotene supplementation: a postintervention follow-up. JAMA. 2003;290(4):47

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