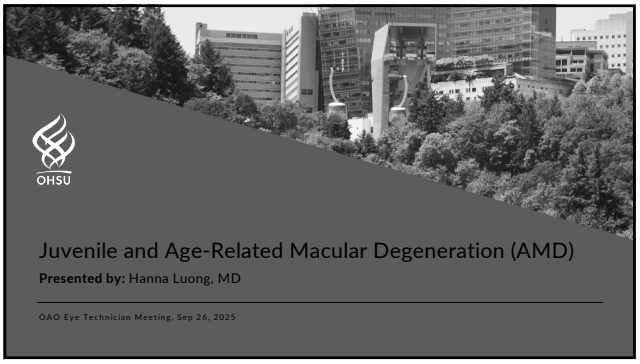

1

Learning Objectives

- Recognize different types of macular degeneration
- Understand the utility of multimodal imaging in the evaluation and management of macular degeneration
- Review current and investigational management strategies for dry and wet AMD

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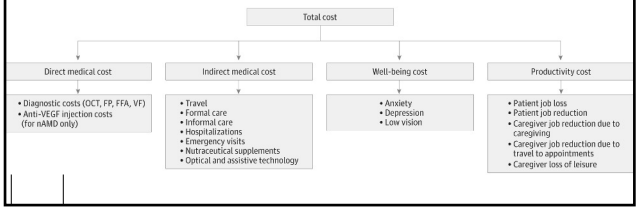
Overview

- AMD is leading cause of blindness in age >50
- Projected prevalence of 288M by 2040
- Significant visual morbidity, healthcare burden



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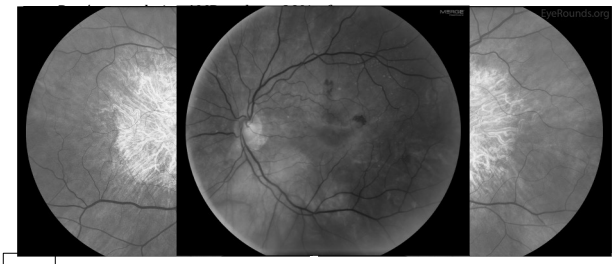
Classification



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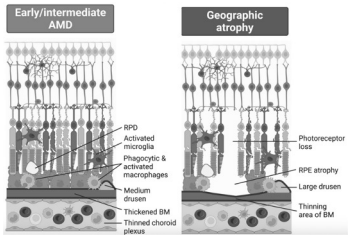
Dry AMD - Pathophysiology

- Dysfunction and degeneration of RPE cells
- Accumulation of drusen and photoreceptor loss
- Progression to geographic atrophy



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Dry AMD – Clinical Features

- Soft>hard, large>small drusen
- Subretinal drusenoid deposits (SDD)
- Pigment migration
- Geographic atrophy

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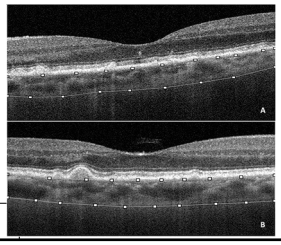
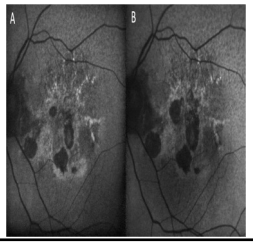
Dry AMD – Imaging

- OCT: drusen, SDD
- FAF: subtle pigmentary changes, GA borders





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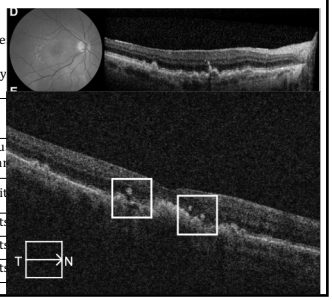
Dry AMD – Estimating Progression

- AREDS Simplified Severity Scale
  - 1 point for the presence of large drusen (≥125 µm)
  - 1 point for the presence of pigment abnormality
- Fellow eye of neovascular AMD
  - up to 60% 5-year risk



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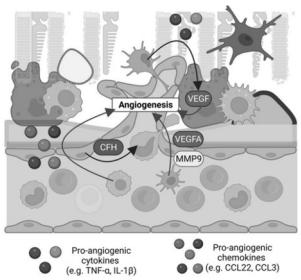
Wet AMD – Pathophysiology

- VEGF-driven choroidal neovascularization (CNV)
- Leakage, hemorrhage, fibrosis



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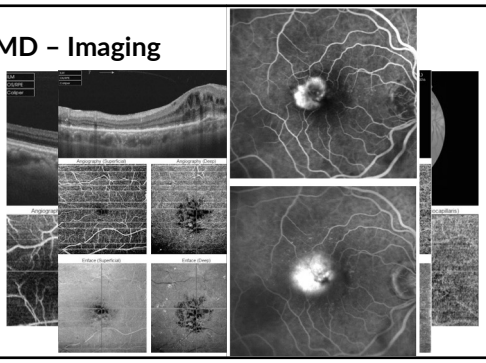
Wet AMD – Imaging

- OCT
- OCT-A
- FA



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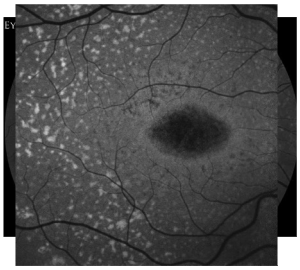
Early Onset/Juvenile Macular Degeneration

- **Stargardt**
  - ABCA4 mutation, typically AR
  - Yellowish flecks
  - Key imaging:
    - FAF: evaluate health of the RPE
    - OCT: evaluate local disease severity
    - ERG: diagnose and prognosticate



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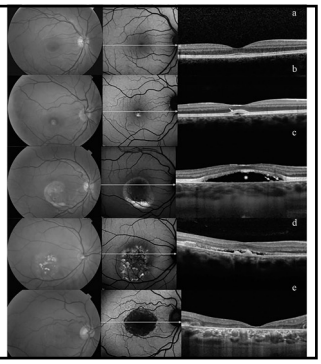
Early Onset/Juvenile Macular Degeneration

- **Best vitelliform macular dystrophy**
  - "Egg yolk," bilateral>unilateral
  - Autosomal dominant
  - Can be minimally visually significant



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Early Onset/Juvenile Macular Degeneration

- **Juvenile retinoschisis**
  - X-linked
  - Nearly 100% are fovea-involving
  - Can lead to RD
  - VA 20/60 to 20/120, worse with age

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Risk Factors for AMD

- Age
- Smoking
- Genetics/family history
- Cardiovascular factors

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AREDS & AREDS2

Table 1. AREDS Vitamin Formulations

	AREDS1	AREDS2
	Daily Dose	
Vitamin C	500mg	500mg
Vitamin E	273mg (400 IU)	273mg (400 IU)
Beta-Carotene	15mg	-
Lutein	-	10mg
Zeaxanthin	-	2mg
Zinc	80mg	25mg
Copper	2mg	2mg

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Lifestyle Prevention

- Smoking cessation
- Mediterranean diet
- UV protection
- Amsler grid monitoring

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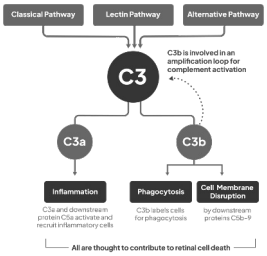
Dry AMD: Geographic Atrophy Treatments

- Pegcetacoplan
  - C3 inhibitor
  - OAKS and DERBY trials
- Avacincaptad pegol
  - C5 inhibitor
  - GATHER1 and GATHER2 trials



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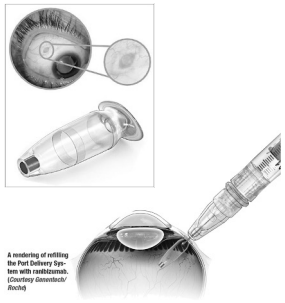
Wet AMD: Treatments

- **Very common:** bevacizumab (off-label), ranibizumab, aflibercept
- **Newer:** faricimab, high-dose aflibercept
- Brolucizumab considerations
- Ranibizumab port delivery system (PDS)
- **Largely supplanted:** laser photocoagulation, PDT



A rendering of refilling the Port Delivery System with ranibizumab. (Courtesy Genentech/Roche)

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Anti-VEGF Regimens

- **Initial loading** = 3 monthly injections (all agents)
- After loading:
  - **Fixed:** e.g. aflibercept 2 mg q8w or ranibizumab q4w
  - **Treat-and-extend:** extend by 2 weeks if dry, shorten if recurrence (common for ranibizumab/aflibercept/faricimab)
  - **PRN:** check q4-8w; reinject for fluid/vision loss
- Escalation

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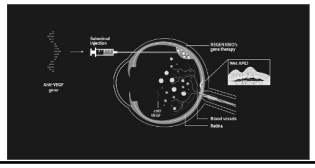
Investigational Therapies

- Gene therapy for nAMD
  - ABBV-RGX-314 (Regenxbio/AbbVie): uses an AAV8 vector to encode an anti-VEGF protein
    - Delivered either subretinally or into the suprachoroidal space
  - Ixo-vec (Adverum): intravitreal injection of genes to produce aflibercept
- OpRegen
  - Subretinal injection of RPE cells to target GA



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Low Vision Referral

- Refer when central vision loss or functional limitation
- Goals:
  - Maximize remaining vision
  - Improve reading, mobility, and independence
  - Reduce depression, falls, and caregiver burden
- Magnifiers
- Rehab services

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Key Takeaways

1. AMD is dysfunction of the RPE–Bruch's membrane–choriocapillaris complex
2. Use multimodal imaging
3. Manage dry AMD by modulating disease progression; manage wet AMD with anti-VEGF

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Q&A

1. What predictors do you use when evaluating the risk of progression from early/intermediate AMD to GA? What have you observed on GA growth rate between patients?
2. Do you care about non-foveal GA?
3. Does your management differ when addressing types 1 vs. 2 vs. 3 CNV?
4. What has been your experience with pegcetacoplan or avacincaptad? How about the ranibizumab PDS?

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Thank You

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