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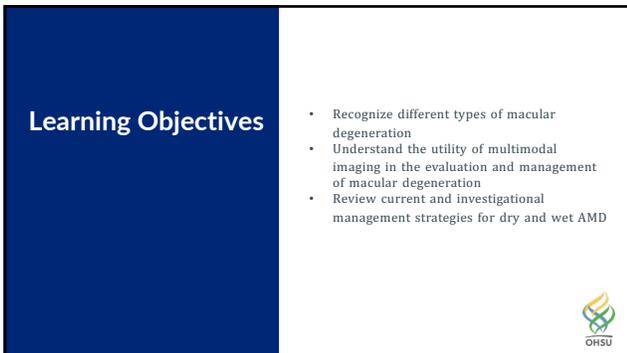
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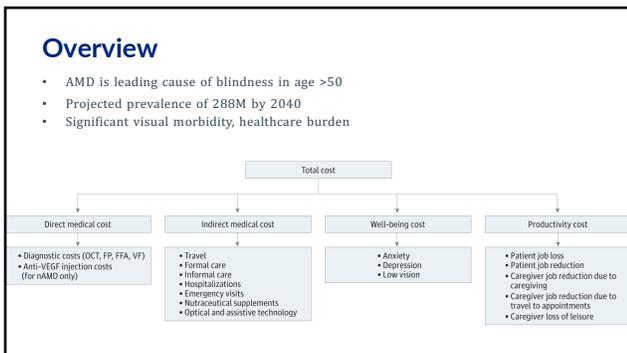
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### Classification



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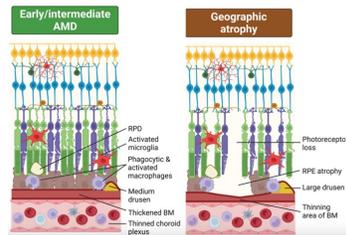
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### Dry AMD - Pathophysiology

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



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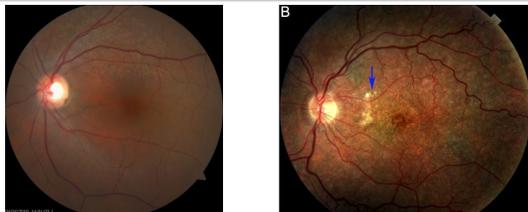
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### Dry AMD - Clinical Features

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



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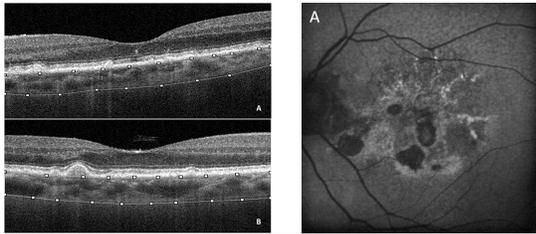
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### Dry AMD - Imaging

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



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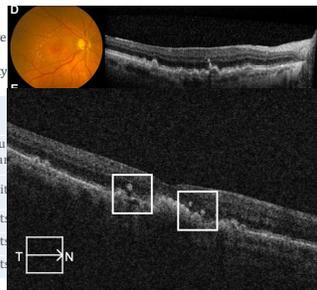
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### Dry AMD - Estimating Progression

- AREDS Simple Severity Scale
  - Hyperreflective foci (HFF) in eye
  - SDD drusen ( $\geq 125 \mu\text{m}$ )
  - increasing drusen volume
  - drusen collapse/ooze
- Fellow eye **Arteriovascular AMDs** up to 60% 5-year risk

0	No large drusen pigment char
1	1 point in eit
2	2 total point
3	3 total point
4	4 total point



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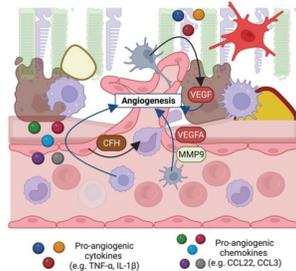
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### Wet AMD - Pathophysiology

- 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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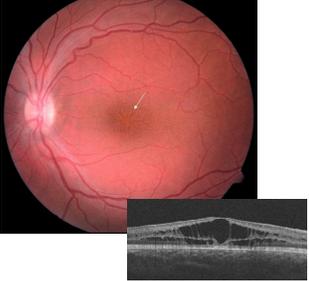
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### Early Onset/Juvenile Macular Degeneration

- 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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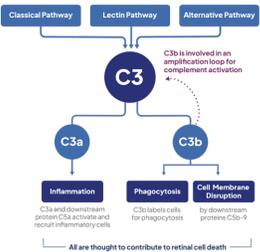
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### Dry AMD: Geographic Atrophy Treatments

- 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



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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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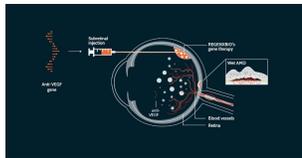
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### Investigational Therapies

- 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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