Retinal Care in Optometry: When to Manage and When to Co-manage

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1

Disclosures

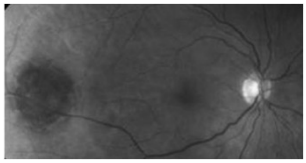
- Consultant or Speaker
- **Speaker bureau/Advisory Board**
  - Apellis/Bigen
  - Astellas
  - Optos
  - Notal Vision
  - Heidelberg
  - LKC
  - Orasis
  - Visible Genomics
  - B&L
  - AbbVie/RGX
  - Alcon Surgical
  - Neurotech

All relevant relationships have been mitigated

2

Clinical Decision Making & Challenges

- Patient has moved to your area and wants to establish with your office and have her contact lenses prescription updates.

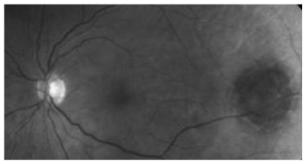


3

3

Clinical Decision Making & Challenges

- How do we decide what to do with this coincidental findings?



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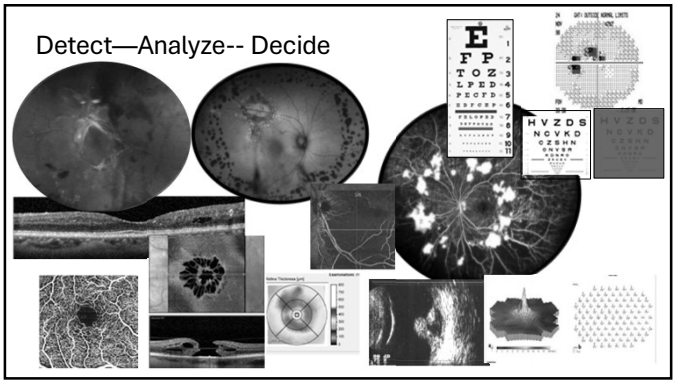
4

What Happened Here? Is it a guessing game or an educated guess?

5

Detect—Analyze-- Decide



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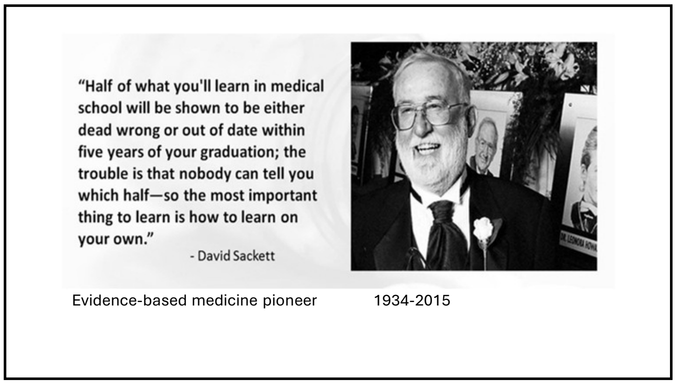
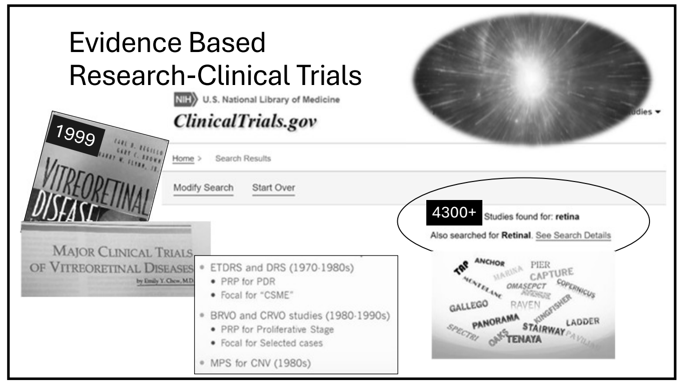

"Half of what you'll learn in medical school will be shown to be either dead wrong or out of date within five years of your graduation; the trouble is that nobody can tell you which half—so the most important thing to learn is how to learn on your own."
- David Sackett
Evidence-based medicine pioneer
1934-2015

8


Evidence Based
Research-Clinical Trials
1999
VITREORETINAL DISEASE
MAJOR CLINICAL TRIALS OF VITREORETINAL DISEASES
U.S. National Library of Medicine
ClinicalTrials.gov
Home
Search Results
Modify Search
Start Over
4300+
Studies found for: retina
Also searched for Retinal. See Search Details
ETDRS and DRS (1970-1980s)
PRP for PDR
Focal for "CSME"
BRVO and CRVO studies (1980-1990s)
PRP for Proliferative Stage
Focal for Selected cases
MPS for CNV (1980s)
ANCHOR
PIER
CAPTURE
OMASPECT
GALLEGO
RAVEN
PANORAMA
STAIRWAY
LADDER
TENAYA

9

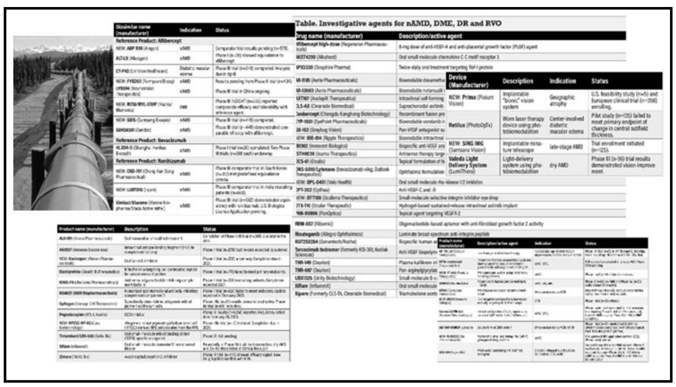
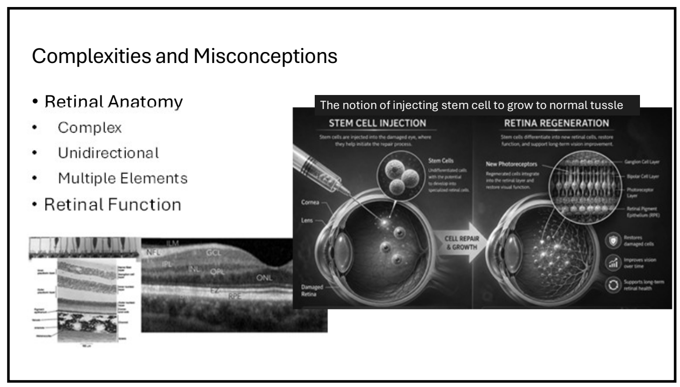
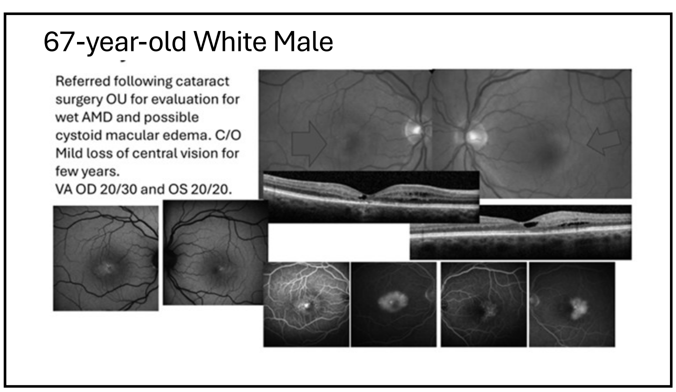


Table. Investigative agents for nAMD, DME, DR and RVO

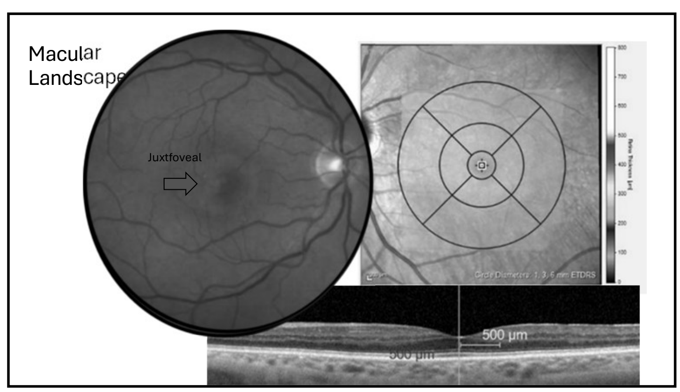
10


Complexities and Misconceptions
• Retinal Anatomy
• Complex
• Unidirectional
• Multiple Elements
• Retinal Function
The notion of injecting stem cell to grow to normal tussle
STEM CELL INJECTION
RETINA REGENERATION
CELL REPAIR & GROWTH

13


67-year-old White Male
Referred following cataract surgery OU for evaluation for wet AMD and possible cystoid macular edema. C/O Mild loss of central vision for few years.
VA OD 20/30 and OS 20/20.

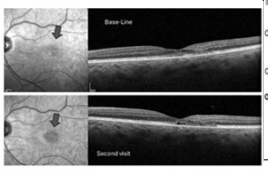
14


Macular
Landscape
Juxtfoveal
500 µm

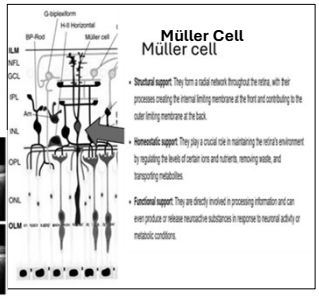
15

The lecture objective is not discussing disease state or treatment. However, this is an important topic.

- MacTel is a rare bilateral, neurodegenerative retinal disease that can lead to vision loss.
- Disfunction of Muller cells reduces the production of neuroprotective factors resulting in loss of photoreceptors



48-Y-O
WF
Loss of EZ
And Vision
In 6 months



16

Old Classification: Gass-Boldi

New Grading

MacTel Type 2 — Multimodal Imaging Classification
MacTel Project Report No. 10 • Chew et al., 2023

MULTIMODAL IMAGING GUIDES SEVERITY

GRADE	ESSENTIAL FEATURE
0	No lesions
1	Noncentral ellipsoid zone (EZ) break
2	Central EZ break
3	Noncentral pigment
4	OCT hyper-reflectivity + EZ break, no pigment
5	Central pigment, no exudative neovascularization
6	Exudative neovascularization ± central pigment

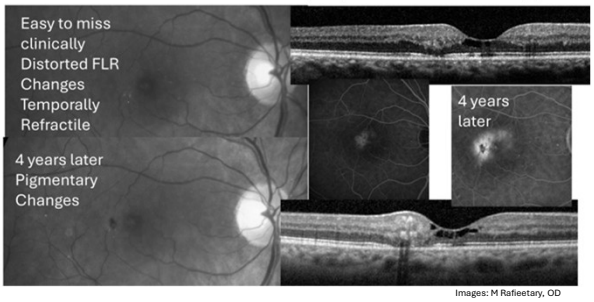
LESS SEVERE → MORE SEVERE

EZ = ellipsoid zone • OCT = optical coherence tomography

Chew EY et al. *Ophthalmology Science*. 2023;3(2):100261.

17

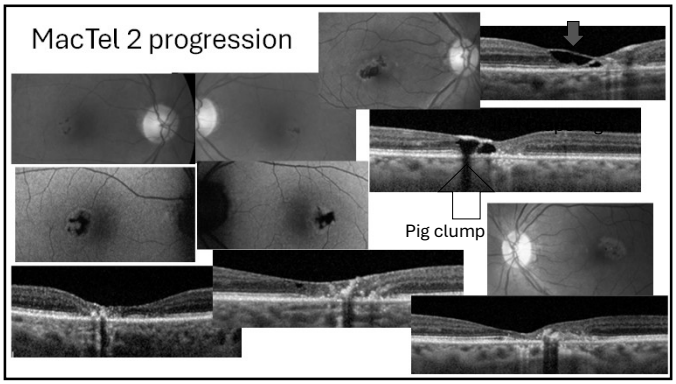
MacTel 2 Presentation (Depends on severity)



Images: M Rafieetary, OD

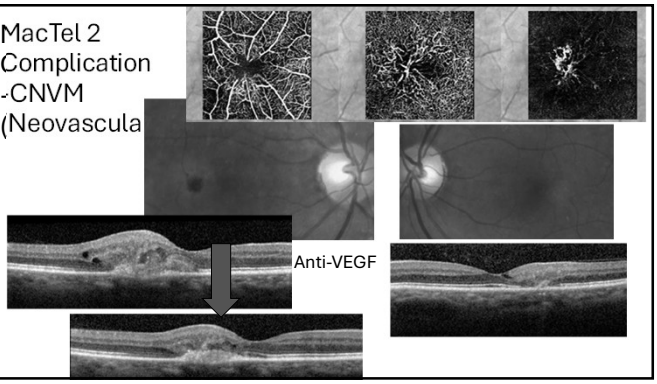
18

MacTel 2 progression



19

MacTel 2 Complication -CNVM (Neovascula



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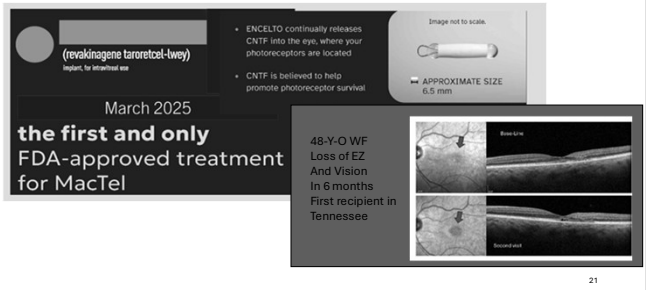
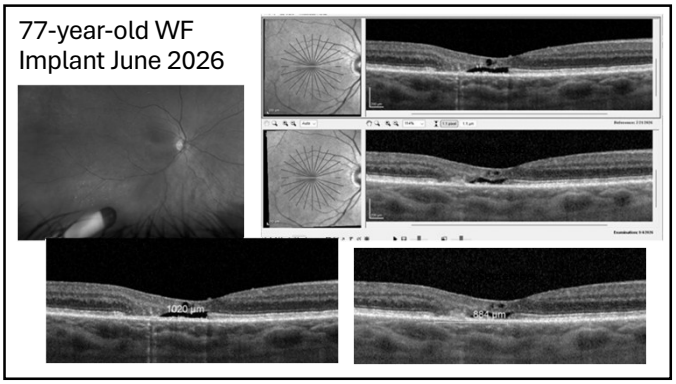


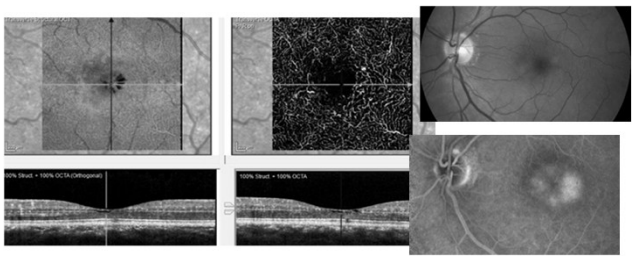
21

77-year-old WF
Implant June 2026



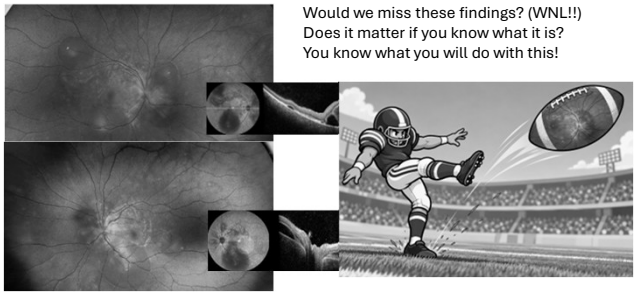
22

Be on the lookout for MacTel 2 it matters more now
It is most likely more common than realized!



23

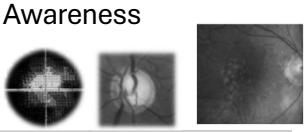
Knowledge Base
Demographic-Diagnostic- Context (18 YO AfAM F recent vision loss)



Would we miss these findings? (WNL!!)
Does it matter if you know what it is?
You know what you will do with this!

24

Awareness



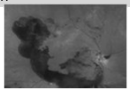
CDC: In 2019, an estimated 19.8 million (12.6%) Americans aged 40 and older were AMD[1]

1.49 million (0.94%) were living with vision threatening AMD (Underestimation)

CDC: In 2022, the CDC estimates that approximately 4.2 million Americans of all ages have glaucoma, with 1.5 million experiencing vision-affecting glaucoma

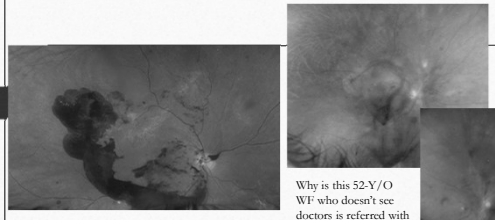
CDC: In 2021 across all ages, an estimated 9.6 million people in the United States were living with diabetic retinopathy (DR). Of these, 1.84 million were living with vision-threatening DR

In the United States, myopia affects a significant portion of the population, with an estimated prevalence of around 40% (136 M)
MYOPIC MAC DEG



25

If so common

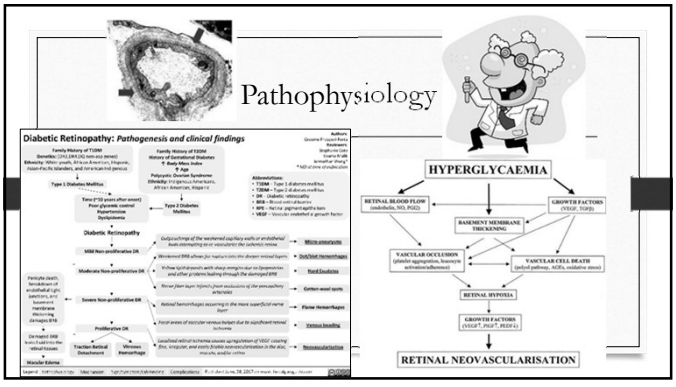


Why should the be the first visit of this 40 Y/O WF?

Why is this 52-Y/O WF who doesn't see doctors is referred with dx of retinitis?

26

Pathophysiology



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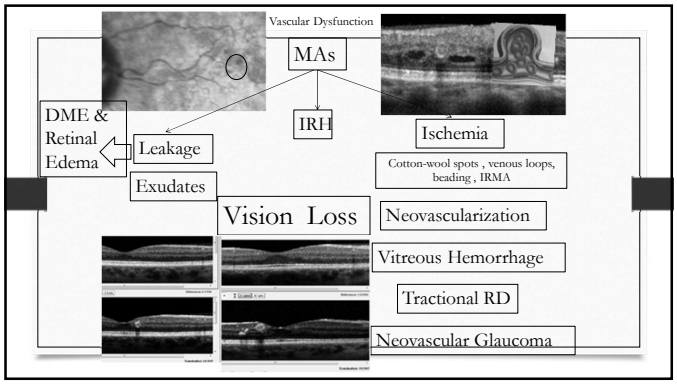

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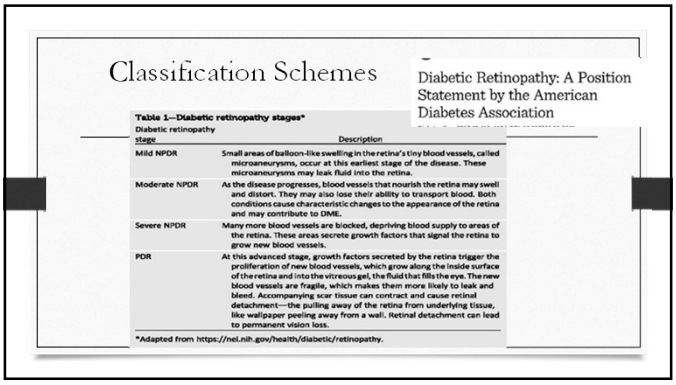

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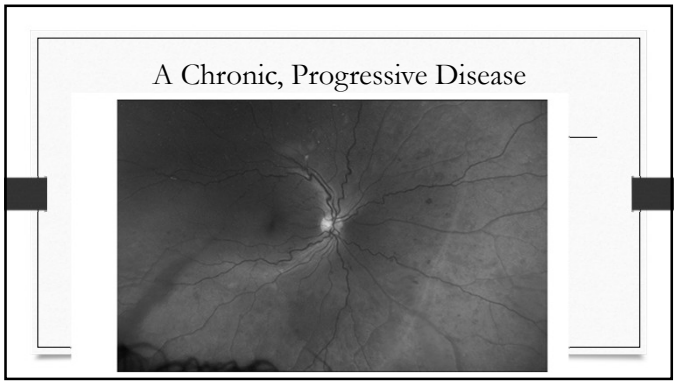

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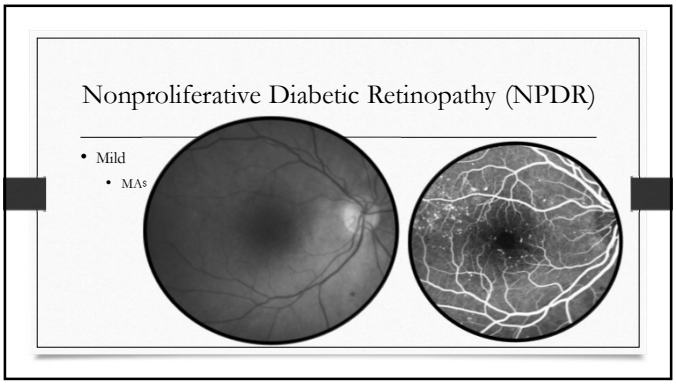

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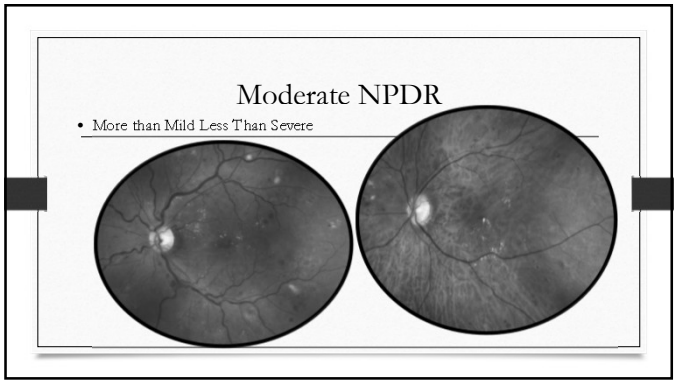

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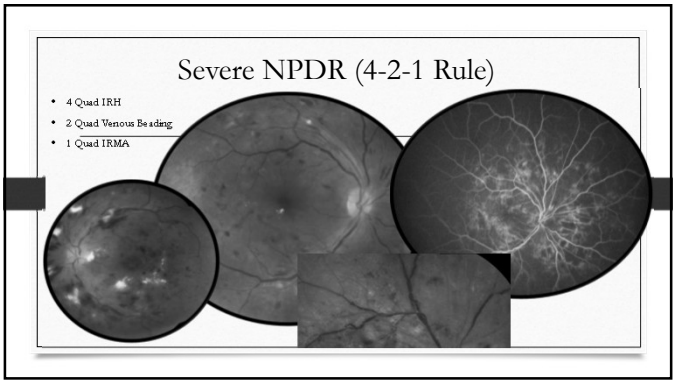
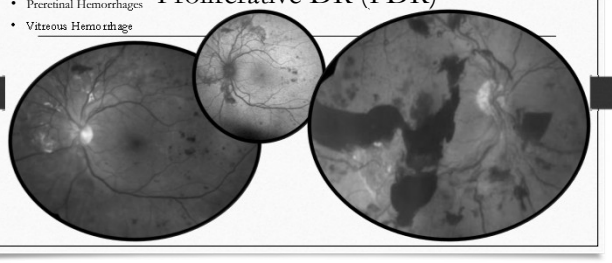


33

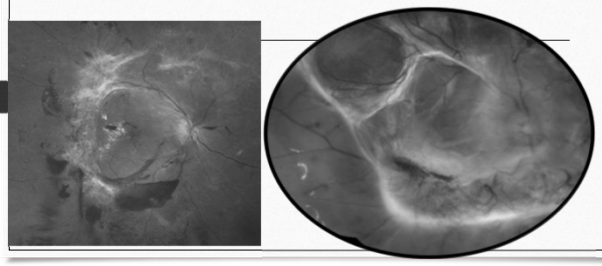
Proliferative DR (PDR)

- Neovascularization
- Preretinal Hemorrhages
- Vitreous Hemorrhage



34

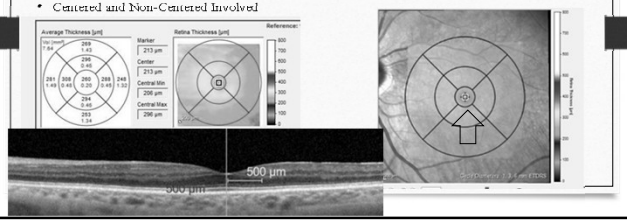
High-risk PDR



35

Diabetic Macular Edema (DME)
No Longer CSME!

- Can be Present at Any Stage of DR (Increased Incidence with DR Progression)
- Centered and Non-Centered Involved



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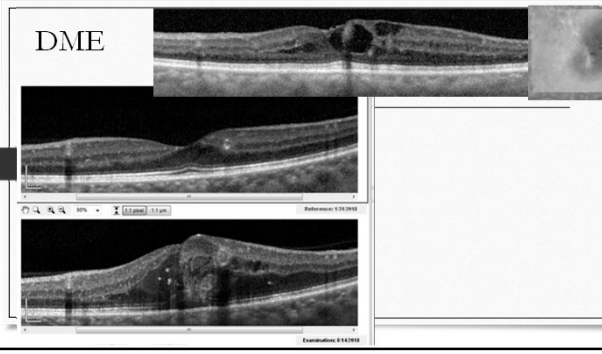
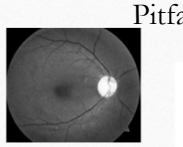
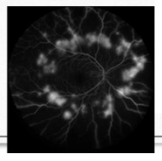
DME

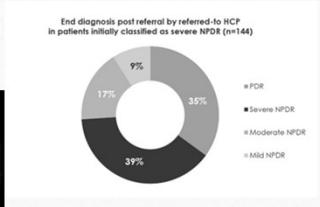


37

Pitfalls of Staging

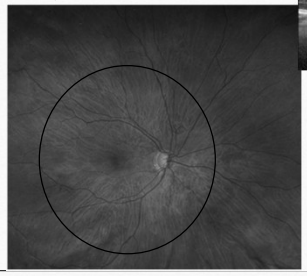


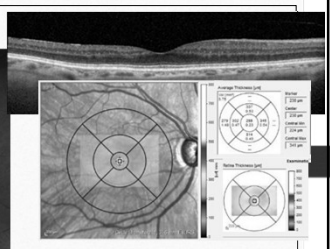




38

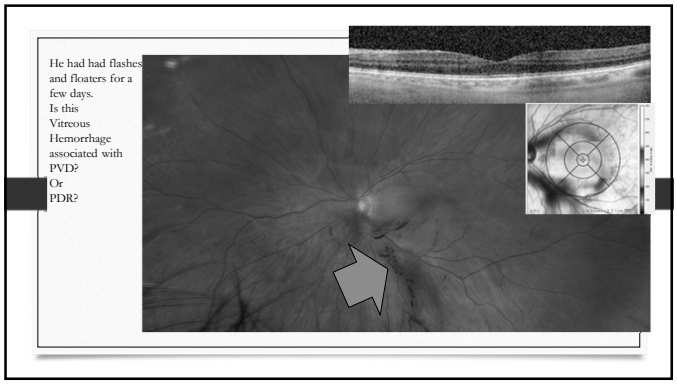
71-year-old WM DM for 43 years, insulin-dependent for last 5 years, well controlled. 20/20





Staging?
None….Mild….Moderate….Severe…PDR?

39



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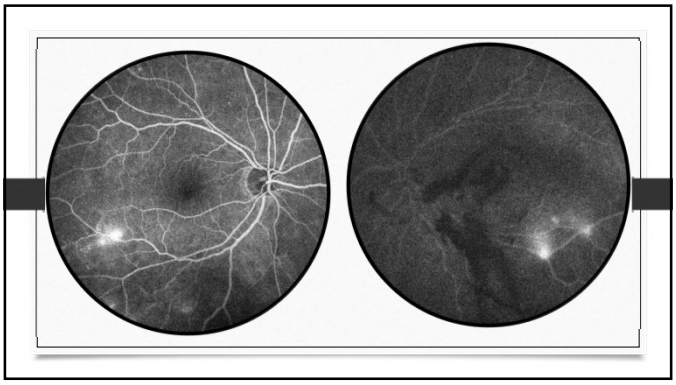

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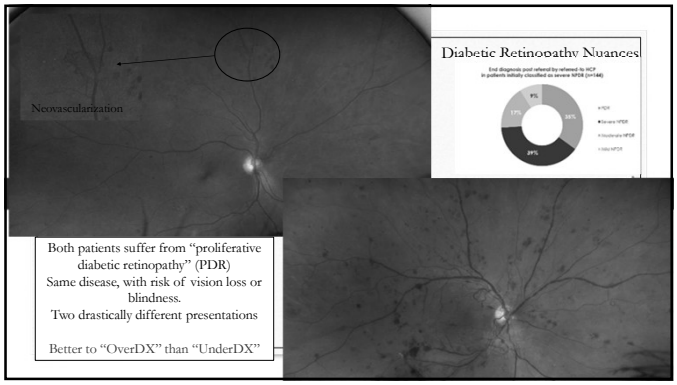

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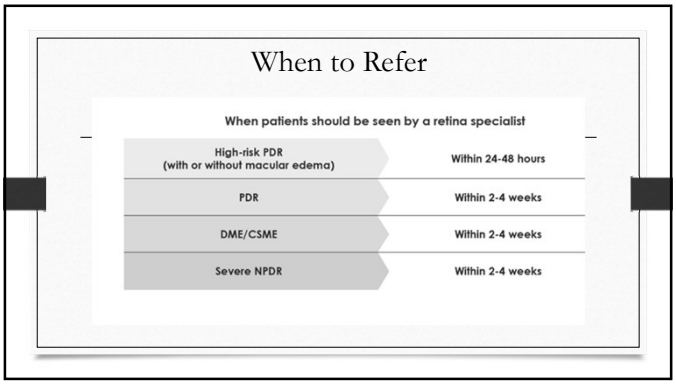

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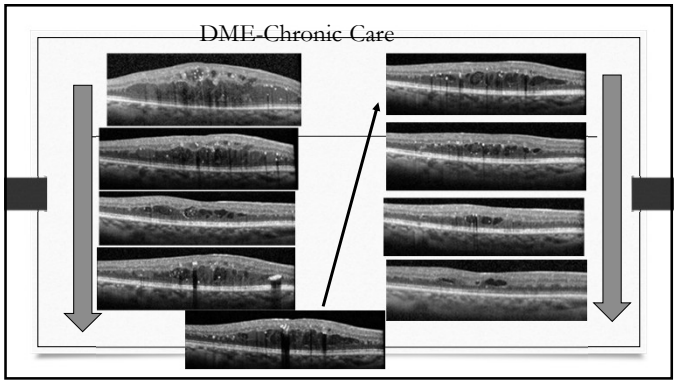

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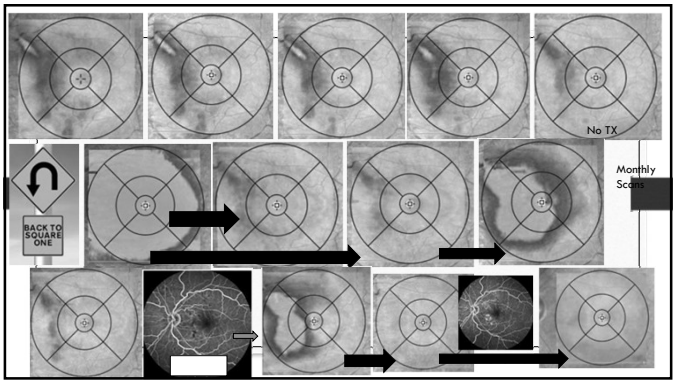

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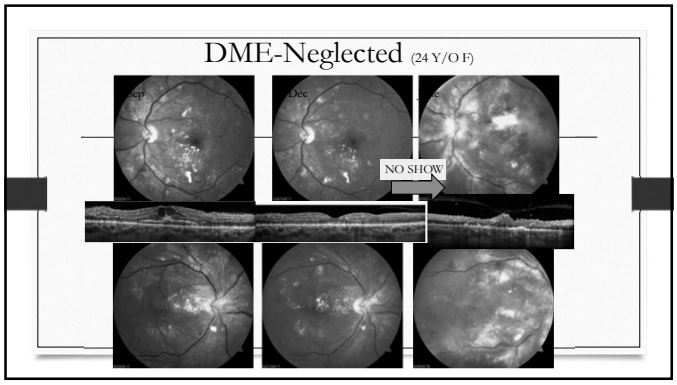

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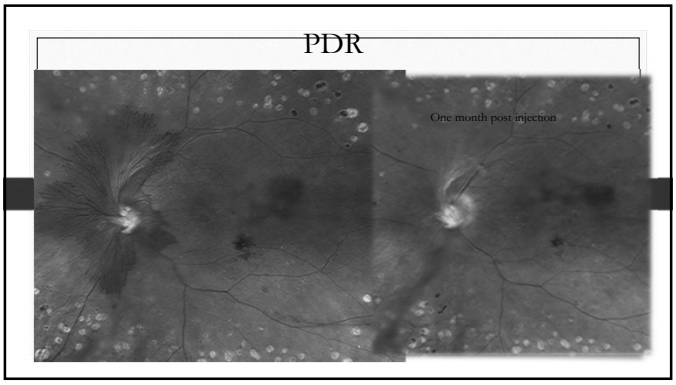

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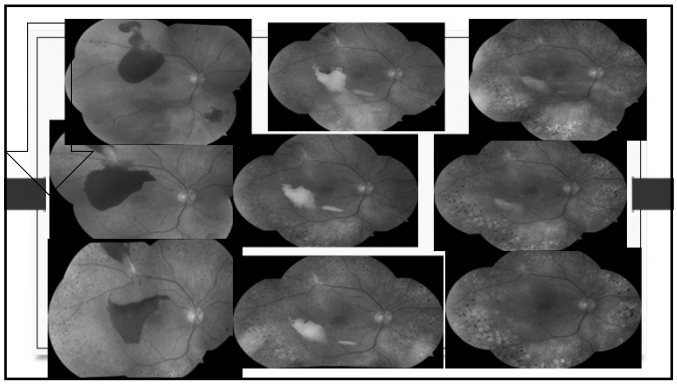

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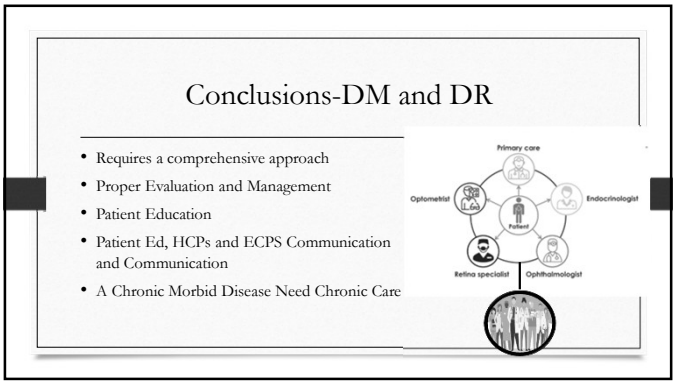

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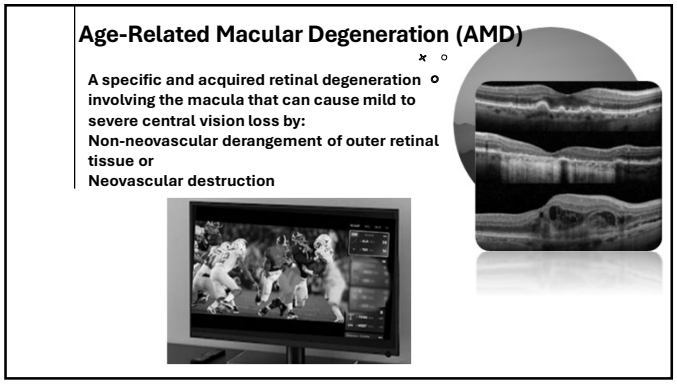

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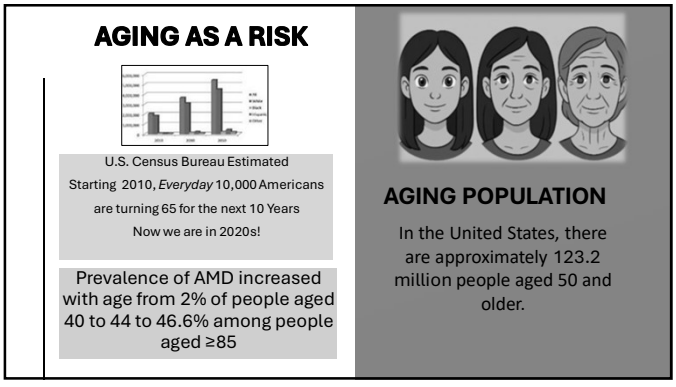


51

OTHER RISK FACTORS

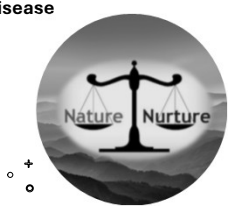
AMD is a Multi-Etiologic Disease

Non-modifiable
Ethnicity
Anatomic and Physiologic Variations
Low macular Pigment, Color or the Iris

Modifiable

Smoking

Dietary Habits
Cardiovascular Disease
Increased BMI
Sleep Apnea
Medications



15 years ago-Aspirin Debate, **Now GLP 1 agonists debate.....**

52

Genetics Factors and of AMD

- Non-Mendelian
- More than 30 genes
- Complement Pathway
  - CFH, CFHR1, CFHR3, C3, C2, CFB, C9, CFI
- Other Pathways
  - ARMS2, TIMP3, ABCA1, APOE, VEGF, FBLN5
- Others
  - HTRA1, CX3CR1, RECC6, FGF2, Y402H

Lung Cancer 8%-15% inherited genetic mutation[1]
Coronary Artery Disease 40%-60%[2]
Type 2 Diabetes 10%-15%[3] (Varies per source)
Colorectal Cancer 5%-10%[4]
AMD 70%[5] (46-71%)

Phenotype probability differs amongst various genotype variations

1) https://ccr.cancer.gov/news/article/genetics-not-just-smoking-influence-small-cell-lung-cancer-risk
2) https://www.ahajournals.org/doi/10.1161/circresaha.115.306566#:~:text=Coronary%20artery%20disease%20(CAD)%20has,4
3) Florez Jcet al. Genetics of Type 2 Diabetes. PMID: 33651556.
4) https://www.cancer.gov/types/colorectal/hp/colorectal-genetics-pdq#:~:text=About%2075%25%20of%20patients%20with,overall.%5B3%2C4%5D
5) Warwick A, Genetics and genetic testing for age-related macular degeneration. Eye (Lond). 2018. PMID: 29125146;PMCID: PMC5944647.

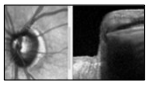
53

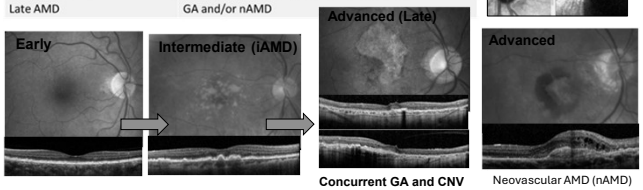
AMD Classification

Beckman Classification

Classification	Clinical Findings
No AMD	No drusen and no RPE abnormalities
Normal aging changes	Drusen ≤ 63 µm and no RPE abnormalities
Early AMD	Drusen > 63 µm and ≤ 125 µm and no RPE abnormalities
Intermediate AMD	Drusen > 125 µm and/or RPE abnormalities
Late AMD	GA and/or nAMD

Drusen Size
Small: < 63 µm
Medium: 64 – 124 µm
Large: > 125 µm



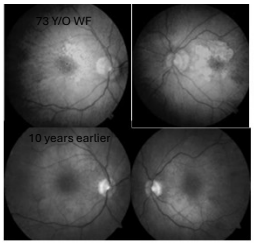


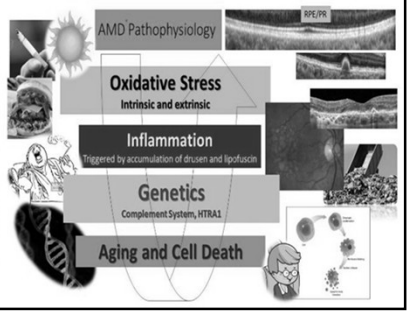
Concurrent GA and CNV

Neovascular AMD (nAMD)

54

Pathogenesis of Progression



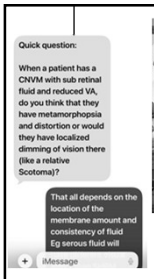


55

How do we diagnose AMD

- Consideration
  - Pre-Clinically Evident
  - Early.....to.....late
- Based on
  - Presenting HX, Symptoms
  - Risk Assessment

56



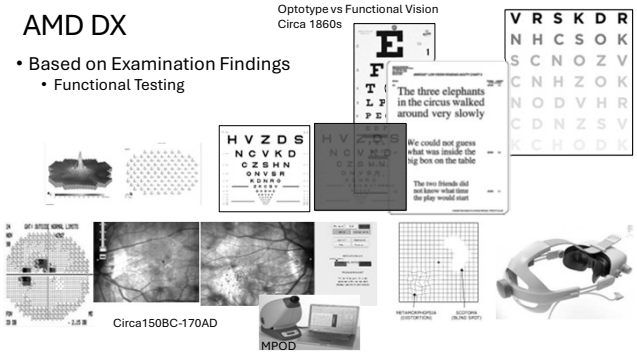
Metamorphopsia is a form of distortion
Distortion = blurry, stretched vision
Metamorphopsia = bent lines
Scotoma is a blind spot
Dimming is seeing dark
Ultimately "vision" is a primary sense like any other of our senses the experience can differ from one person to another

57

AMD DX

- Based on Examination Findings
  - Functional Testing

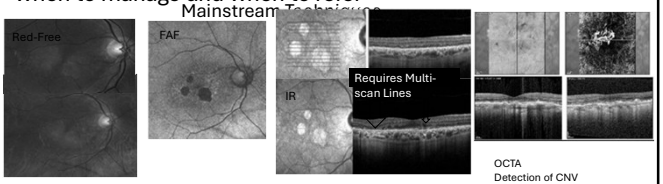
Optotype vs Functional Vision
Circa 1860s



59

Diagnosis-Utilization of Imaging Technologies help us to know when to manage and when to refer

Mainstream Technique



OCTA
Detection of CNV

Color Fundus Photography (CFP)
(+)Most Commonly Available
(+)Documentation
(±)Image Manipulation (Red-Free)
(-)Early Lesions Difficult to Detect
(-)No prognostic Value

Fundus Autofluorescence (FAF)
(+) Diagnostic Value
(+) Prognostic Value
(-)Availability
(-)Familiarity

Enface
Infrared (IR) or Near (NIR)
(+)Early detection of drusen and reticular pseudodrusen (RPD)
(+) Early GA detection
And serial follow-up
(-)Device Dependent

OCT
(+)Pre-GA
(+)GA
(+)CNV
(+)(+)(+)
(-)Interpretation skill

60

OCT-the work horse

Literature Search Points to OCT, as being the most used technology for diagnosis of AMD

RESEARCH ARTICLE

Optical coherence tomography and color fundus photography in the screening of age-related macular degeneration: A comparative, population-based study

Edoardo Midena[1,2]*, Luisa Frizziero[2], Tommaso Torresin[1], Paolo Boscolo Todaro[1], Giacomo Miglionico[1], Elisabetta Pilotto[2]

1 Department of Ophthalmology, University of Padova, Padova, Italy, 2 IRCCS-Fondazione Bietti, Rome, Italy

* edoardo.midena@unipd.it

Conclusion: OCT provided gradable images in almost all examined eyes, compared to limited CFP efficiency. Moreover, OCT images allowed to detect more AMD eyes compared to gradable photos. OCT imaging appears to significantly improve the power of AMD screening in a general, unselected population, compared to CFP alone.

Midena E, et al . Optical coherence tomography and color fundus photography in the screening of age-related macular degeneration: A comparative, population-based study. PLoS One. 2020 Aug PMID: 32797085; PMCID: PMC7428158.

61

Regardless, AMD is often undiagnosed

- Neely et al. Evaluated the prevalence of undiagnosed AMD in primary eye care setting
- 1288 eyes from 644 patients

75%
No AMD per medical record (n=968)

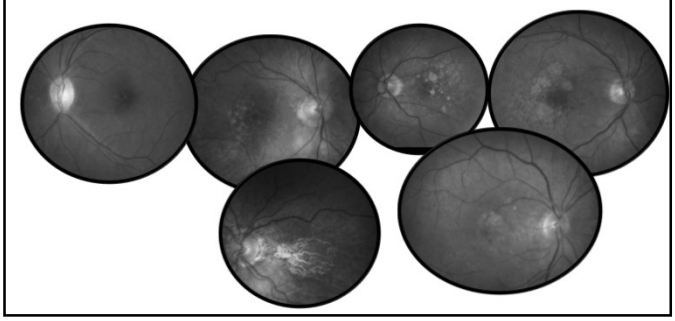
24.8%
AMD despite no diagnosis in medical record (n=320)

30% large drusen
10% hyperpigmentation
13.4% hypopigmentation
77.8% small drusen
78.1% intermediate drusen

Reference: Neely DC, et al. *JAMA Ophthalmol*. 2017;135(6):570-575.

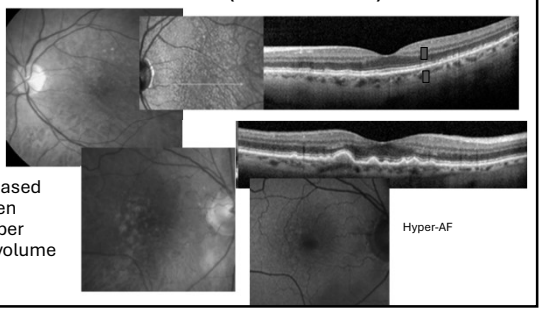
62

Challenges Clinical Diagnosis and Course of AMD



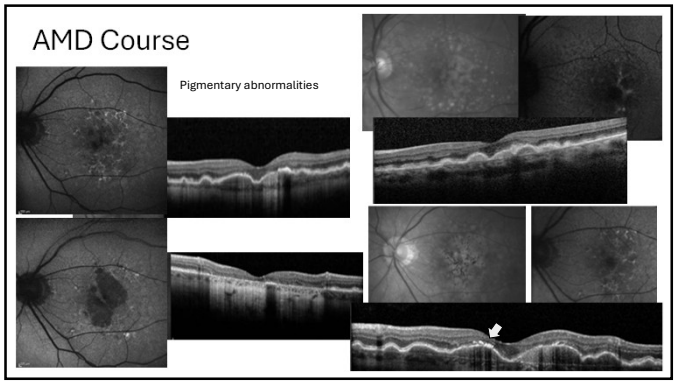
63

Progression Indicators (Biomarkers)



- Increased drusen number and volume

64



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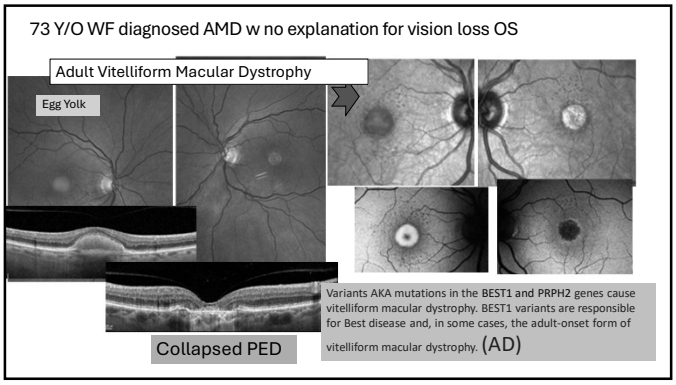

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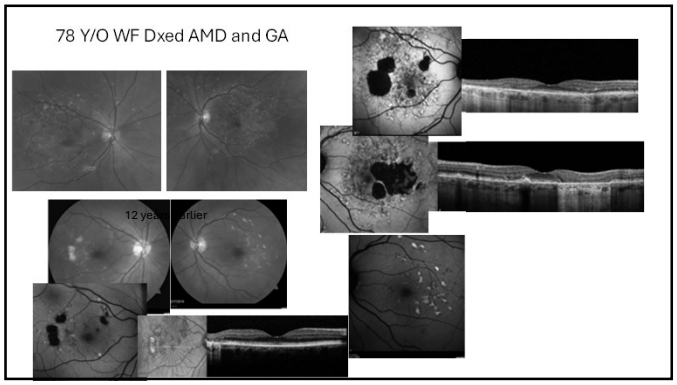

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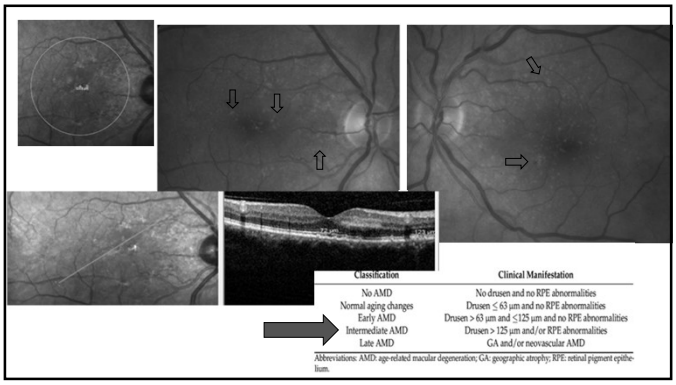

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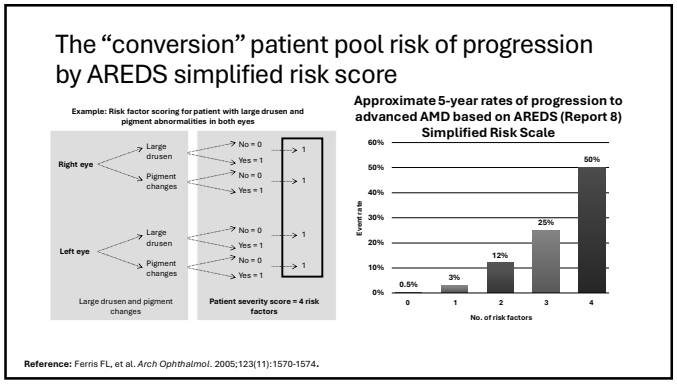

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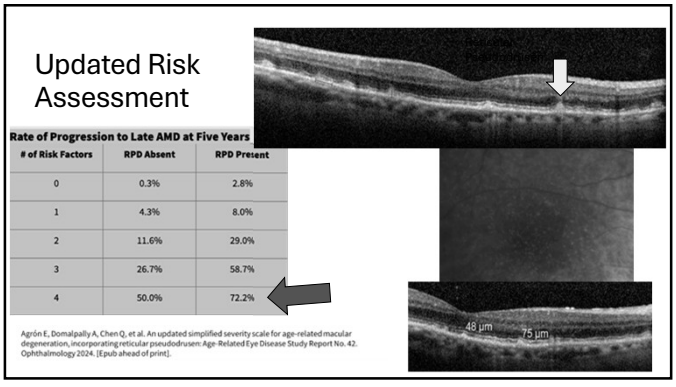
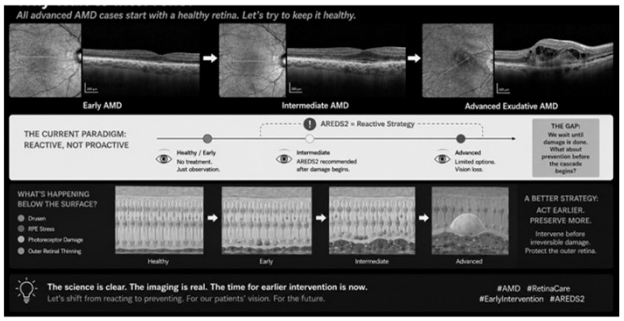


70

Reactive Management



71

AMD Management

- Atrophic or Dry AMD
  - Smoking Cessation
  - Management of Comorbidities
  - Nutrition and Supplements
  - **Low Vision Rehabilitation******
  - Patient Education and Proper Follow-up Care
- GA an Advanced form of dry AMD- TX
- Wet or nAMD
  - Intravitreous Anti-VEGF
    - Various Agents
  - PDS
  - In the pipeline (including gene therapy)

72

AREDS (2001):

Studied patients with intermediate or advanced AMD

Formulation:

Vitamin C (500 mg), Vitamin E (400 IU), Beta-carotene (15 mg), Zinc (80 mg) + Copper (2 mg)

Outcome:

↓ 25% risk of progression to advanced AMD over 5 years

AREDS2 (2013):

Tested modifications to improve safety and efficacy

Changes Tested:

Replaced beta-carotene with lutein (10 mg) & zeaxanthin (2 mg)

Added omega-3 fatty acids (DHA/EPA)

Outcome:

Lutein/zeaxanthin = safer alternative (↓ lung cancer risk in smokers)

Omega-3s = no added benefit

Zinc: 25 mg vs. 80 mg → no significant difference

Recommended for patients with intermediate or advanced AMD

Or patients who has advanced one eye

AREDS2 10-year assessment

Adding Lutein/Zeaxanthin to the original formula provided a 10% additional reduction in progression to late AMD

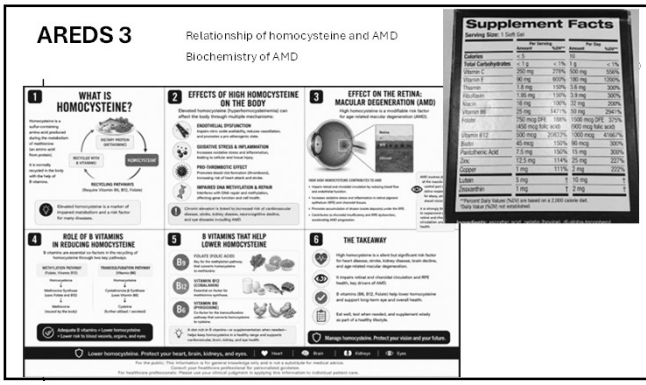
Avoid beta-carotene in smokers or former smokers

73

AREDS 3

Relationship of homocysteine and AMD

Biochemistry of AMD



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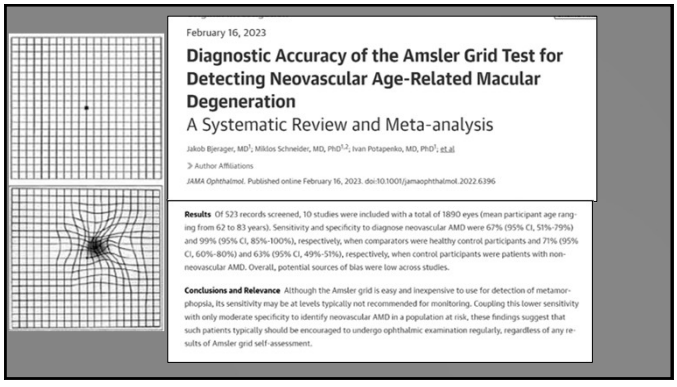


February 16, 2023

Diagnostic Accuracy of the Amsler Grid Test for Detecting Neovascular Age-Related Macular Degeneration

A Systematic Review and Meta-analysis

Jakob Bjerager, MD[1]; Miklos Schneider, MD, PhD[1,2]; Ivan Potapenko, MD, PhD[3]; et al

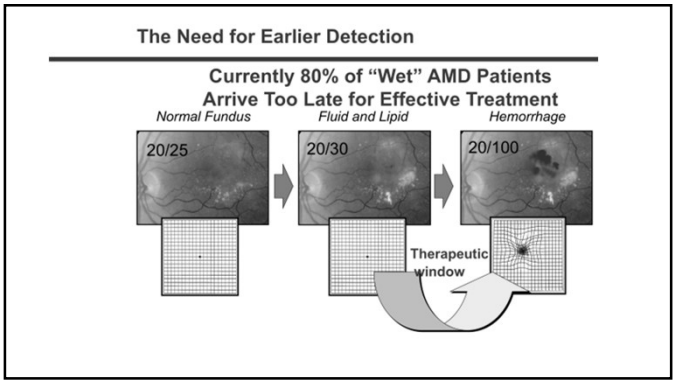
Author Affiliations

JAMA Ophthalmol. Published online February 16, 2023. doi:10.1001/jamaophthalmol.2022.6396

Results Of 523 records screened, 10 studies were included with a total of 1890 eyes (mean participant age ranging from 62 to 83 years). Sensitivity and specificity to diagnose neovascular AMD were 67% (95% CI, 51%-79%) and 99% (95% CI, 85%-100%), respectively, when comparators were healthy control participants and 71% (95% CI, 60%-80%) and 63% (95% CI, 49%-51%), respectively, when control participants were patients with non-neovascular AMD. Overall, potential sources of bias were low across studies.

Conclusions and Relevance Although the Amsler grid is easy and inexpensive to use for detection of metamorphopsia, its sensitivity may be at levels typically not recommended for monitoring. Coupling this lower sensitivity with only moderate specificity to identify neovascular AMD in a population at risk, these findings suggest that such patients typically should be encouraged to undergo ophthalmic examination regularly, regardless of any results of Amsler grid self-assessment.

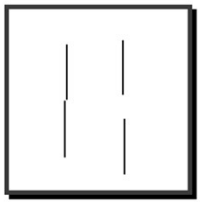
75



76

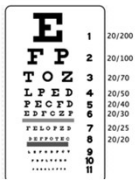
PHP
Preferential
Hyperacuity
Perimeter

Hyperacuity



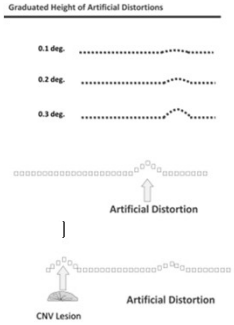
Vernier Resolution (hyperacuity)

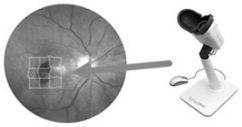
- Two seconds of arc
- 0.03 minutes of arc
- 0.00051 degrees
- **The width of a pencil viewed at 300 m !**



Snellen 20/15 Resolution (standard acuity)
1minute of arc
0.017 degrees

77

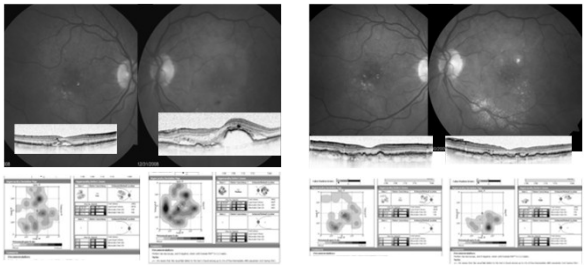




Preferential Hyperacuity Perimetry (PHP) identifies visual distortions caused by, but not limited to, conversion from dry to wet AMD

78

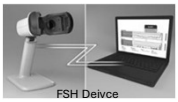
Case Examples Pre- Post- TX

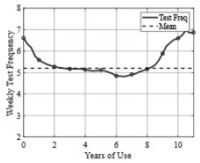


80

Long-term visual outcomes of patients supported by remote monitoring model – ALOFT Study[1]

- Multicenter Study
- 2123 patients 3,334 eyes
  - Mean (SD) of 5.2 weekly tests
- 10 years testing period >1 million tests
- 285 eyes converted to nAMD
  - 52% detected by FSH, 48% symptoms or scheduled visit
  - Mean 6.4 injections per year SD=3.1
- Non-CNV Alerts- every 4.6 years per patient

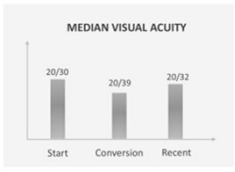

FSH Deivce



[1]Mathai M., et al. Analysis of the Long-term visual Outcomes of ForeseeHome Remote Telemonitoring - The ALOFT study, *Ophthalmology Retina*. (2022)

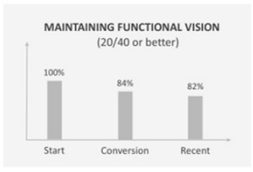
81

ALOFT Study: Visual Acuity Results



Median VA

- Start **of** program – 20/30
- nAMD conversion detected – 20/39
- M**ost recent** visit – 20/32

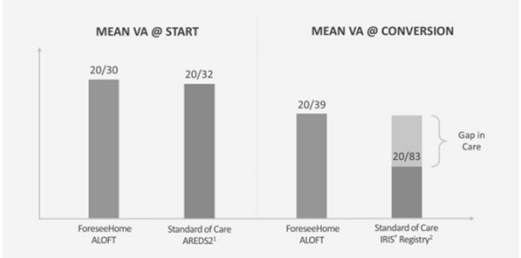


Patients at start with ≥20/40

- Maintaining 20/40 at conversion – **84%**
- Maintaining 20/40 at recent visit – 82%

82

Visual Acuity Results: Comparing ALOFT w/ Standard of Care



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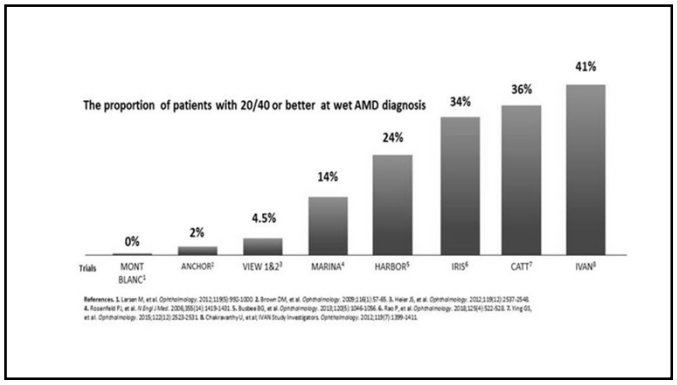

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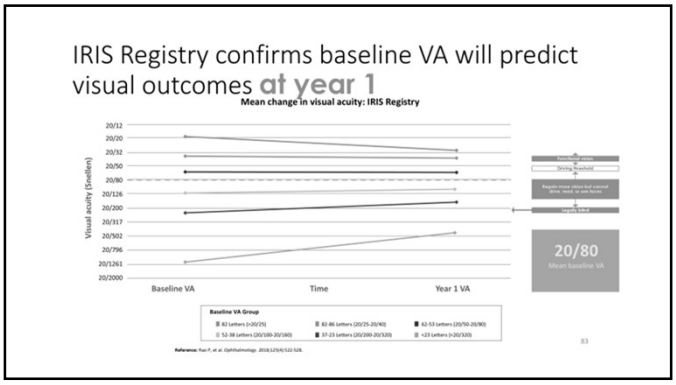

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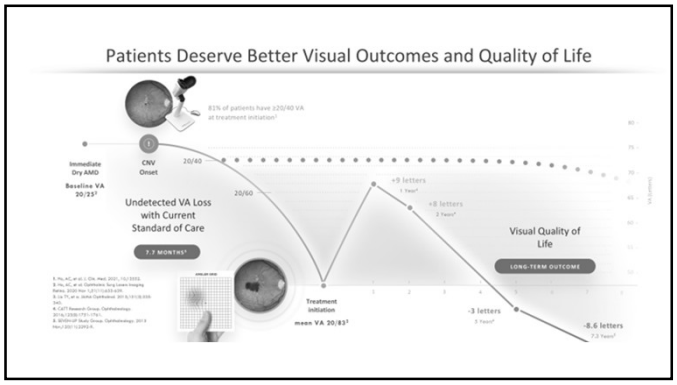

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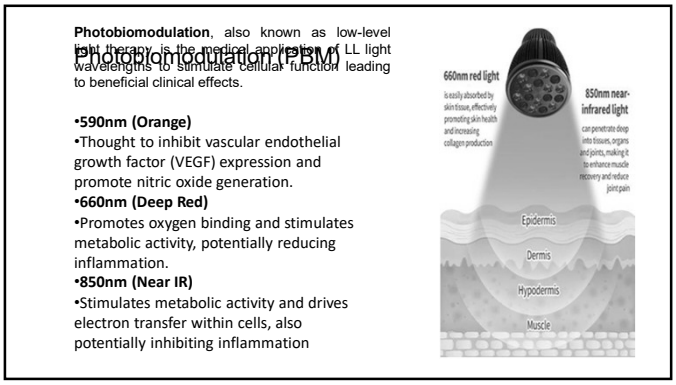

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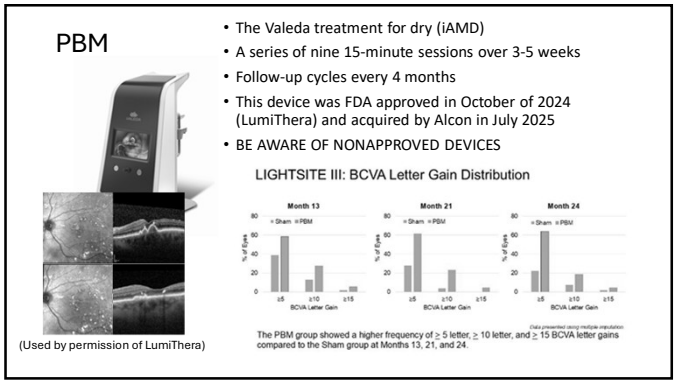
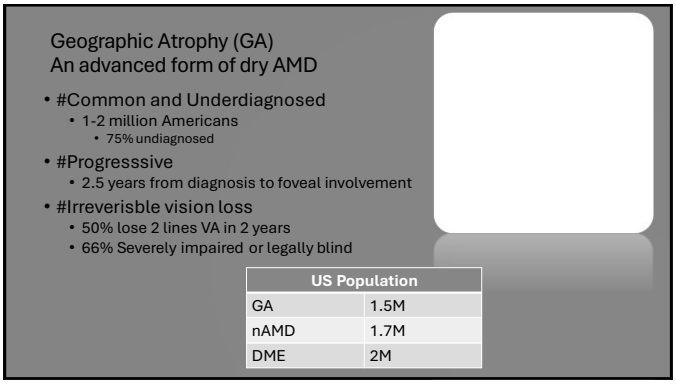


(Used by permission of LumiThera)

88



US Population	
GA	1.5M
nAMD	1.7M
DME	2M

89

EFFECT ON ACTIVITIES OF DAILY LIVING

GA progression harms multiple aspects of your patients' lives[3*]

Patients report GA has a moderate to major negative impact on:

74% Driving

68% Reading

~1 in 5 GA patients become legally blind in their better-seeing eye within 1 year[2]

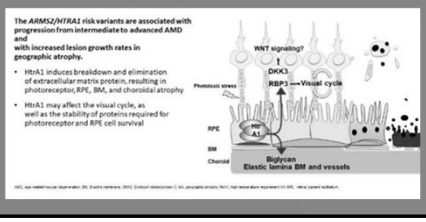
Progression to VA 20/200 or worse at 1 year in better-seeing eyes, % (n/N)[1]

Bilateral GA	Unilateral GA
19.6% (1510/7707)	19.4% (1076/5560)

90

Risk Factors

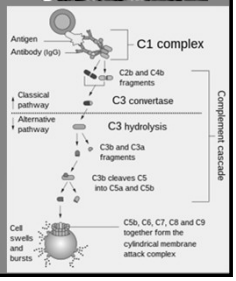
- Aging
  - 4X incidence/10 years after 50 Y/O
- Smoking, poor diet
- Comorbidities: Obesity HTN, Lipid disorders, Sleep Apnea
- Genetics



91

Complement Factor

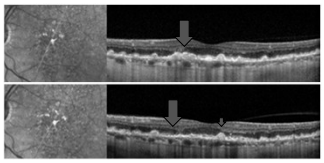
Complement Cascade (System)
-A part of the innate immune system
-A complex biological system
Composed of several proteins and regulators
-Always active, functioning to remove pathogens and biological debris
-Overactivation by aging, disease or **genetic variation** can be damaging to normal tissue biological

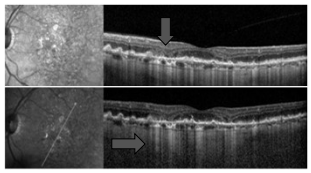


92

OCT- GA Predictors and Biomarkers

- Multiple predictive factors for the development of GA
  - Drusen and pigment epithelial detachment (PED) to Incomplete- (iRORA) and Competed retinal pigment epithelial and outer retinal atrophy (cRORA)

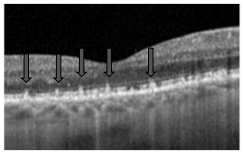


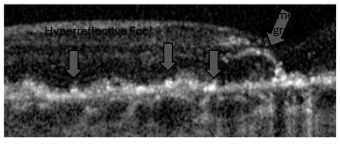


93

OCT- GA Predictors and Biomarkers

- Reticular Pseudodrusen (RPD)
- Hyperreflective Foci and Columns
- Hyperreflective and Hypertransmission Columns



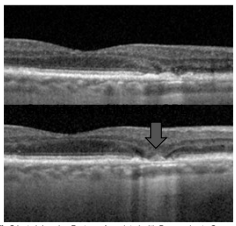


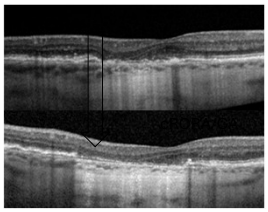
Images: Mohammad Rafieetary, OD

94

OCT- GA Predictors and Biomarkers

- Nascent GA-detected by Subsidence of Inner Retinal Layers



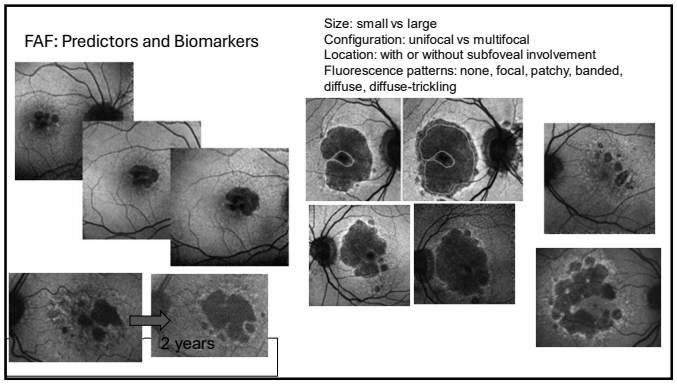


Jaffe GJ, et al. Imaging Features Associated with Progression to Geographic Atrophy in Age-Related Macular Degeneration: Classification of Atrophy Meeting Report 5. Ophthalmol Retina. 2021 Sep;5(9):855-867. doi: 10.1016/j.oret.2020.12.009. Epub 2020 Dec 22. PMID: 33348085.

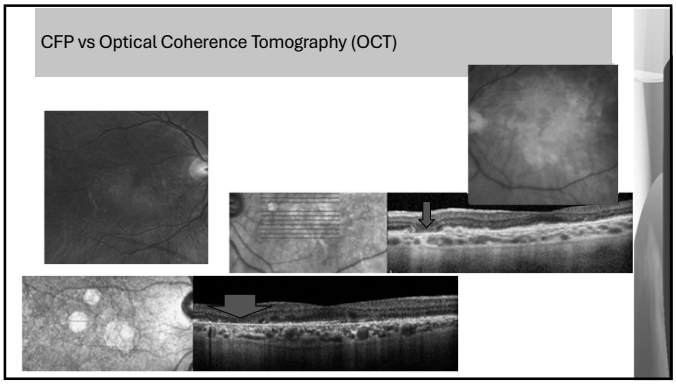
Fleckenstein M, et al. The Progression of Geographic Atrophy Secondary to Age-Related Macular Degeneration. Ophthalmology. 2018 Mar;125(3):369-390.

Images: Mohammad Rafieetary, OD

95



96



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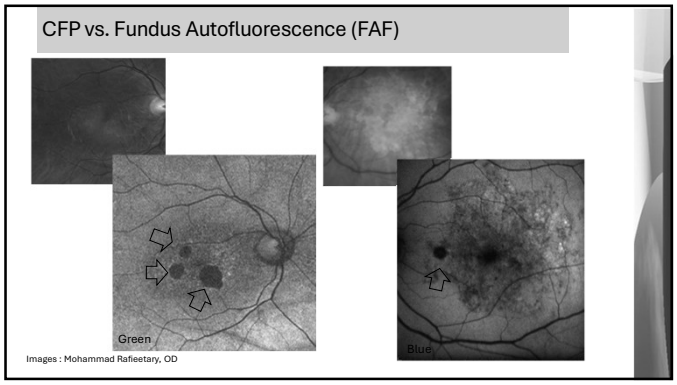

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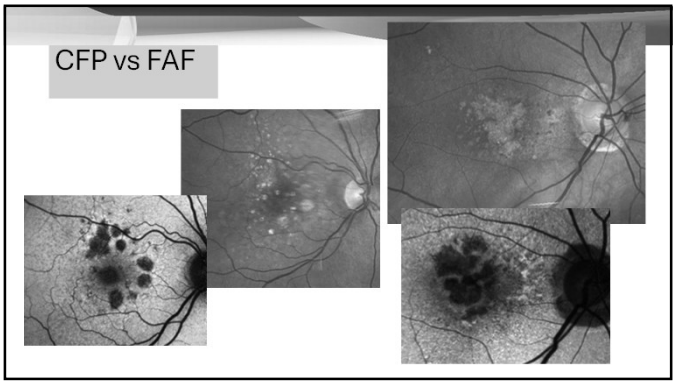

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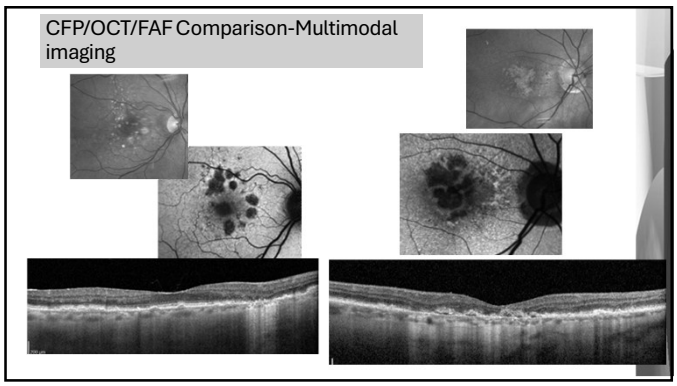

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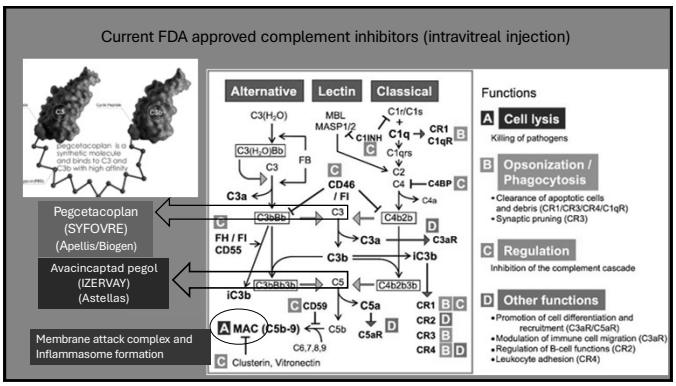
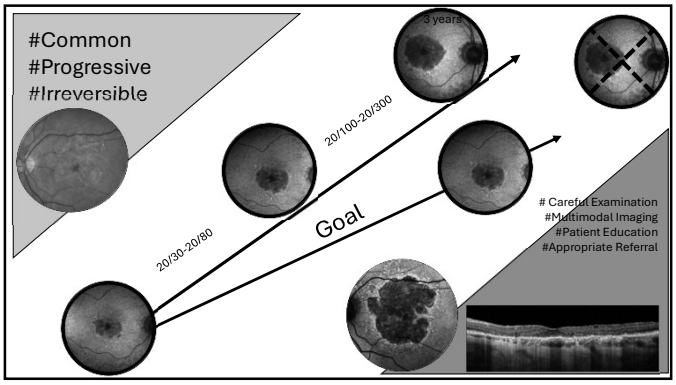


103

CLINICAL TRIAL INFORMATION

104



105

FINAL THOUGHTS

AMD is a commonly encountered condition is optometric practices.

We should use our knowledge, experience, tools and evidenced based information to diagnose and manage patients with this potentially debilitating disease as best as possible.

Thank you!

106