

Age-Related Macular Degeneration

Albert O. Edwards, M.D., Ph.D.

Institute for Retina Research

Presbyterian Hospital of Dallas

Dallas, Texas

www.dallasretina.com

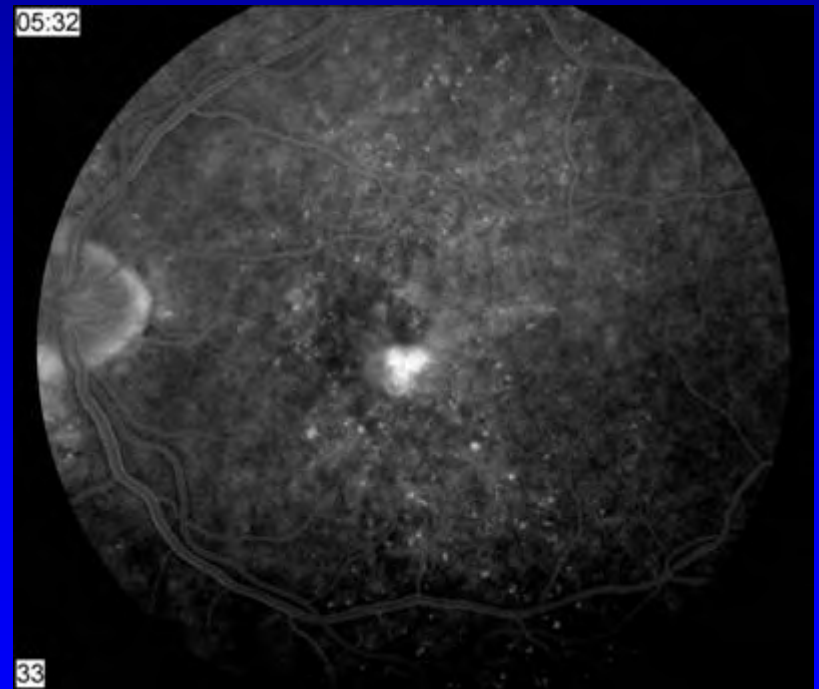
www.irrdallas.org

Case 1

- 58 year-old man
- Exudative AMD diagnosed 4/8/05
- Previous therapy:
 - Laser photocoagulation
 - Photodynamic therapy
- Now has persistent exudation and visual acuity of 20/70

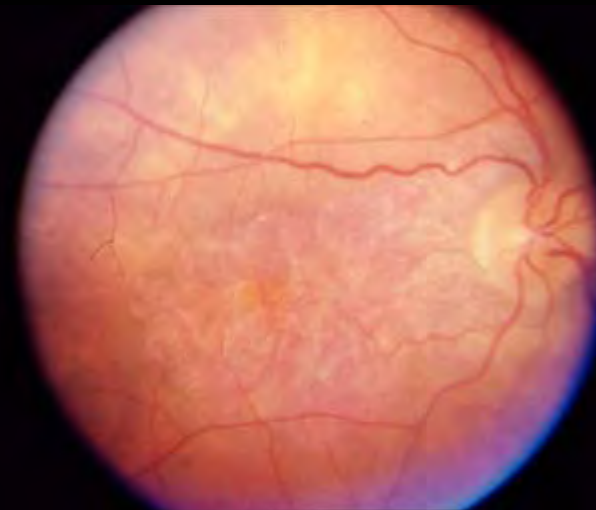
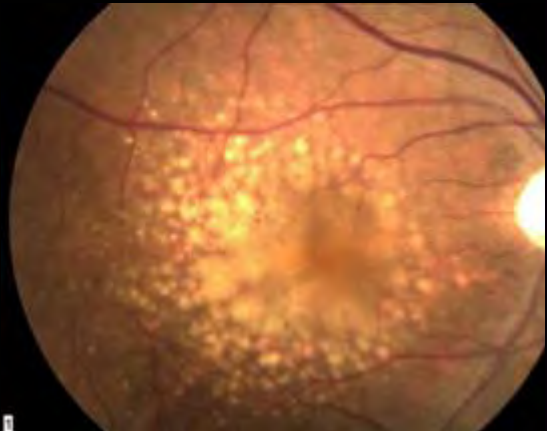


Recent Fluorescein Angiogram





AMD Classification
Early: Drusen, Pigment changes
Late: Atrophy, Exudation



Hypothesis

Causes/Risk Factors for Tissue Injury

Sunlight, Lipofuscin, Anti-retinal antibodies, Excessive complement activation, Systemic inflammation



Excessive Activation of Complement



Maculopathy

Bruch's membrane deposits, drusen, RPE changes, decreased blood flow, hypoxia, inflammatory mediators



Disease Phenotype

Vision loss, Atrophy, Exudation

↑ Genetic and Environmental modifiers ↓

Management of AMD: Overview

Feature	Prevention		Treatment
	Clinical Trial	Epidemiology	
Early	None	<ul style="list-style-type: none"> - Diet - Environment 	None known
Atrophy	AREDS	None known	None known
Exudative	AREDS	<ul style="list-style-type: none"> - Diet - Environment - Lifestyle 	<ul style="list-style-type: none"> - Hot laser - PDT - Anti-VEGF



AMD Eligibility Categories

1. Less than 5-15 small drusen
2. Over 15 small drusen, one intermediate drusen, or pigment
3. About 20 intermediate or one large drusen, or noncentral GA
4. Central GA, CNV, or vision $<20/32$ from AMD in fellow eye



Advanced AMD

Treat the Fellow Eye

Risk of progression at 5 years:

- Category 3: 6%-27%
- Category 4: 43%

Treat High-Risk Patients

Reduction in progression to advanced AMD with Moderate VA loss:

- Category 3: OR = 0.76
- Category 4: OR = 0.52

Bottom Line:

Overall 25% Reduction in development of advanced AMD in category 3 and 4 subjects taking supplements

AMD Prevention: Summary I

- Medical and surgical management
 - AREDS supplements only proven method for preventing complications of AMD in high-risk patients
 - Perform cataract surgery when clinical evidence suggests substantial visual benefit to patient
- Environment
 - Avoid cigarette smoking (multiple studies)
 - Wear protection against sunlight exposure (possible)

AMD Prevention: Summary II

Life style for prevention of AMD

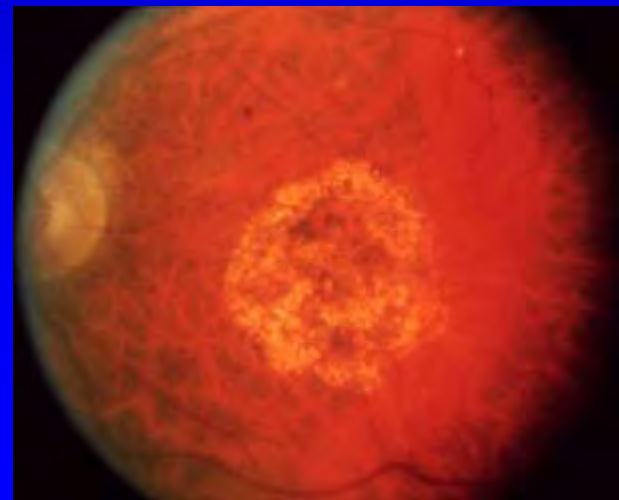
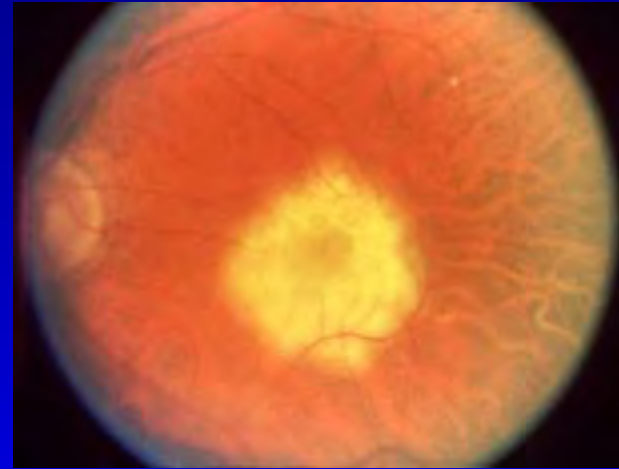
- Heart Healthy Diet
 - Low fat diet (incidence and case-control)
 - Fatty fish > 2 servings per week (4 studies)
 - Leafy green vegetables (some studies)
 - Fruit 3 servings per day (unconfirmed)
 - Consider 2 or more servings of nuts per week (unconfirmed)
- Physical activity (unconfirmed)
- Weight loss (unconfirmed)

Treatment Options for Subfoveal CNV

Extrafoveal and most juxtafoveal
CNV can be managed with
photocoagulation

Laser Photocoagulation

- Thermal burn destroys retina, RPE, choriocapillaris, and CNV
- Cost effective treatment option for extrafoveal CNV and subfoveal CNV with poor initial vision



Photodynamic Therapy

- Photochemical reaction induced by activating verteporfin with 689 nm (red) light
- Relatively greater retention of drug to CNV gives some selectivity to surrounding tissue

Macugen

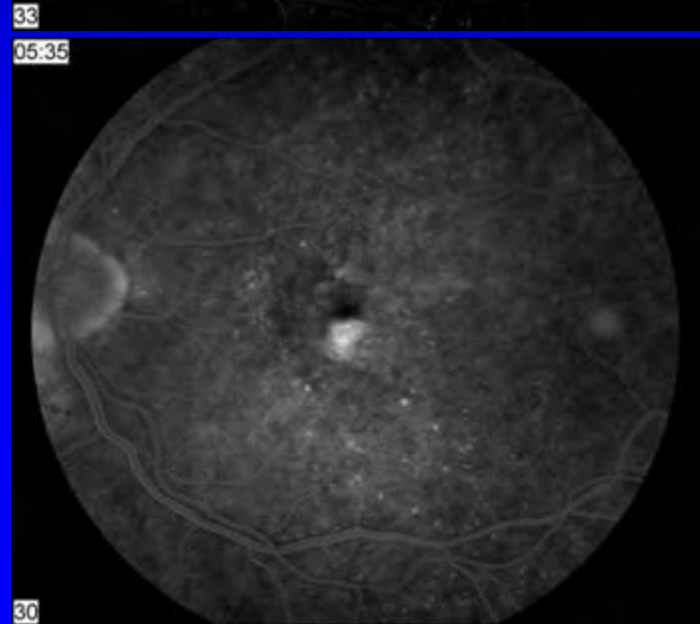
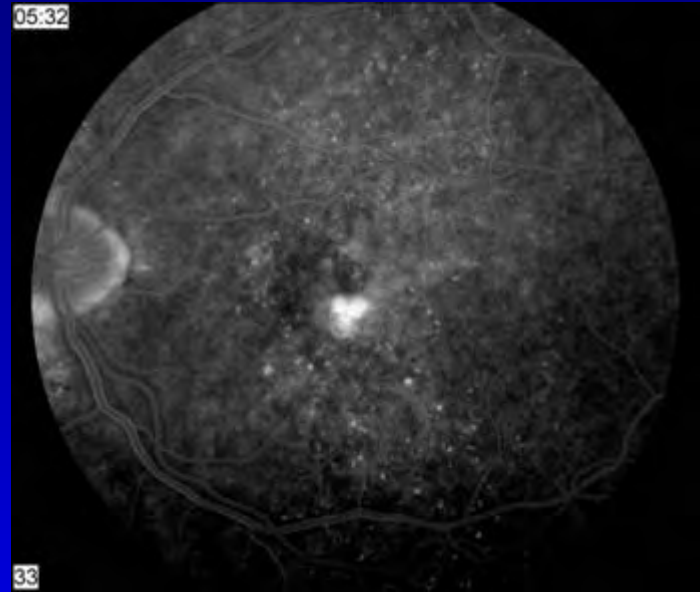
- Pegaptanib: binds extracellular isoform of VEGF (165) up-regulated during pathologic neovascularization
- Does not inhibit revascularization

Lucentis/Avstin

- Ranibizumab: a Recombinant, humanized Fab fragment against VEGF
- Binds all isoforms of VEGF
- Penetrates through all retinal layers unlike full IgG molecule

Returning to our Patient: PL

- Medical Management
 - AREDS
 - Fatty fish
 - Stopped smoking
- Surgical Management
 - Avastin injection
 - Vision improved to 20/30 within 6 weeks



Management of AMD: Current Suggestions

Feature	Prevention		Treatment
	Clinical Trial	Epidemiology	
Early	None	-Fatty fish -Heart healthy diet and lifestyle	None known
Atrophy	AREDS: -Vit C 500 mg -Vit E 400 IU -B-carotene 15 mg -Zinc 80 mg	None known	None known
Exudative		- Fatty fish -Heart healthy diet and lifestyle -Statins?	Lucentis