Diabetic Retinopathy for the Family Doctor

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Denver, CO

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48th Annual Winter Refresher Course

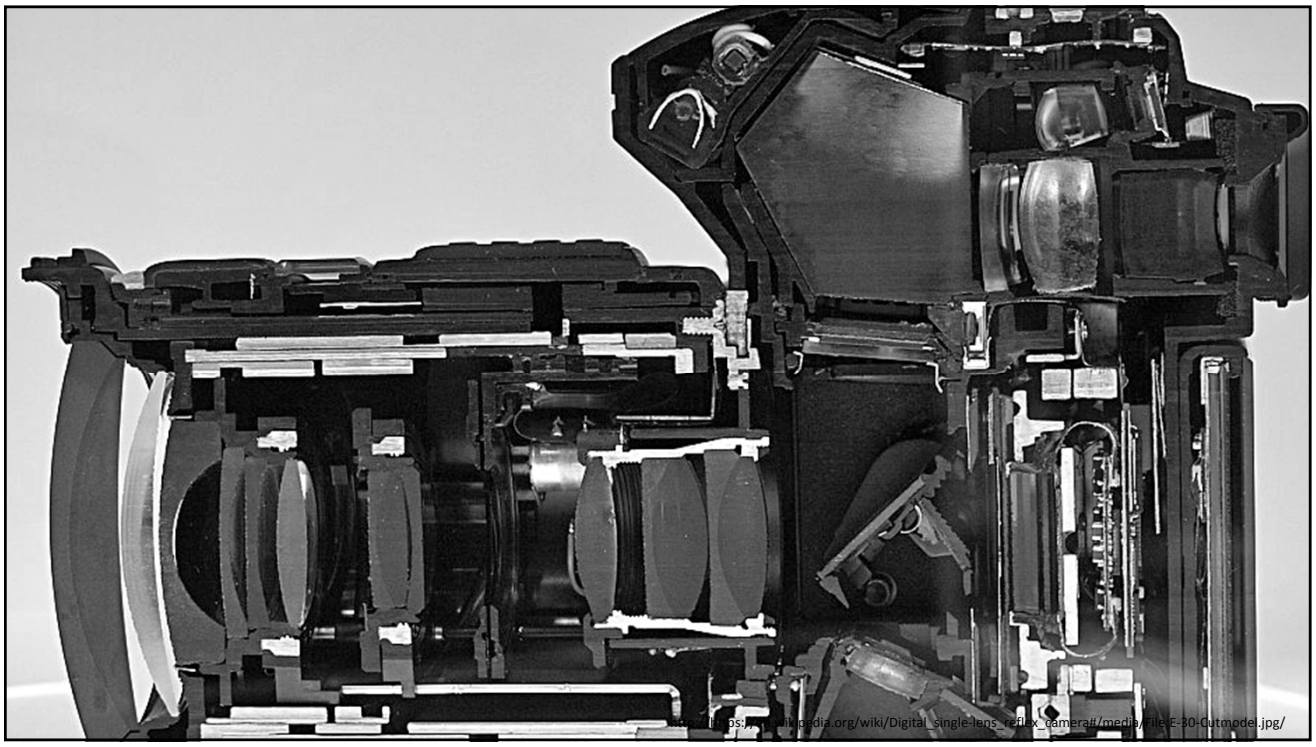
Disclosures

- I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed.
- I do intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

Objectives

1. Refresh yourself with basic ocular anatomy.
2. Understand the various treatment paradigms available for patients with diabetic retinopathy.
3. Review clinical data correlating systemic metrics to severity of diabetic retinopathy.
4. Go out in the world and prevent blindness (among the other complications of DR).

The Camera Analogy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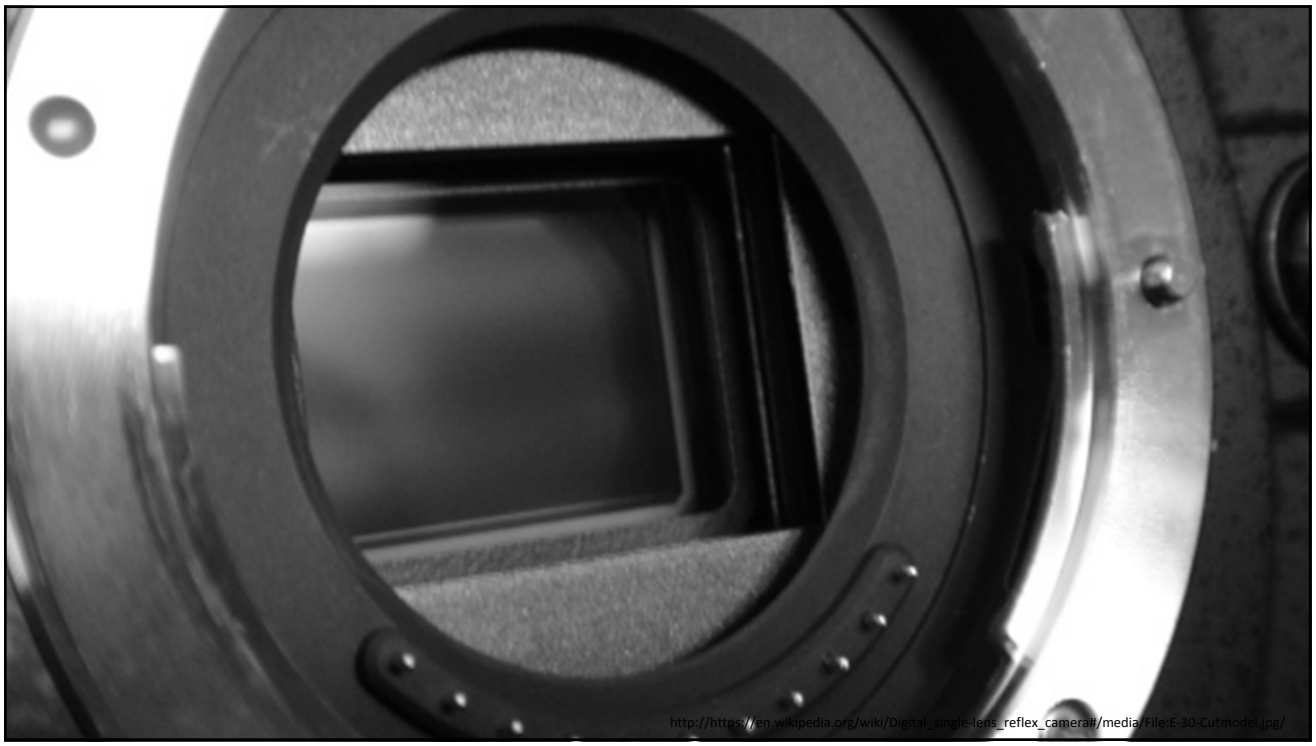
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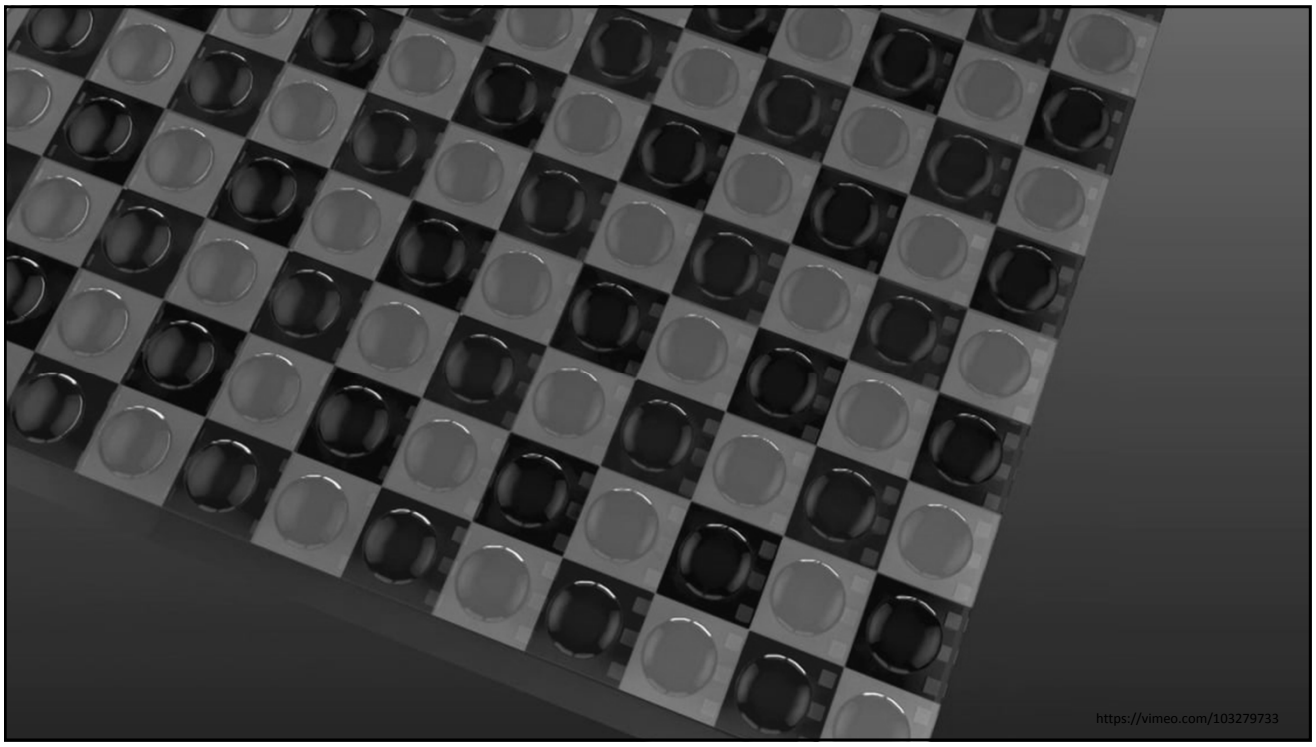
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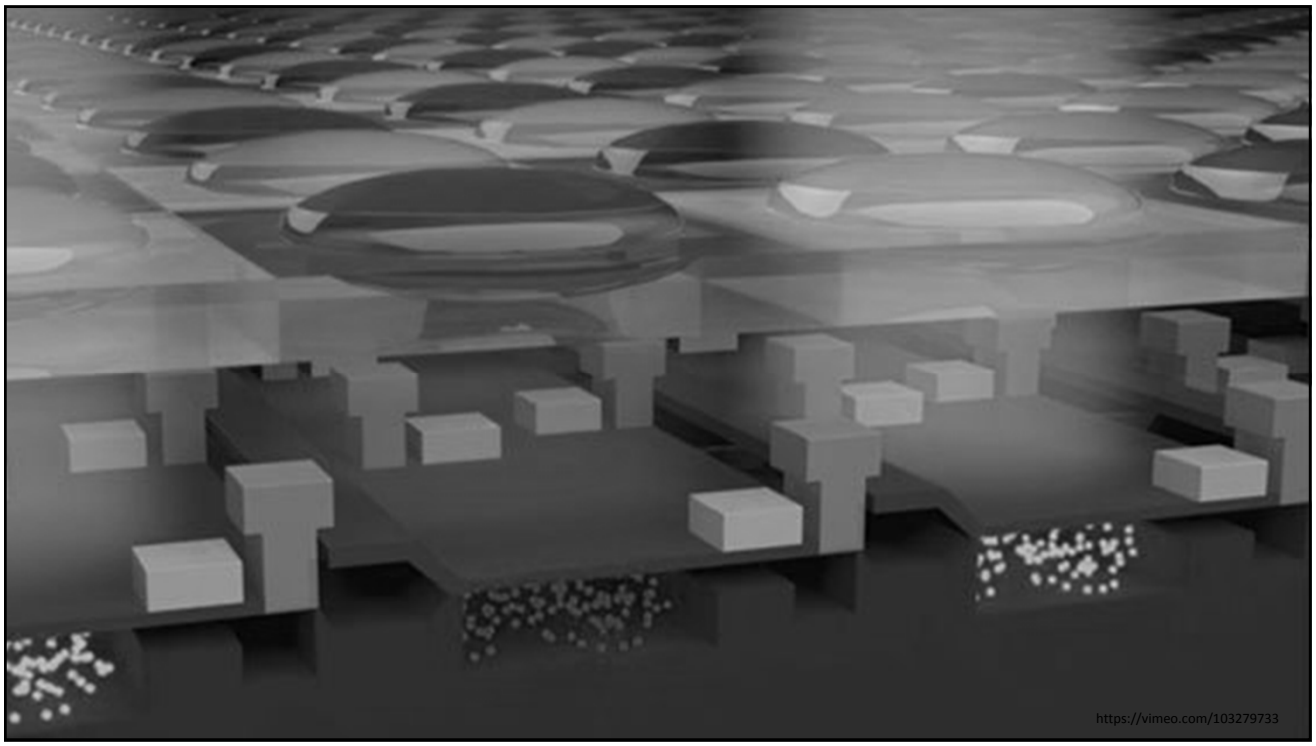
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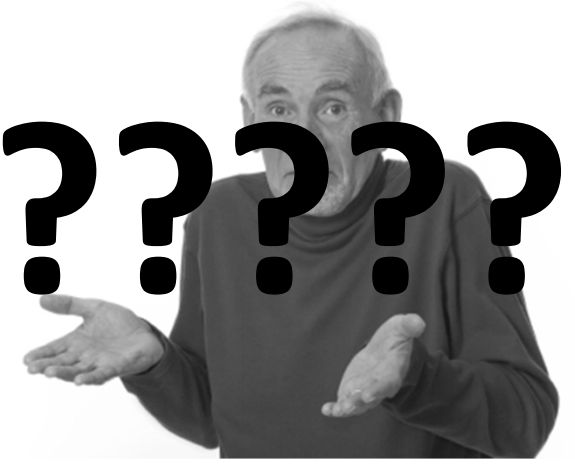
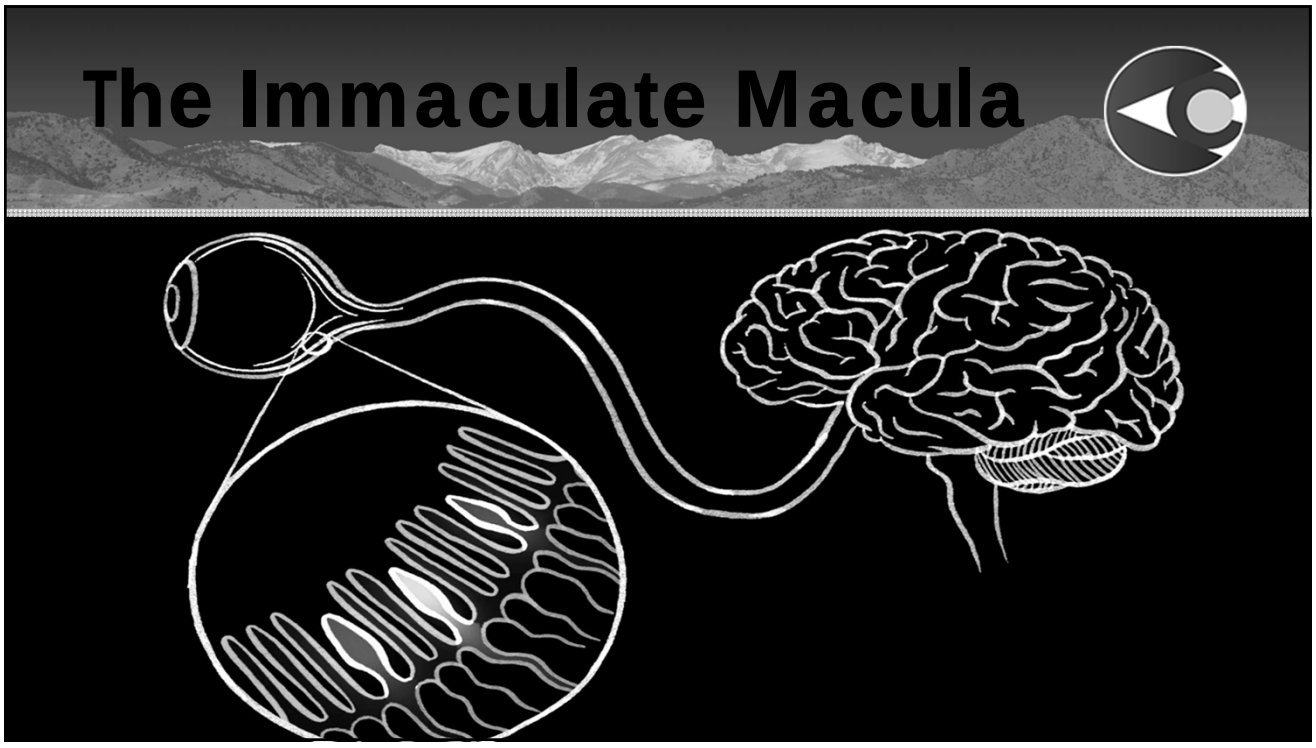
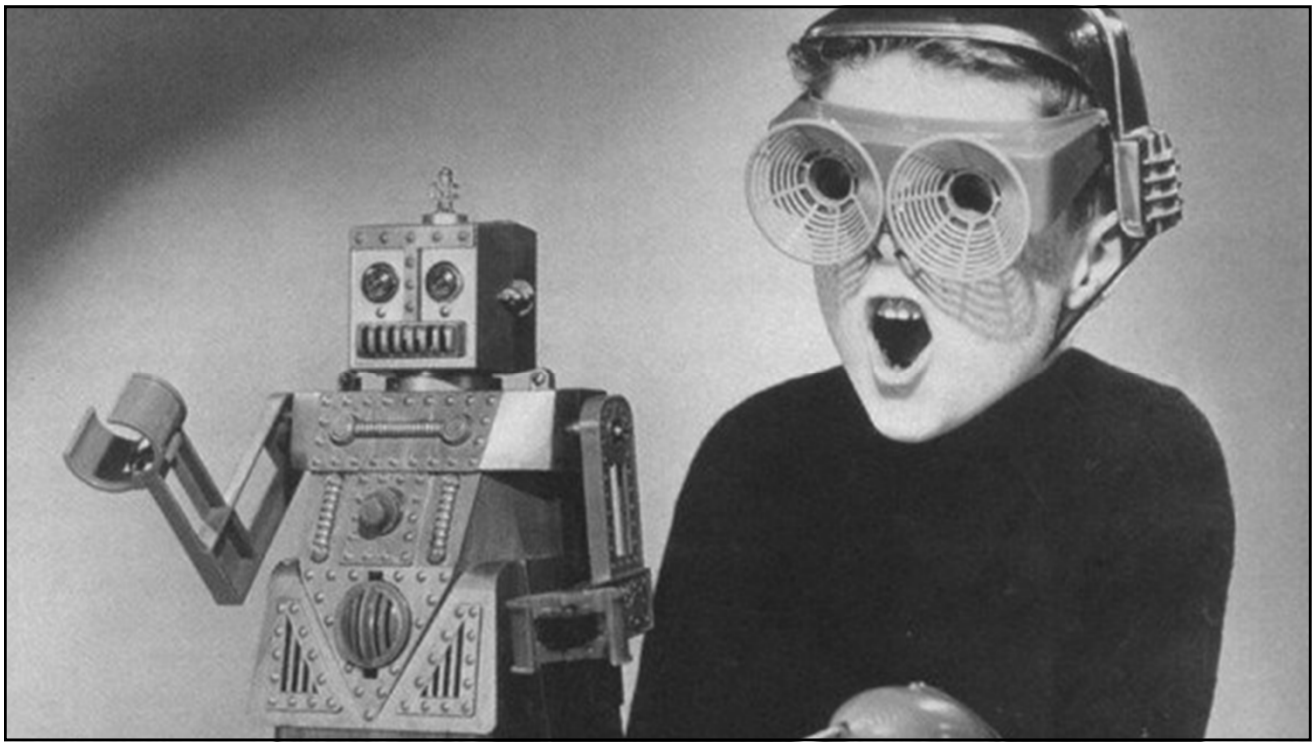



The Immaculate Macula



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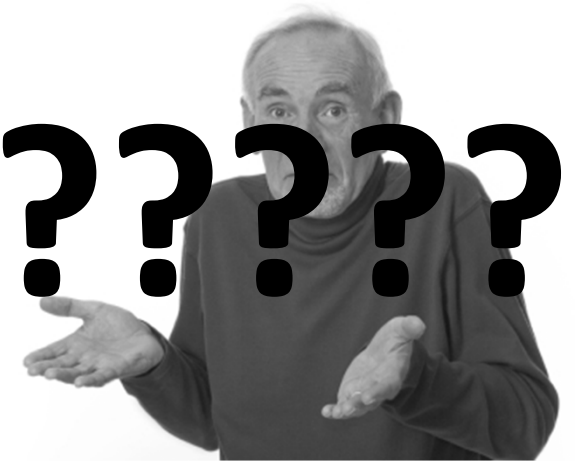

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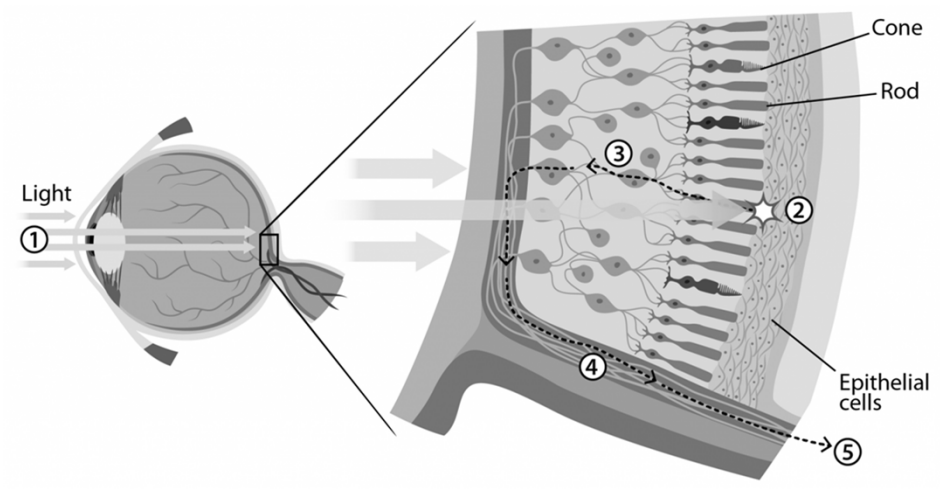

https://askabiologist.asu.edu/rods-and-cones

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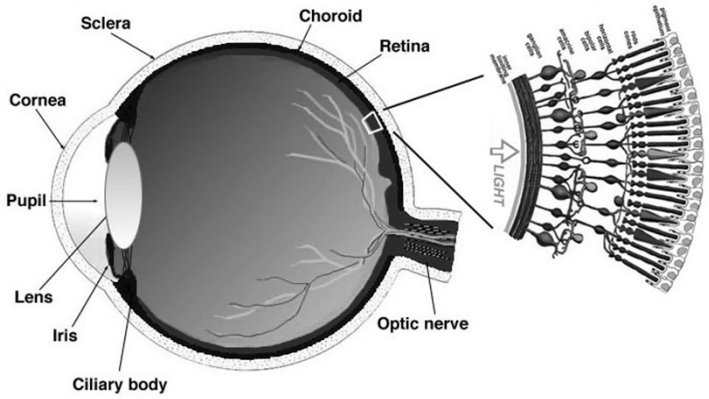

Fig. 1.1. A drawing of a section through the human eye with a schematic enlargement of the retina.

http://webvision.med.utah.edu/book/part-i-foundations/simple-anatomy-of-the-retina/

The Immaculate Macula

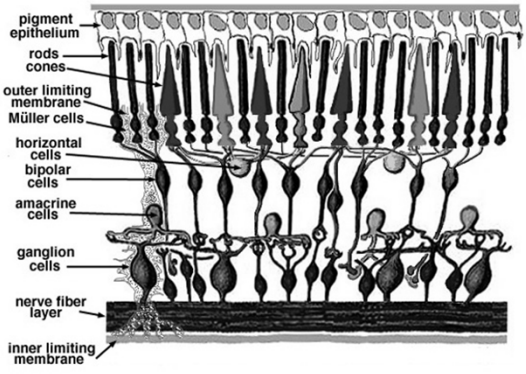

Fig. 2. Simple diagram of the organization of the retina.

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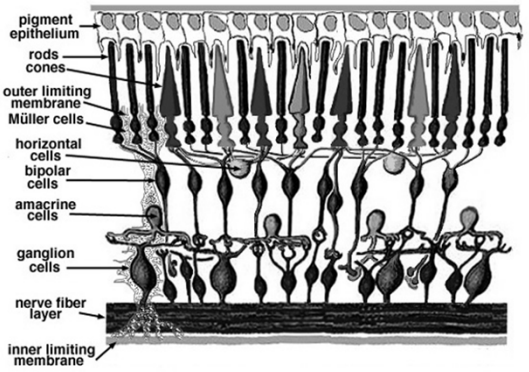

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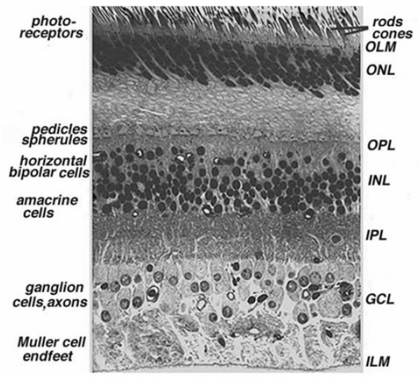

Fig. 3. Light micrograph of a vertical section through central human retina.

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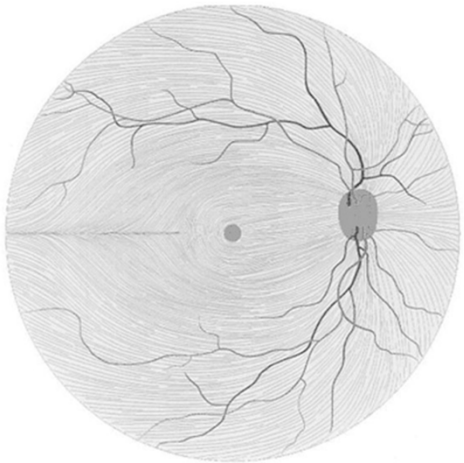

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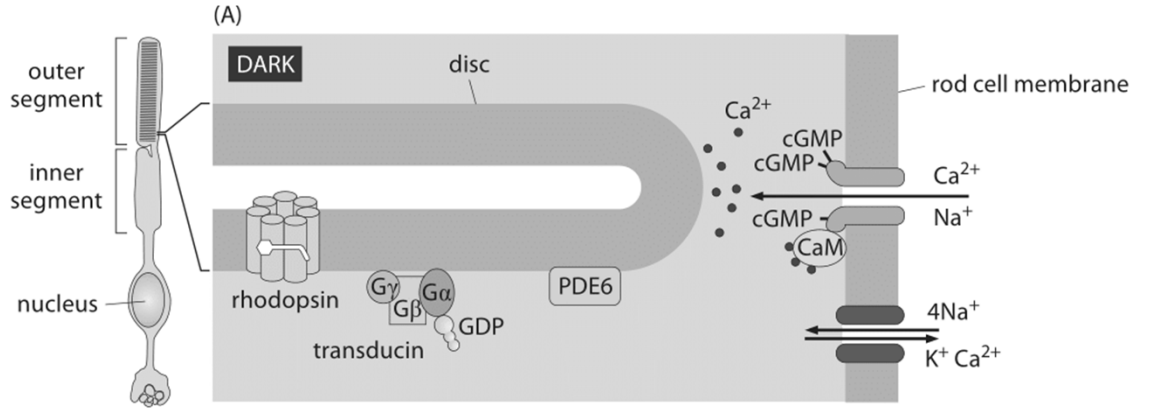

http://book.bionumbers.org/how-many-rhodopsin-molecules-are-in-a-rod-cell/

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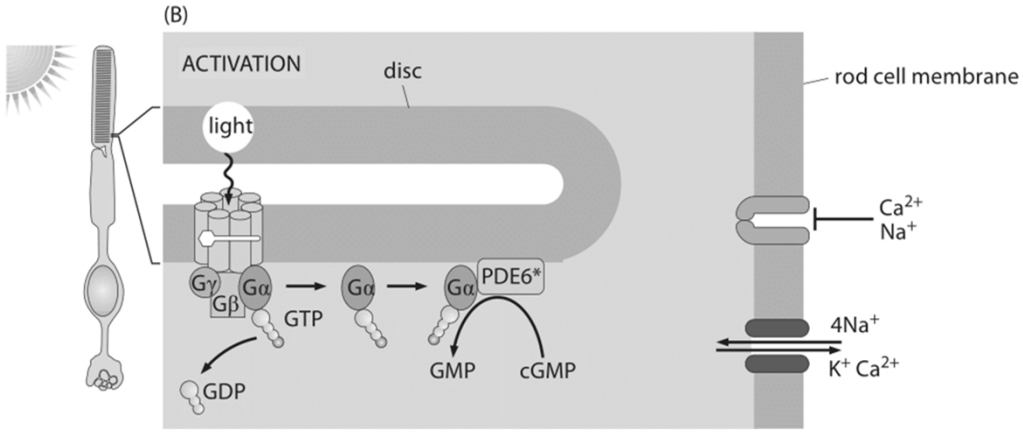

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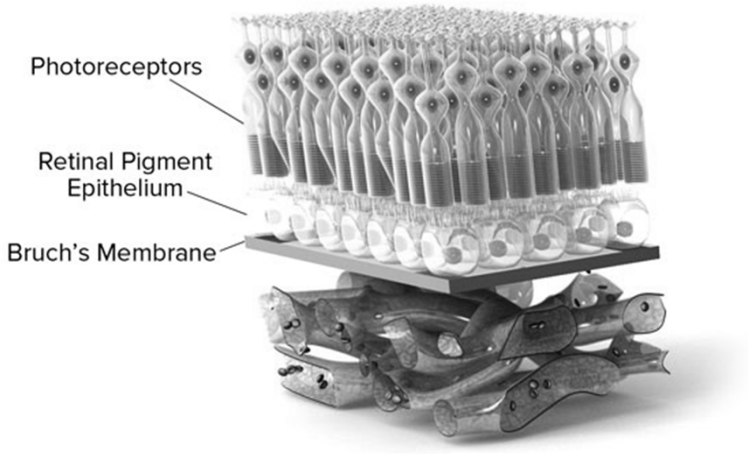

http://101proofsforgod.blogspot.com/2015/12/

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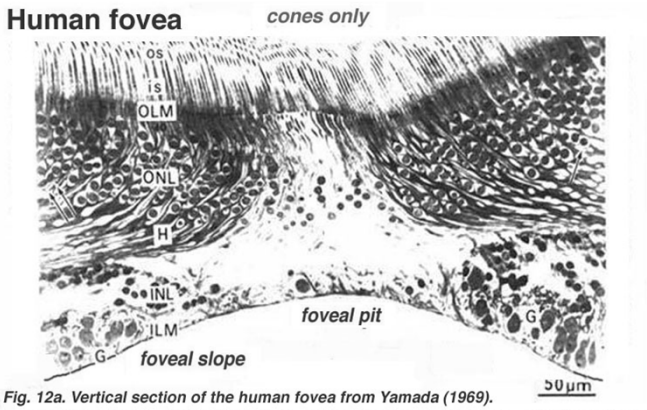

Fig. 12a. Vertical section of the human fovea from Yamada (1969).
os, outer segments; is, inner segments; OLM, outer limiting membrane; ONL, outer nuclear layer
H, Henle fibers; INL, inner nuclear layer; ILM, inner limiting membrane; G, ganglion cells

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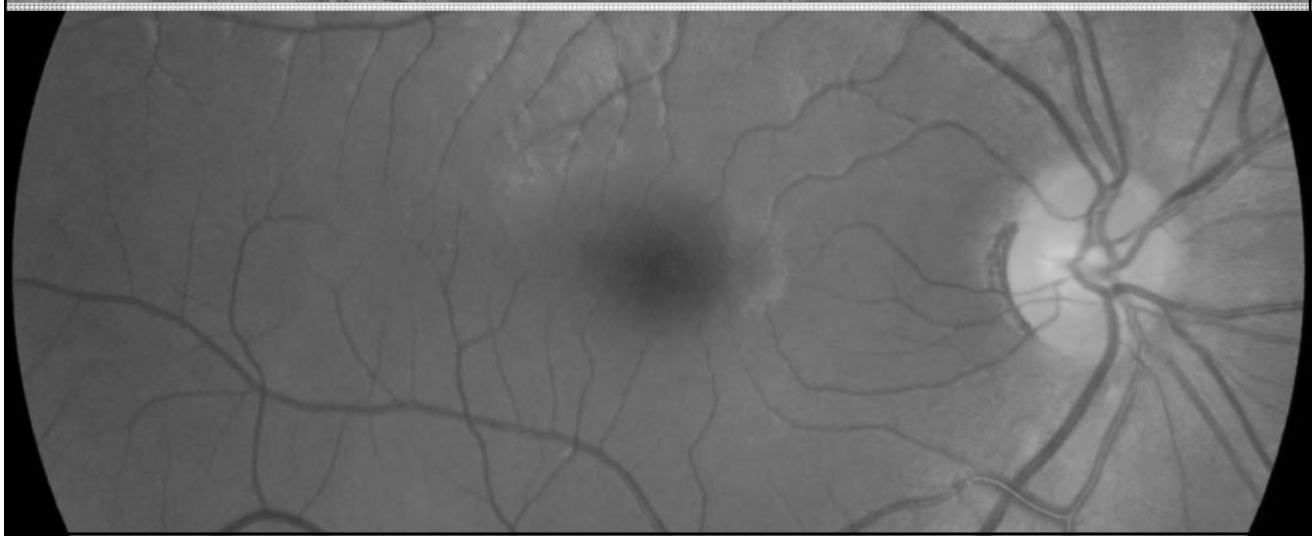
Diagnostics: Photography



Diagnostics: OCT

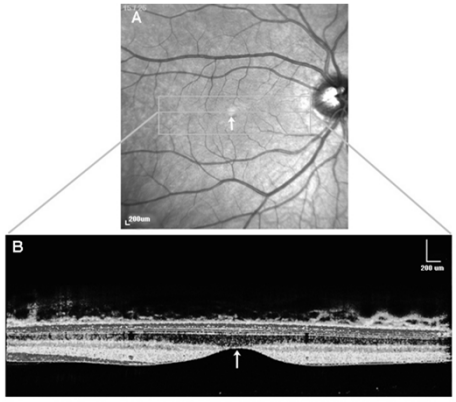
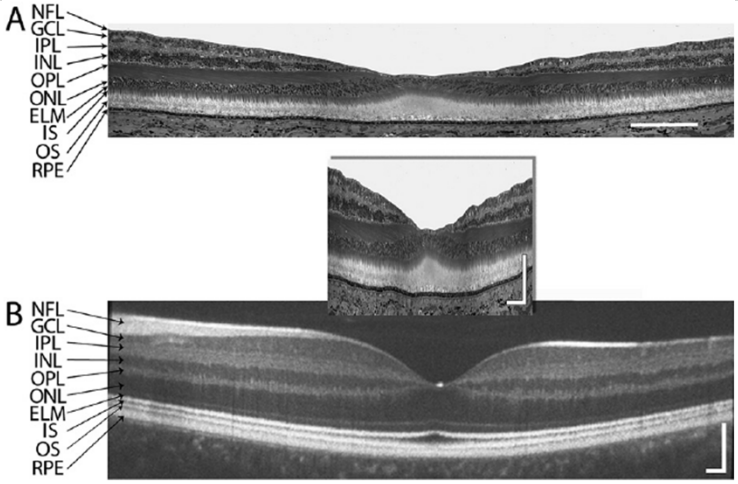


Fig 13a. A) fundus photo of a normal human macula, optic nerve and blood vessels around the fovea. B) Optical coherence tomography (OCT) images of the same normal macula in the area that is boxed in green above (A). The foveal pit (arrow) and the sloping foveal walls with displaced inner retina neurons (green and red cells) are clearly seen. Blue cells are the packed photoreceptors, primarily cones, above the foveal center (pit).

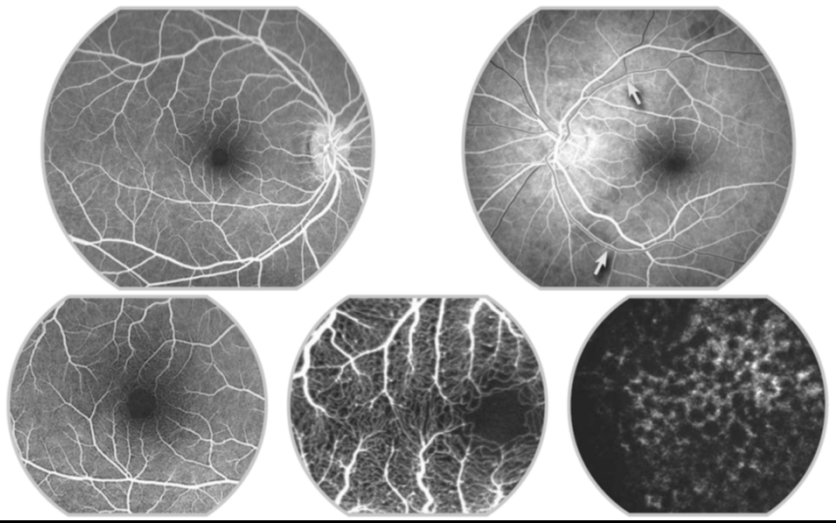
http://webvision.med.utah.edu/book/part-i-foundations/simple-anatomy-of-the-retina/

Diagnostics: OCT



https://www.researchgate.net/figure/236054471_fig7_Fig-7-A-comparison-of-histological-and-OCT-images-of-the-cross-sectional-appearance-of

Diagnostics: Angiography



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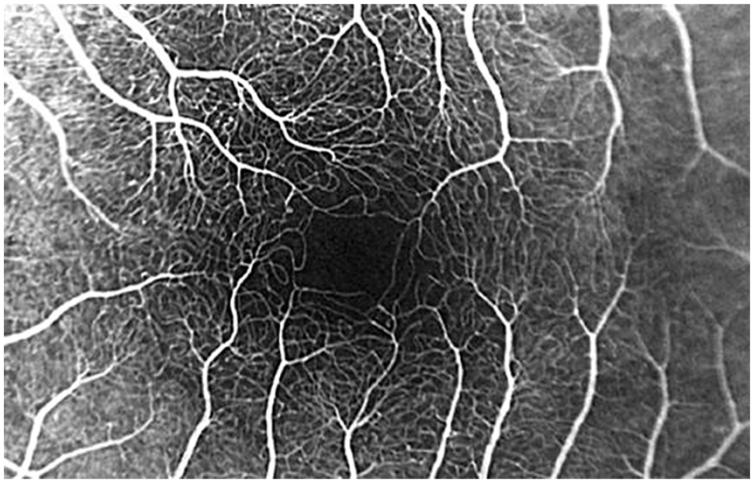

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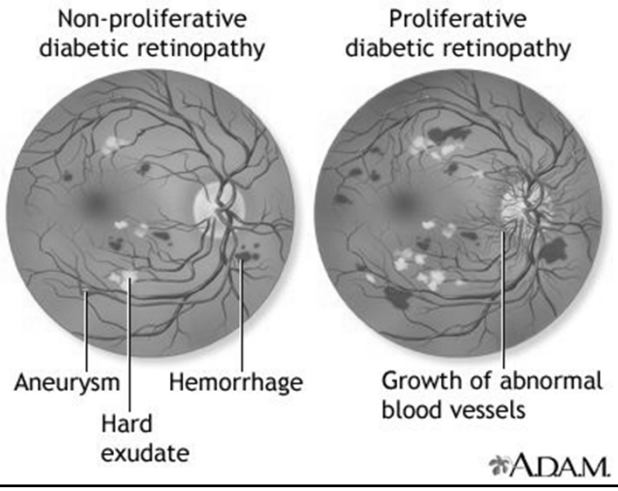
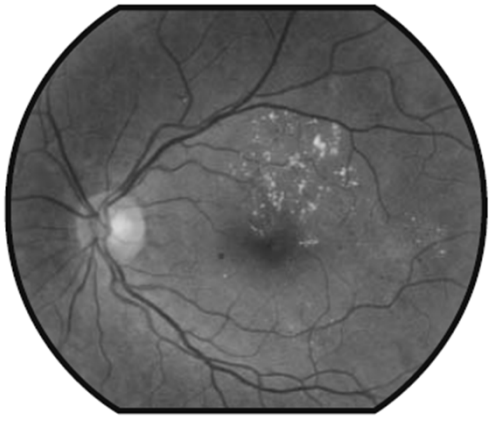
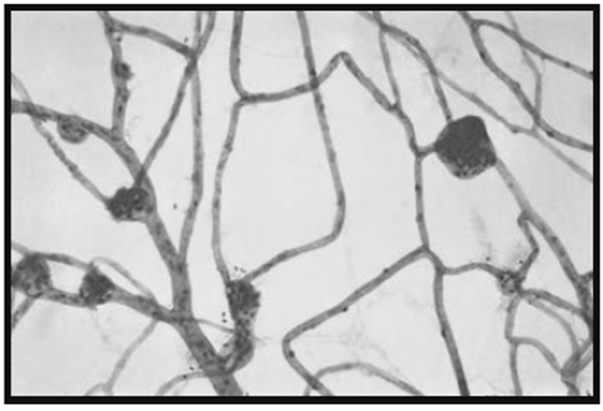
Diagnostics: Angiography

Ocular Manifestations



Mild NPDR





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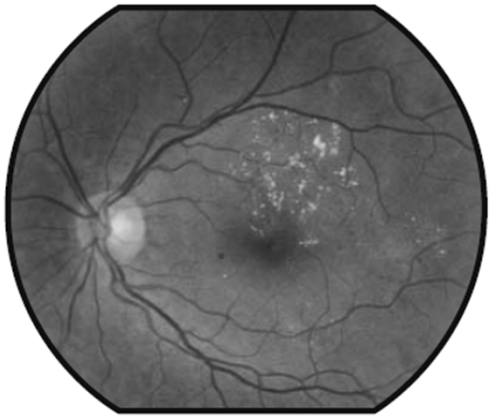
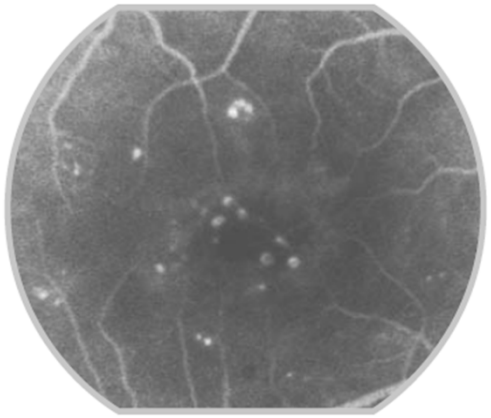
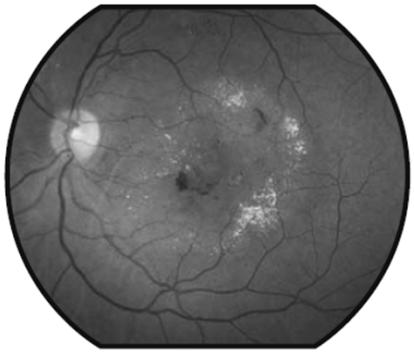
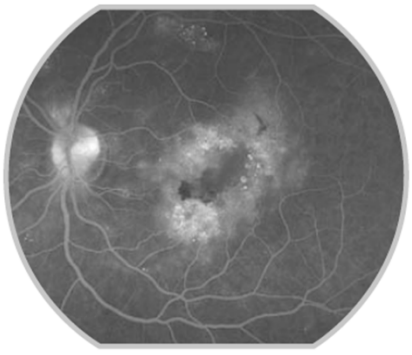


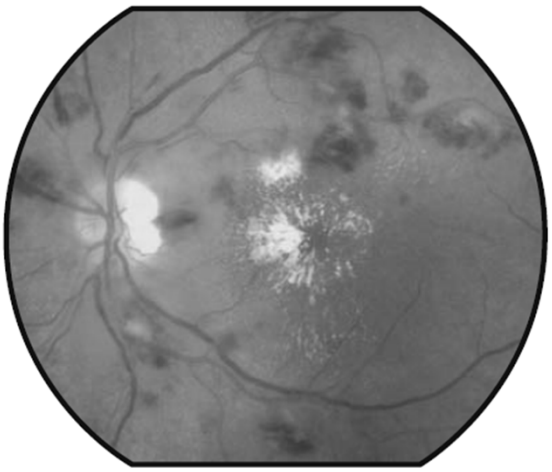


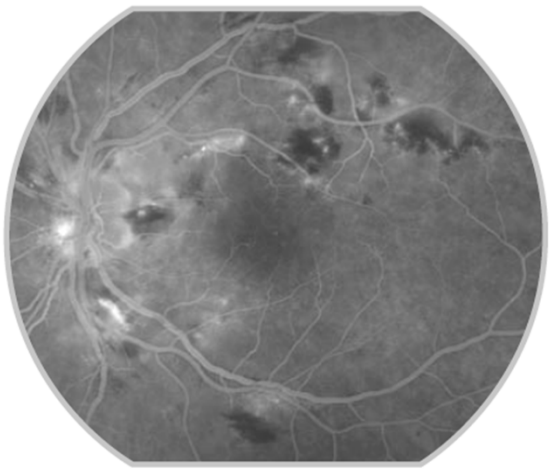
Moderate NPDR





Severe NPDR





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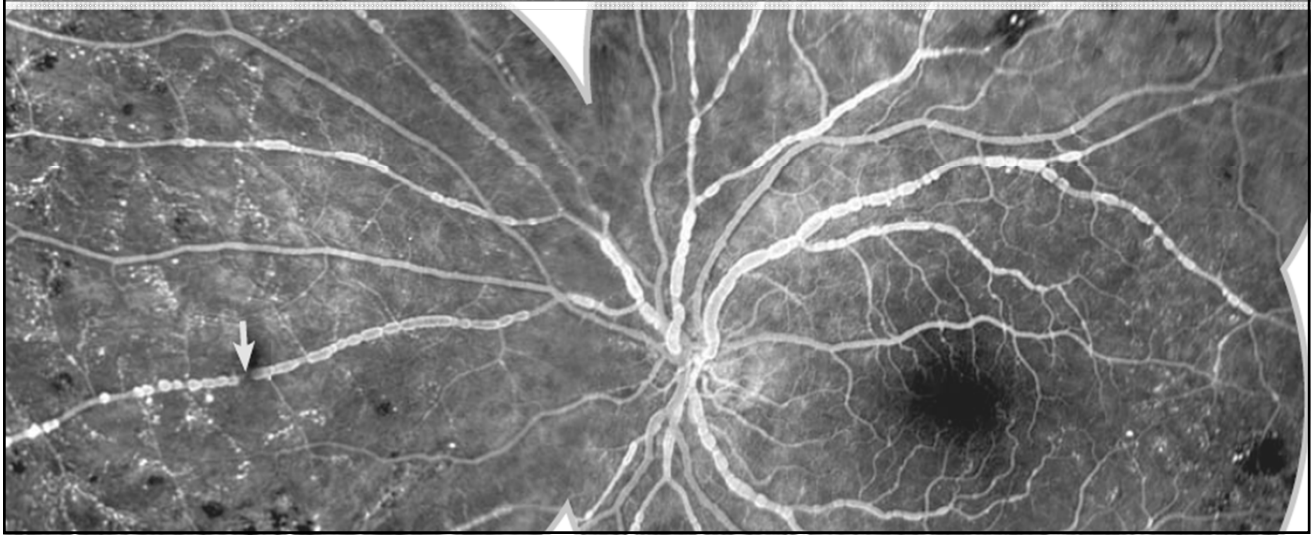
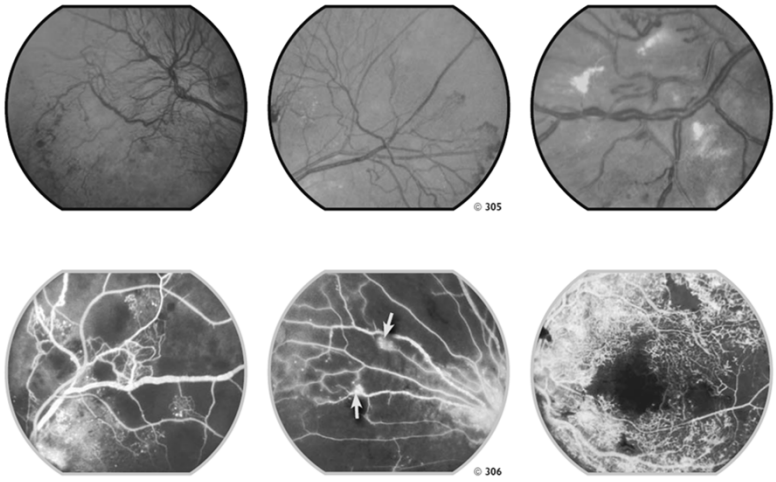


PDR



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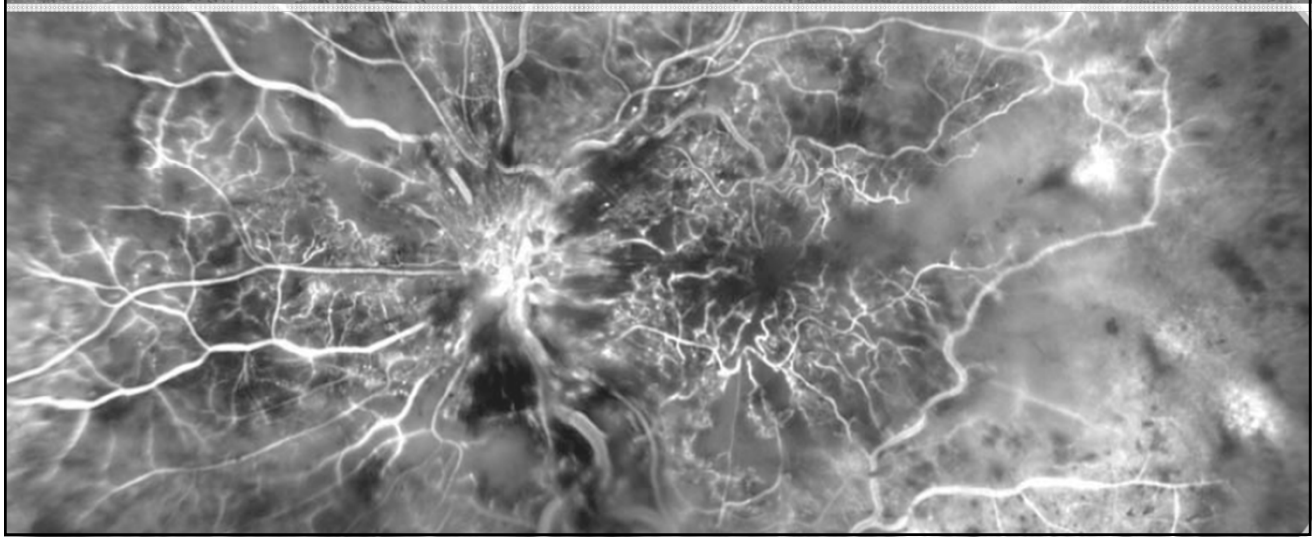
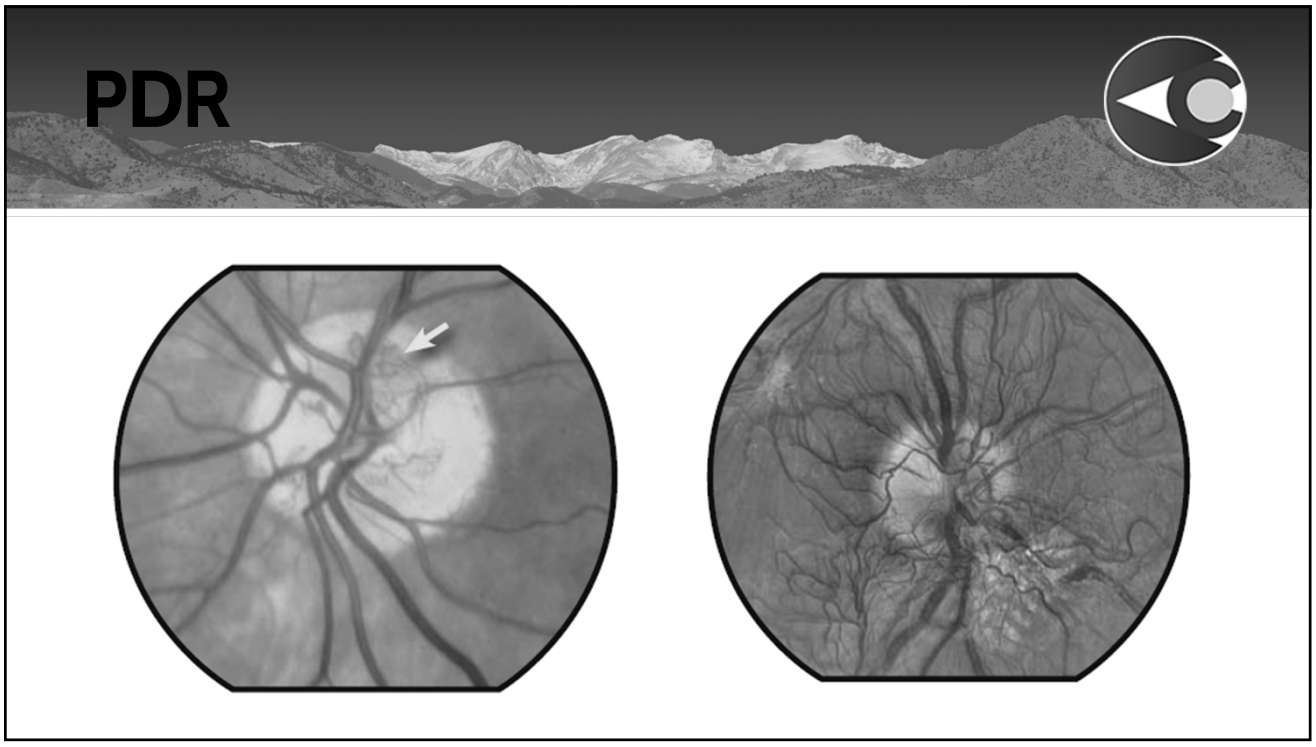
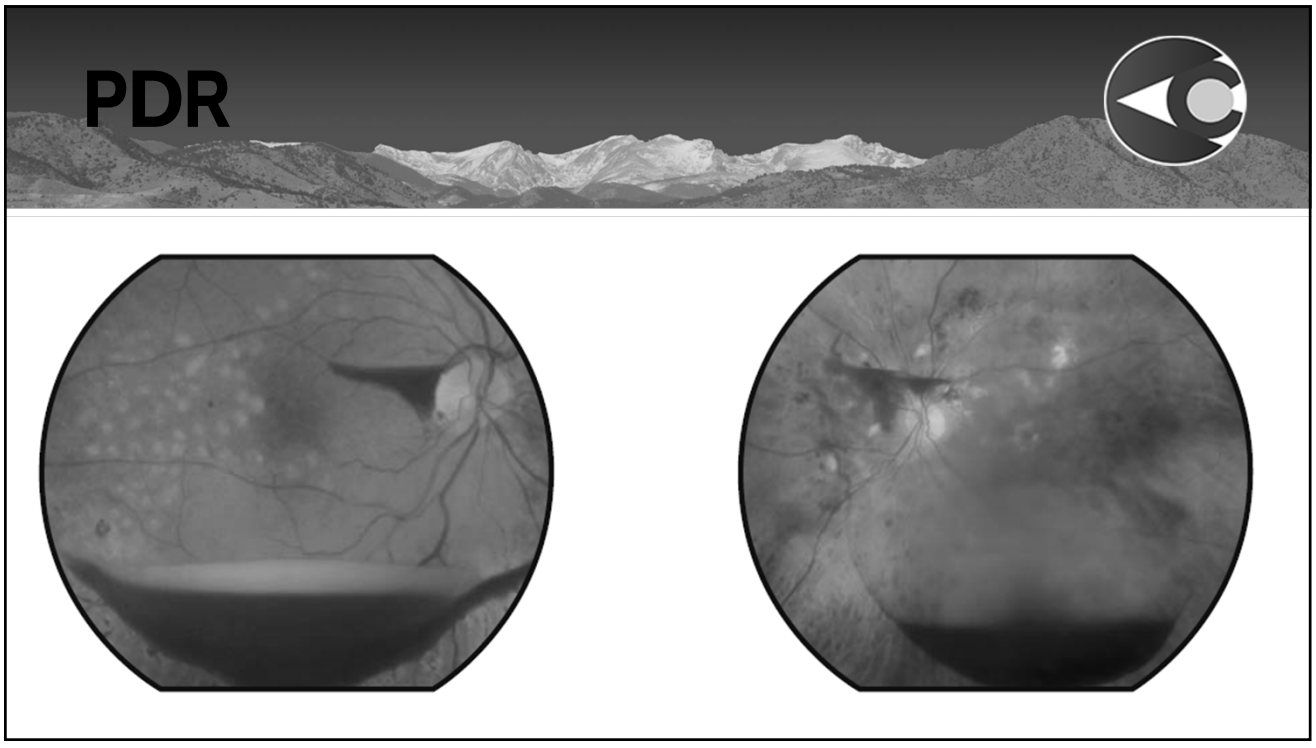
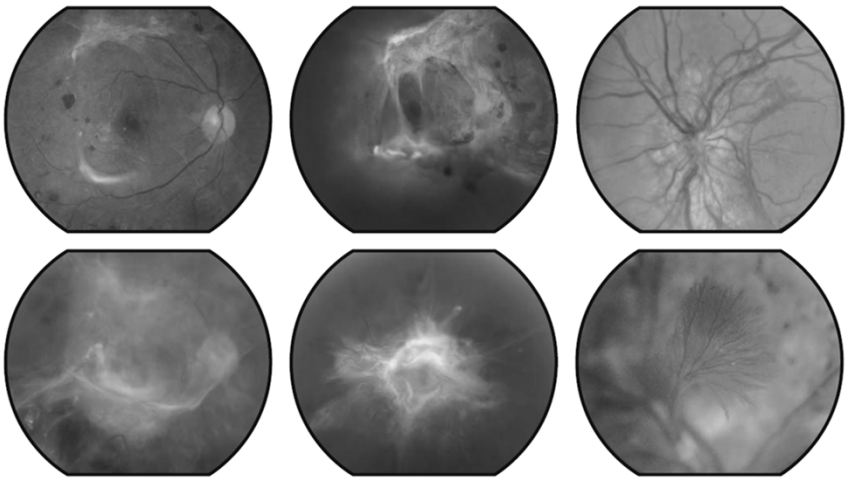



PDR


PDR

PDR



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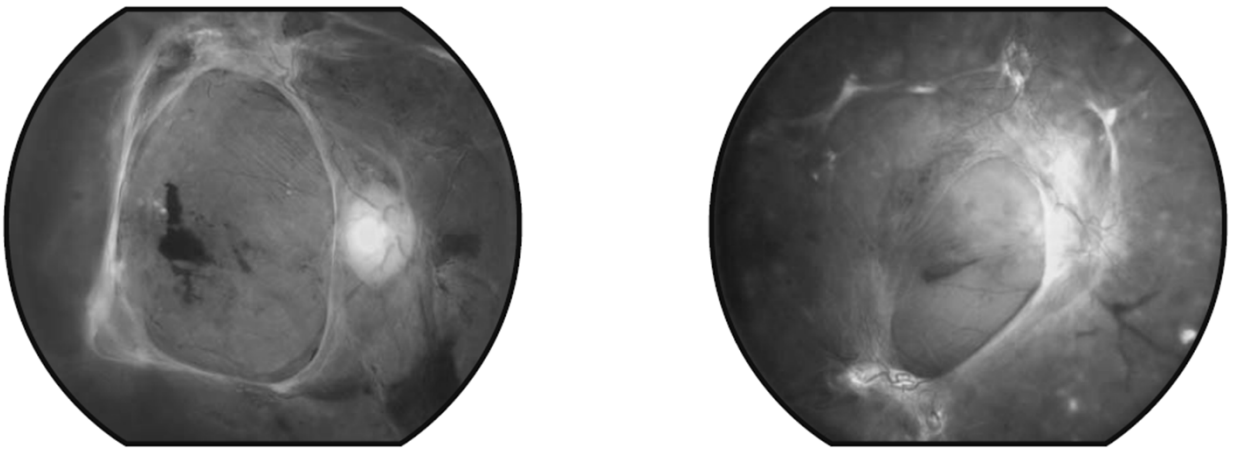

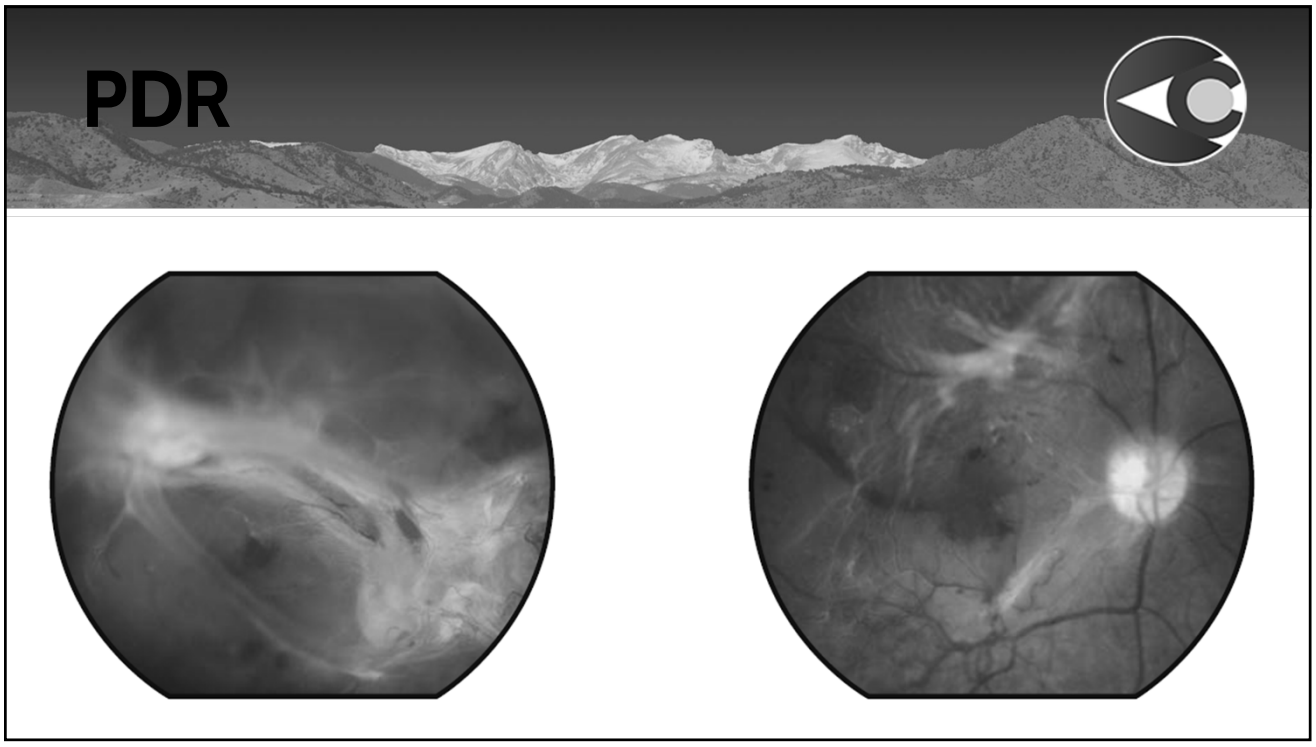
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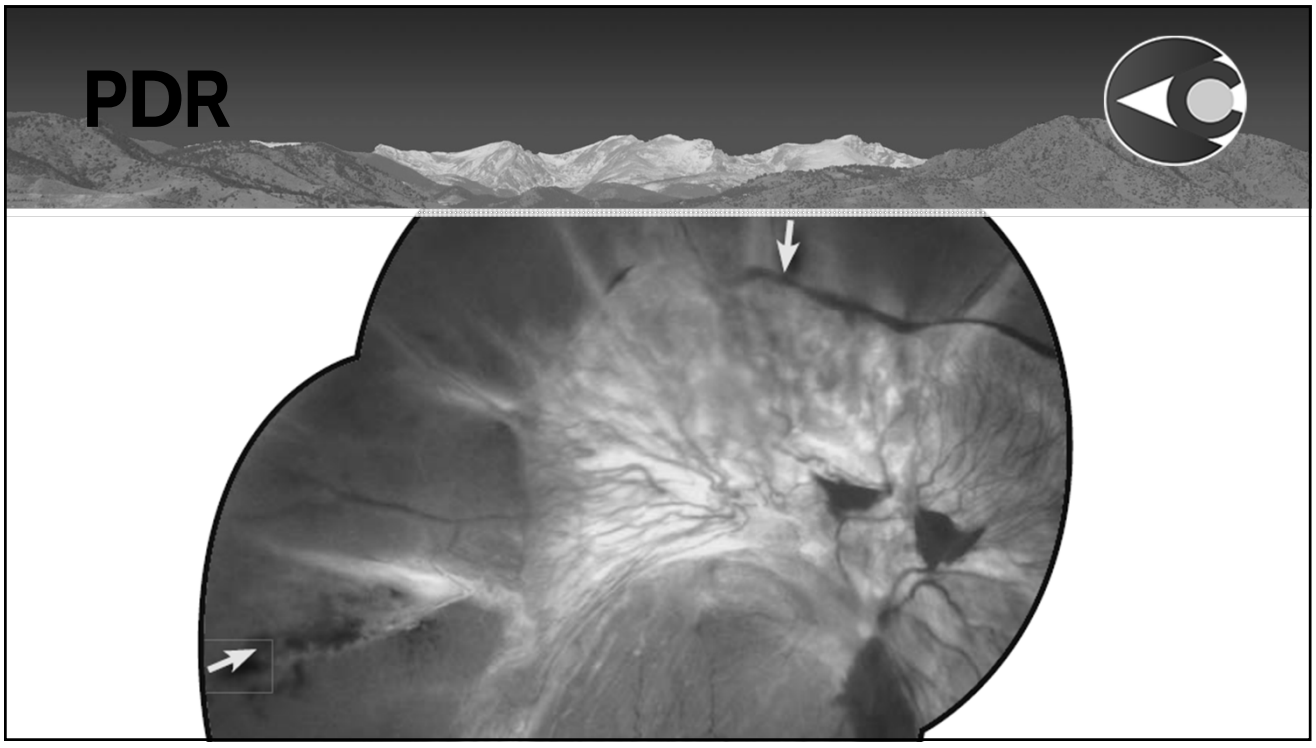
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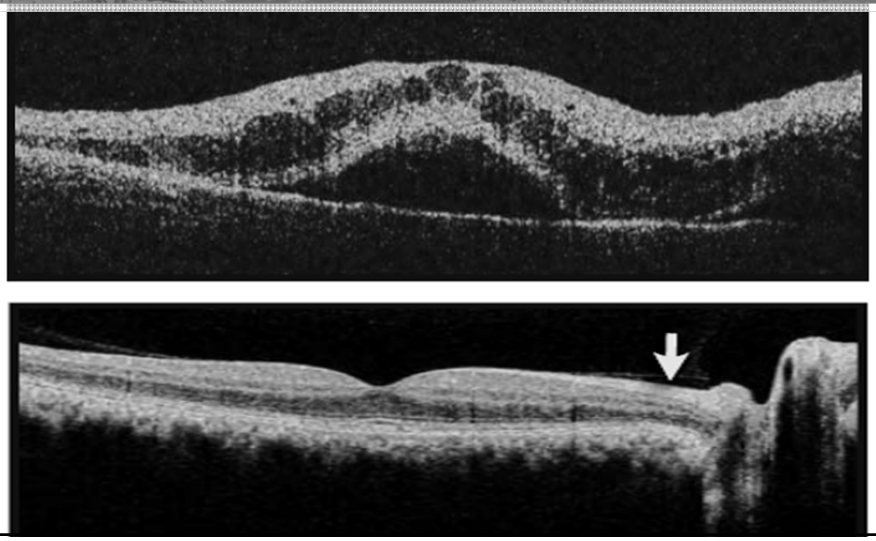
DME

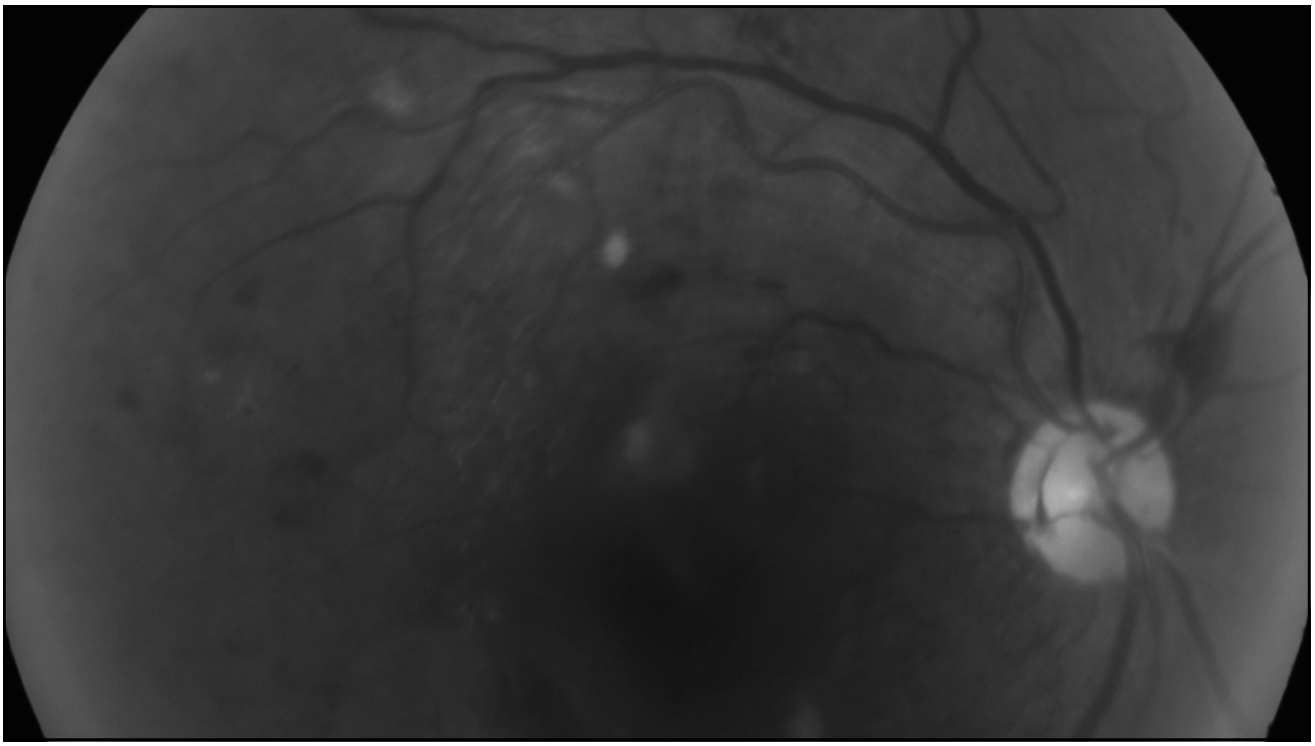
DME

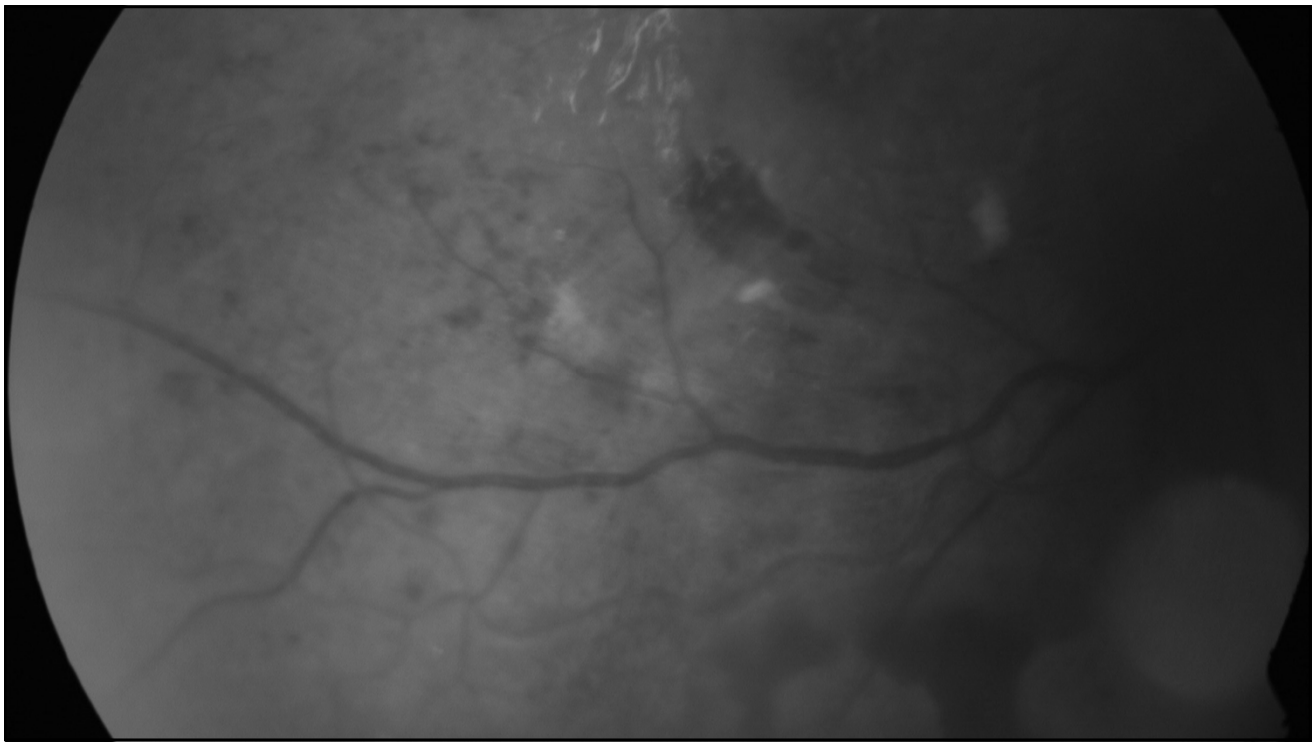


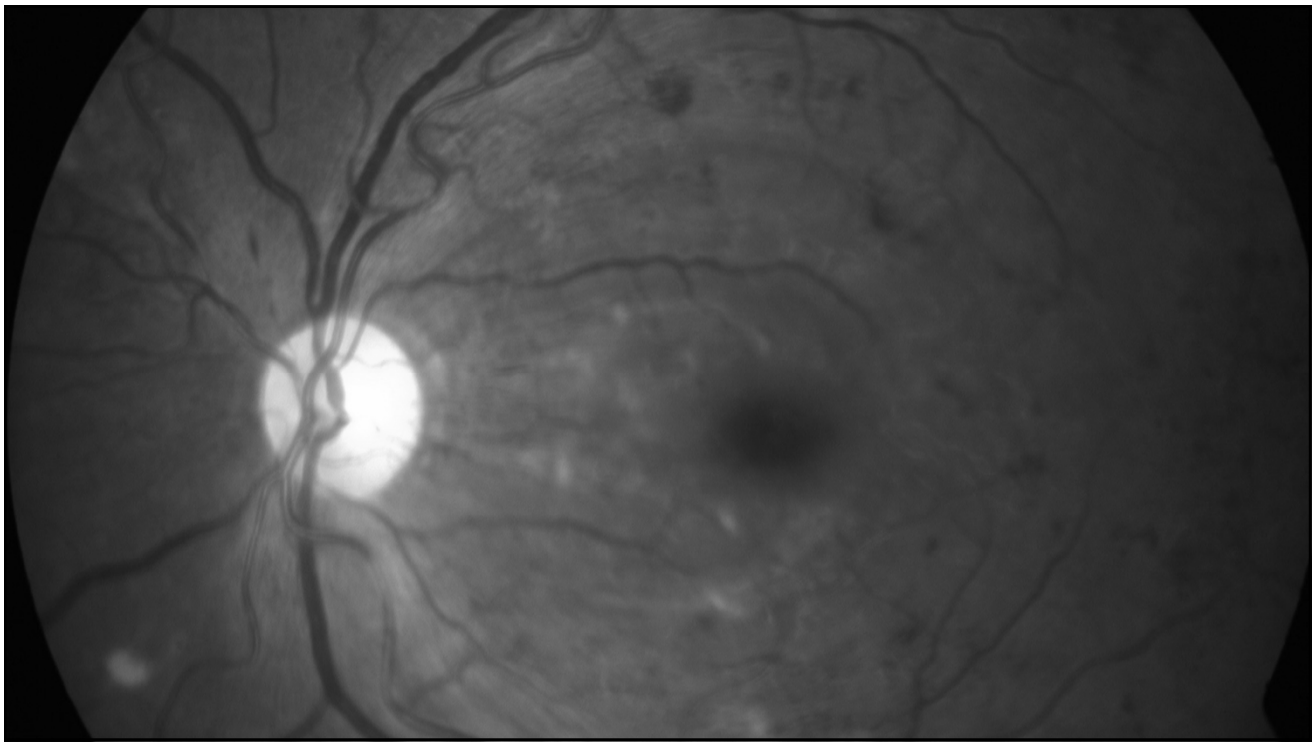
Case 1

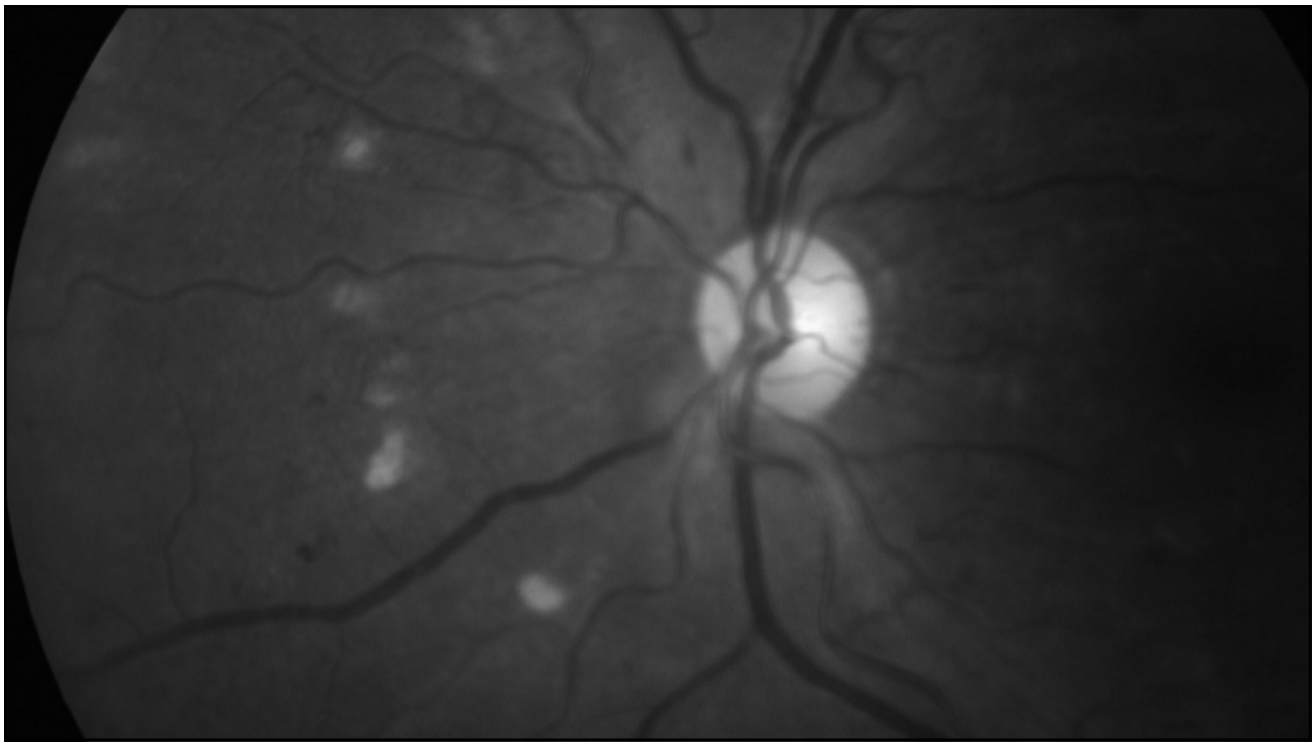
CC

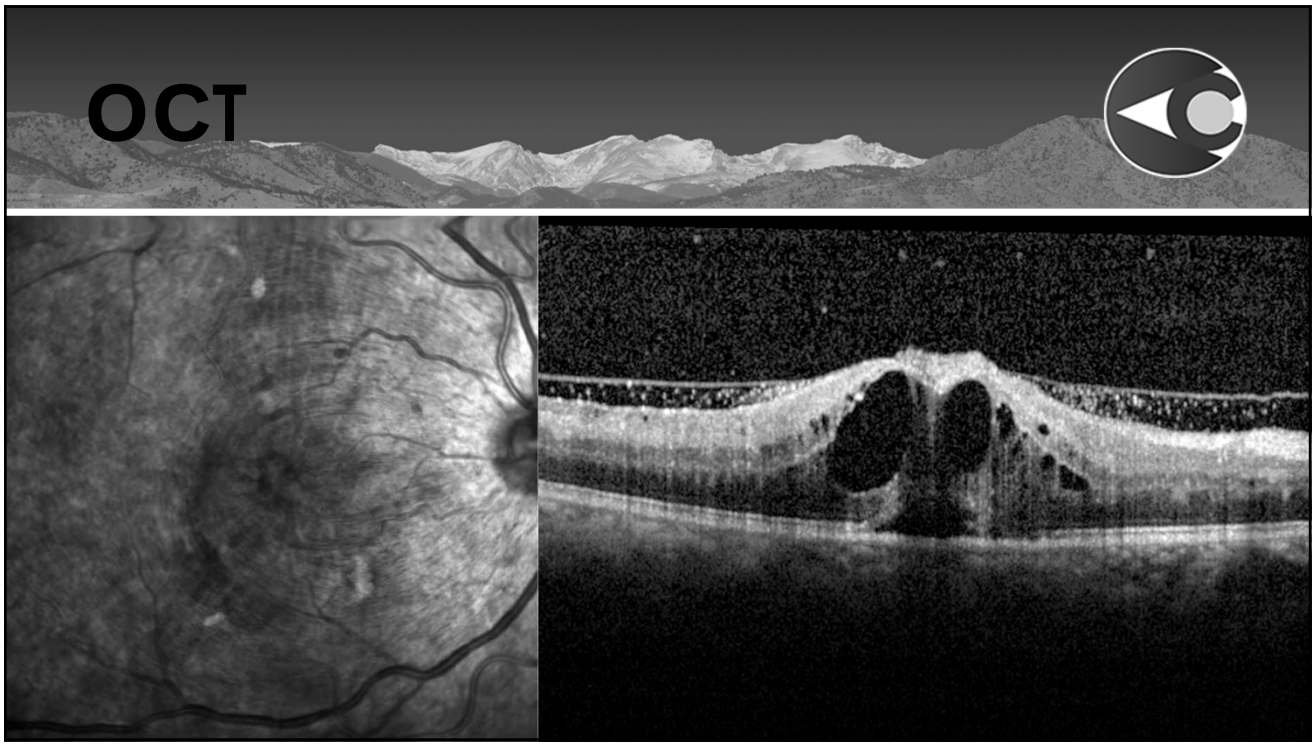
24 y/o Hispanic F presenting with vision loss in the right eye



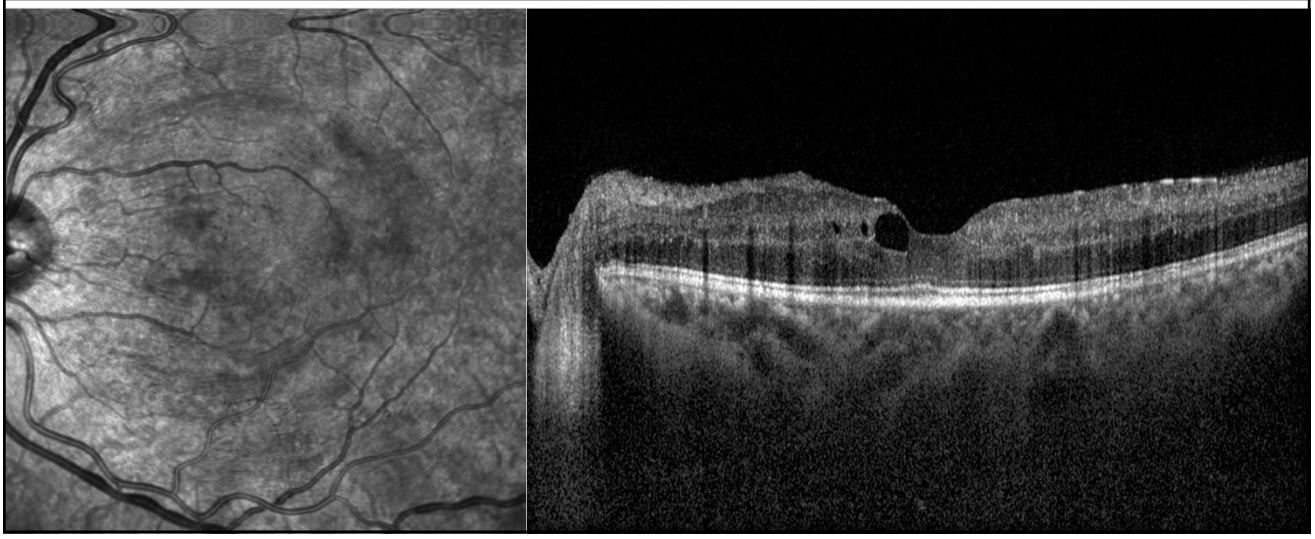







OCT

OCT



PMH

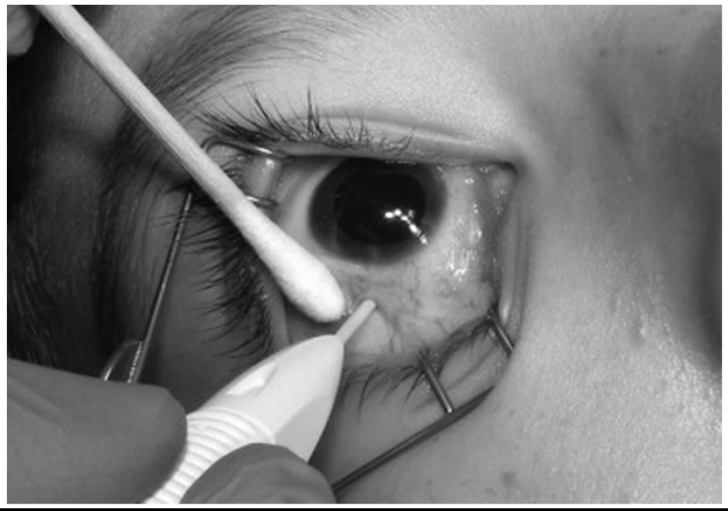
- PMHx: T1DM, 20 weeks pregnant
- MEDS: Insulin, Prenatal Vitamin
- ALLERGIES: None

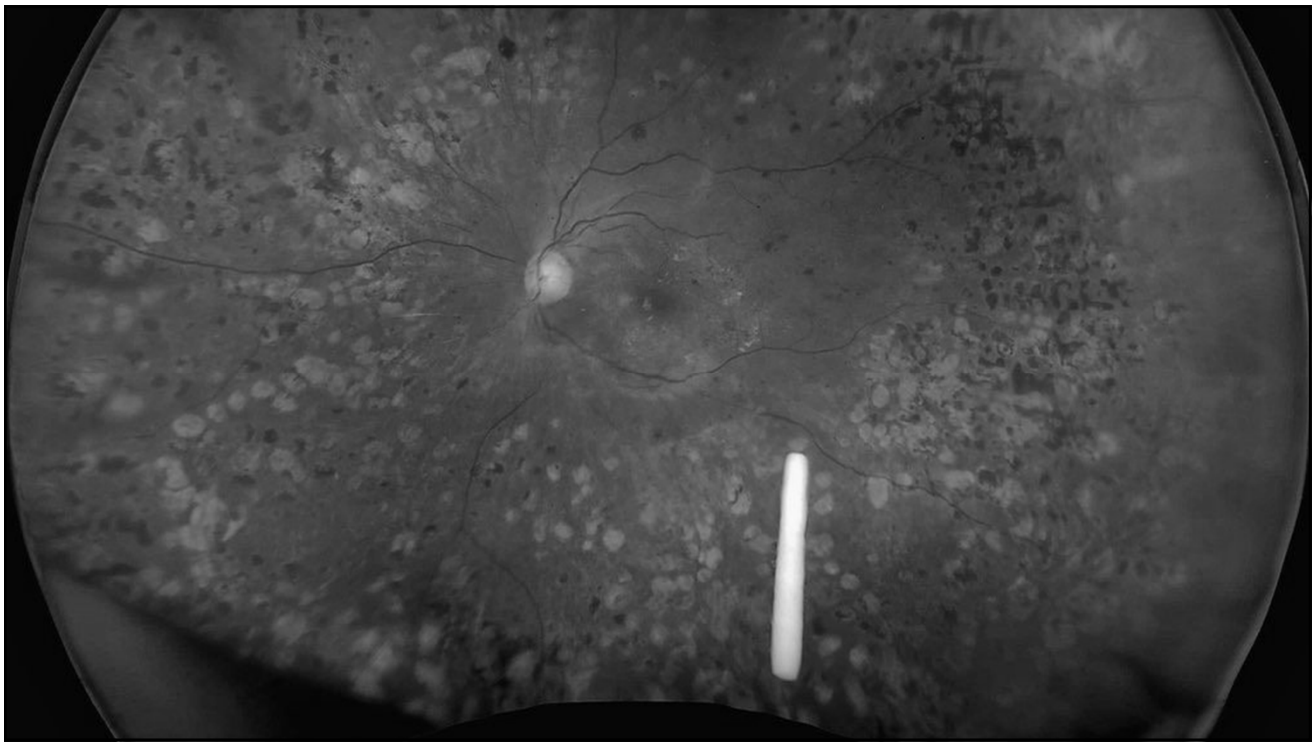
DME Treatment Options

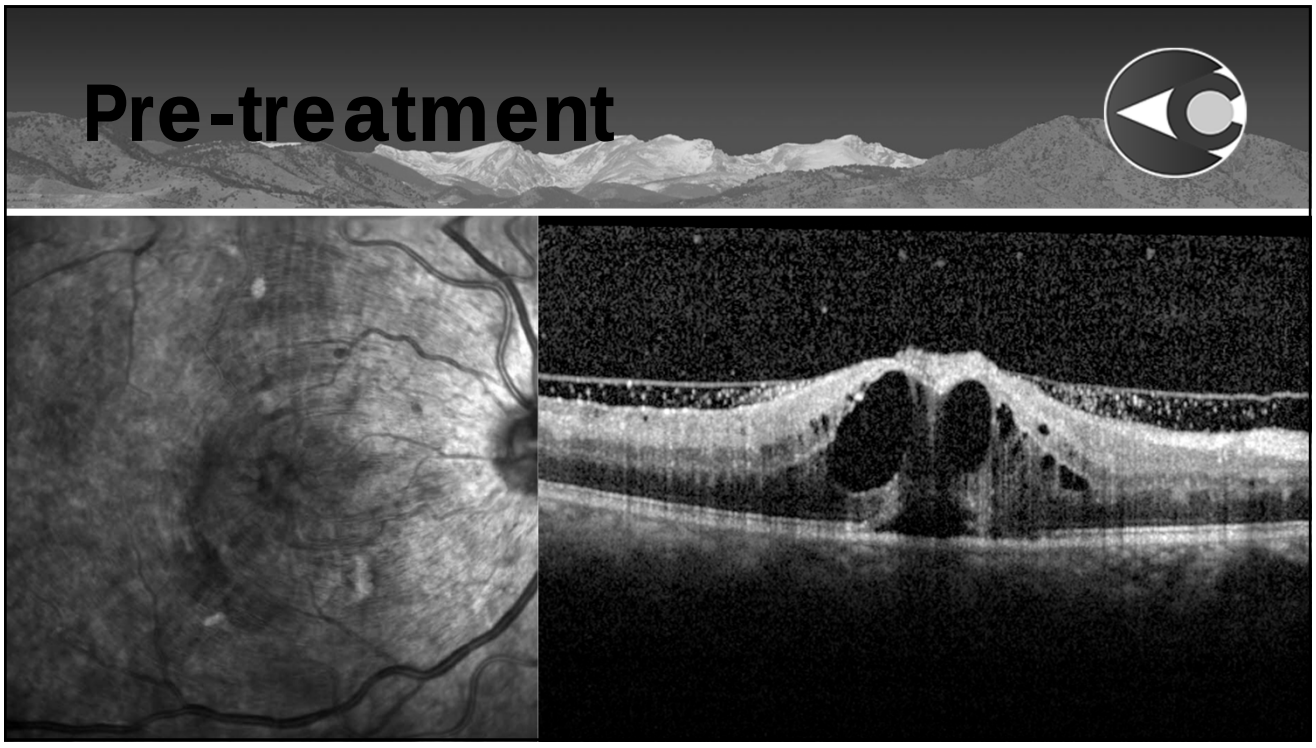
- Observation
- Intravitreal Anti-VEGF
- Intravitreal Steroids

Dexamethasone Implant

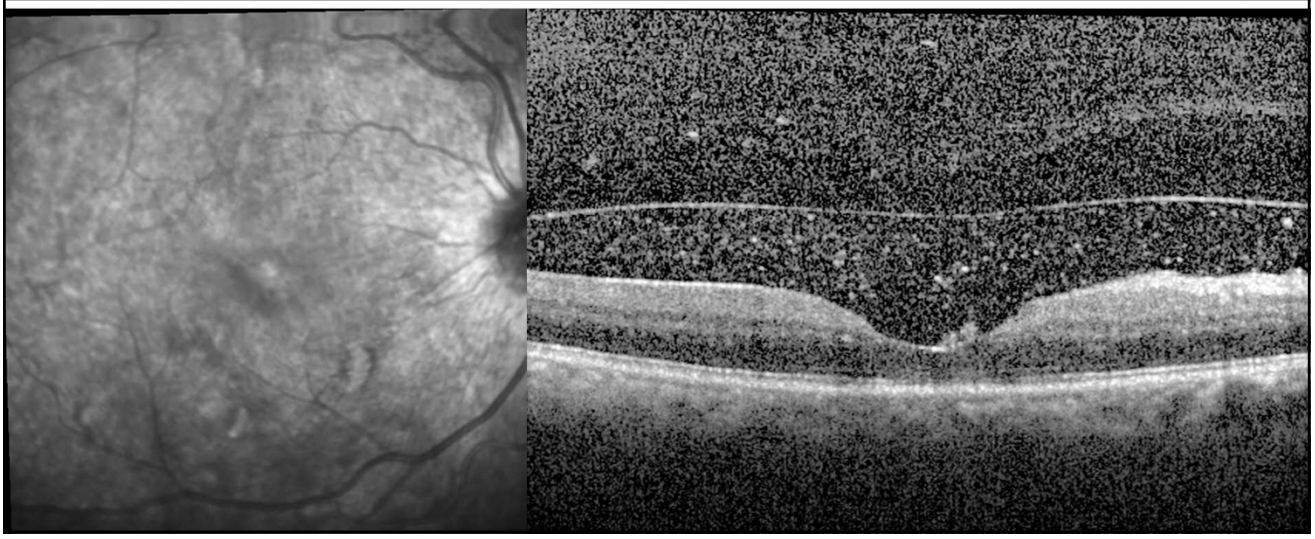
Dexamethasone Implant






Pre-treatment

Post-treatment

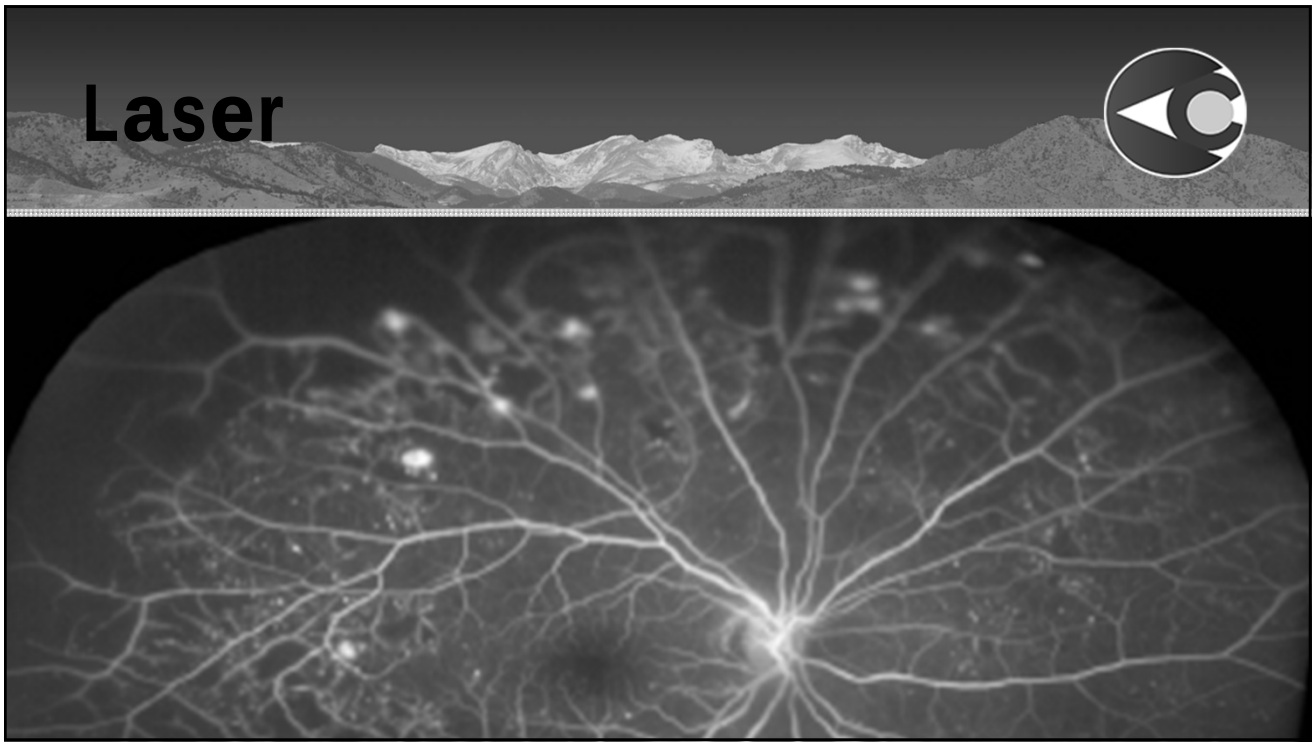


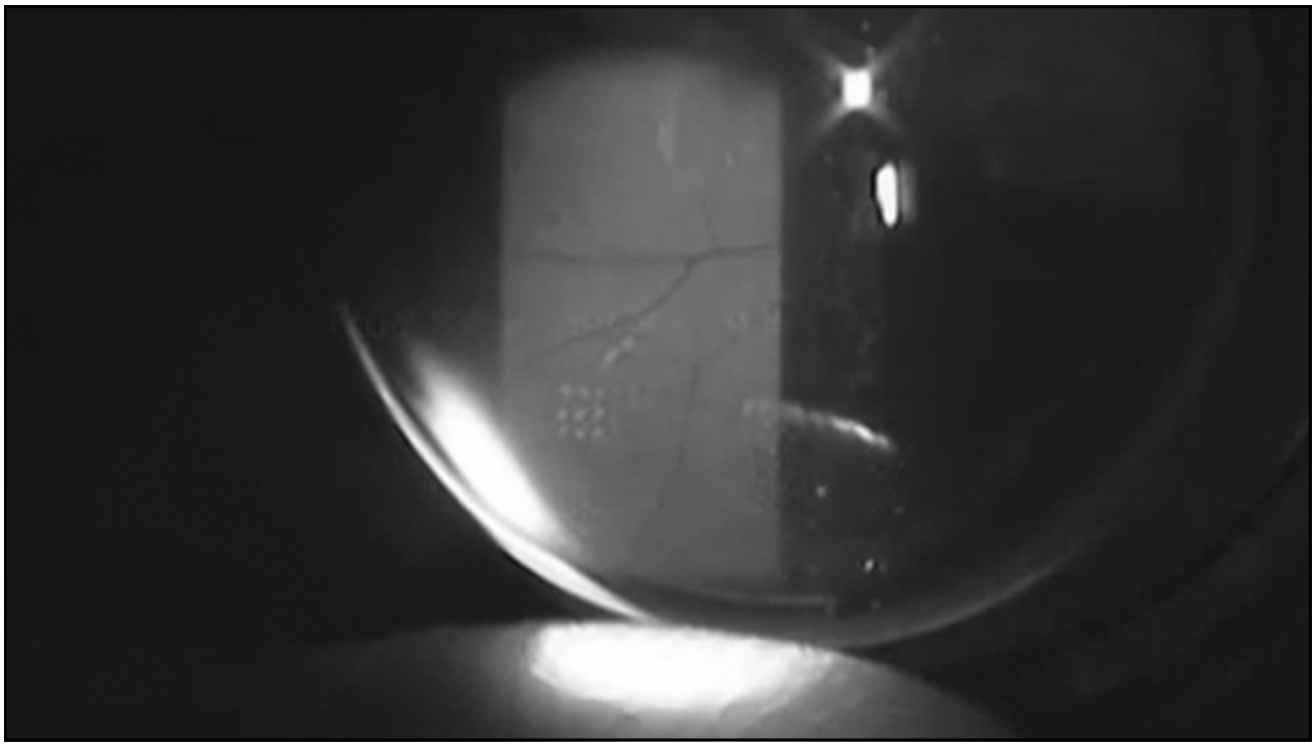
What next?

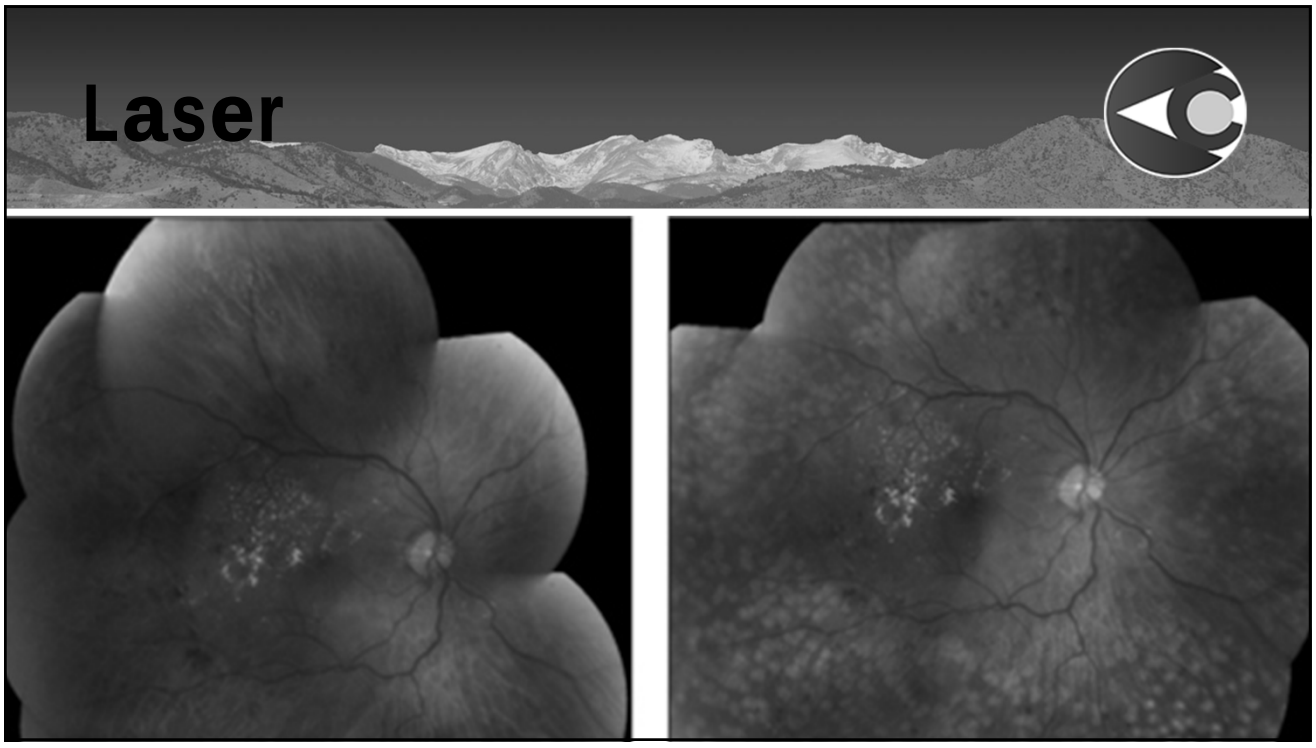
DME has been addressed…

…what about the PDR?


Laser
Cool!


Laser

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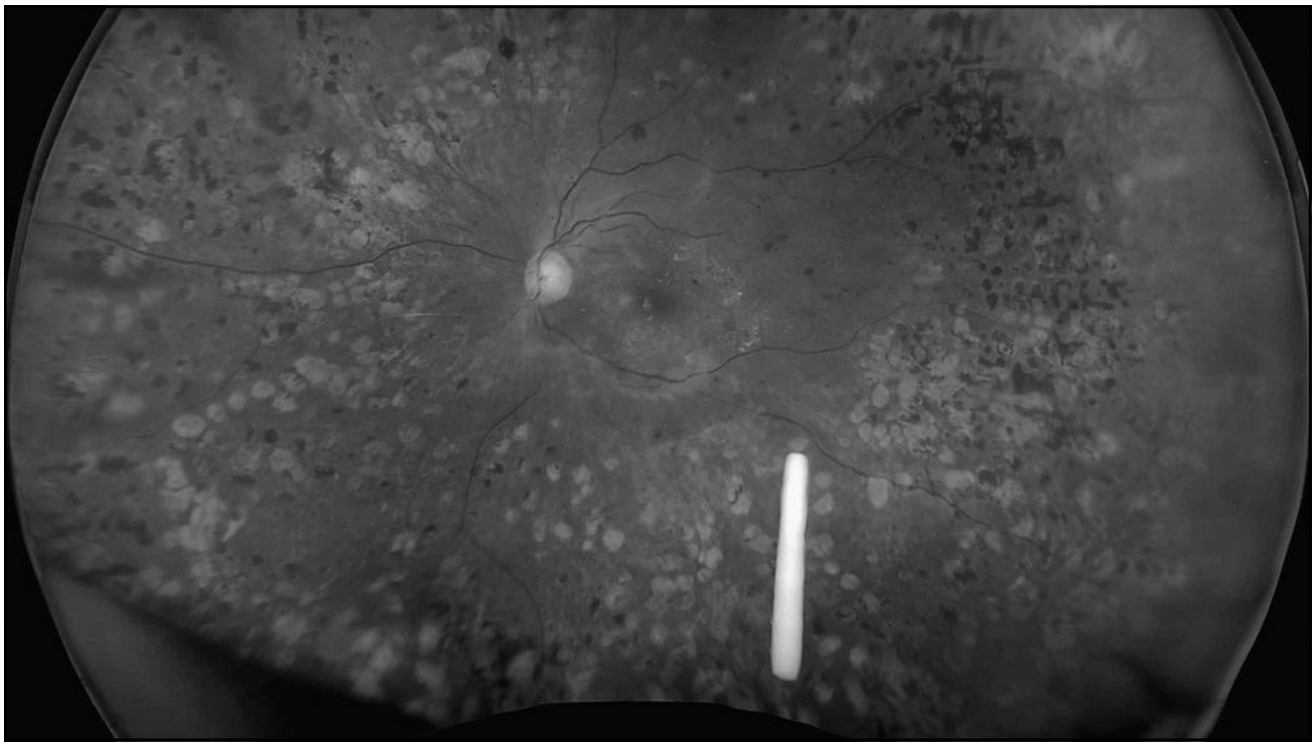


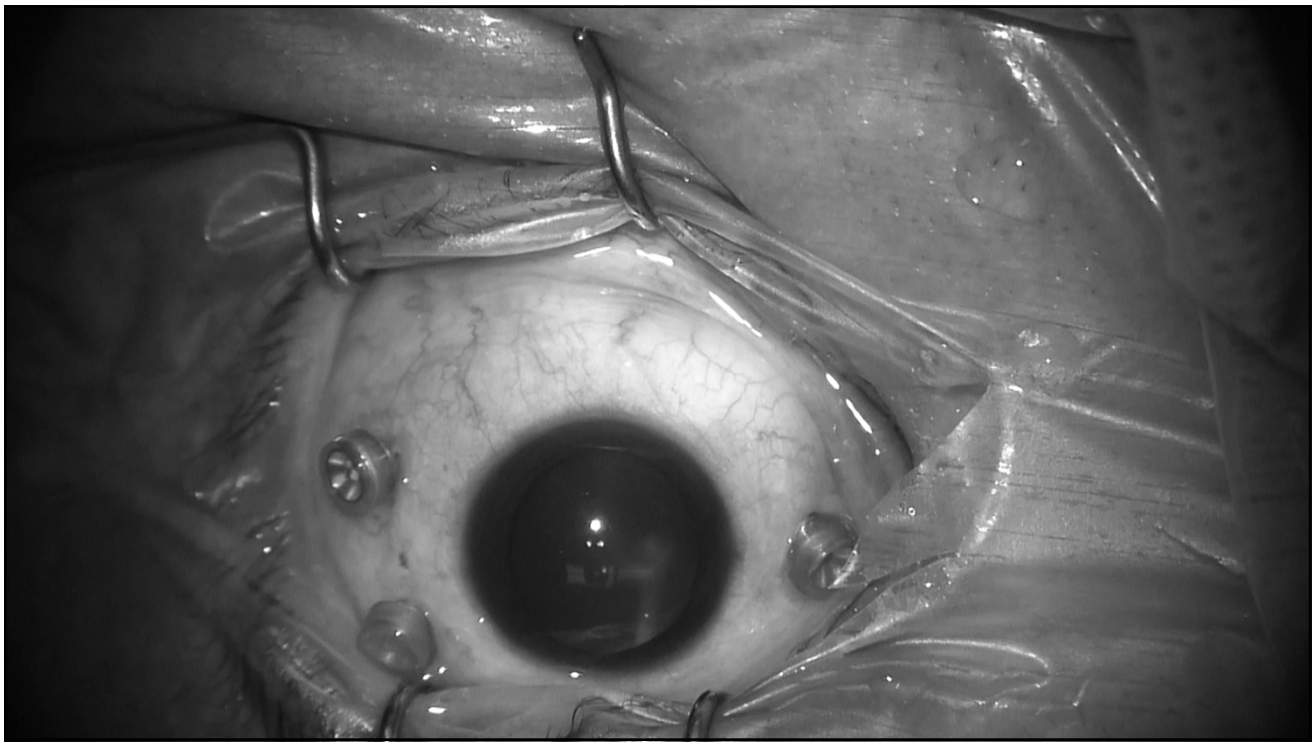
Update

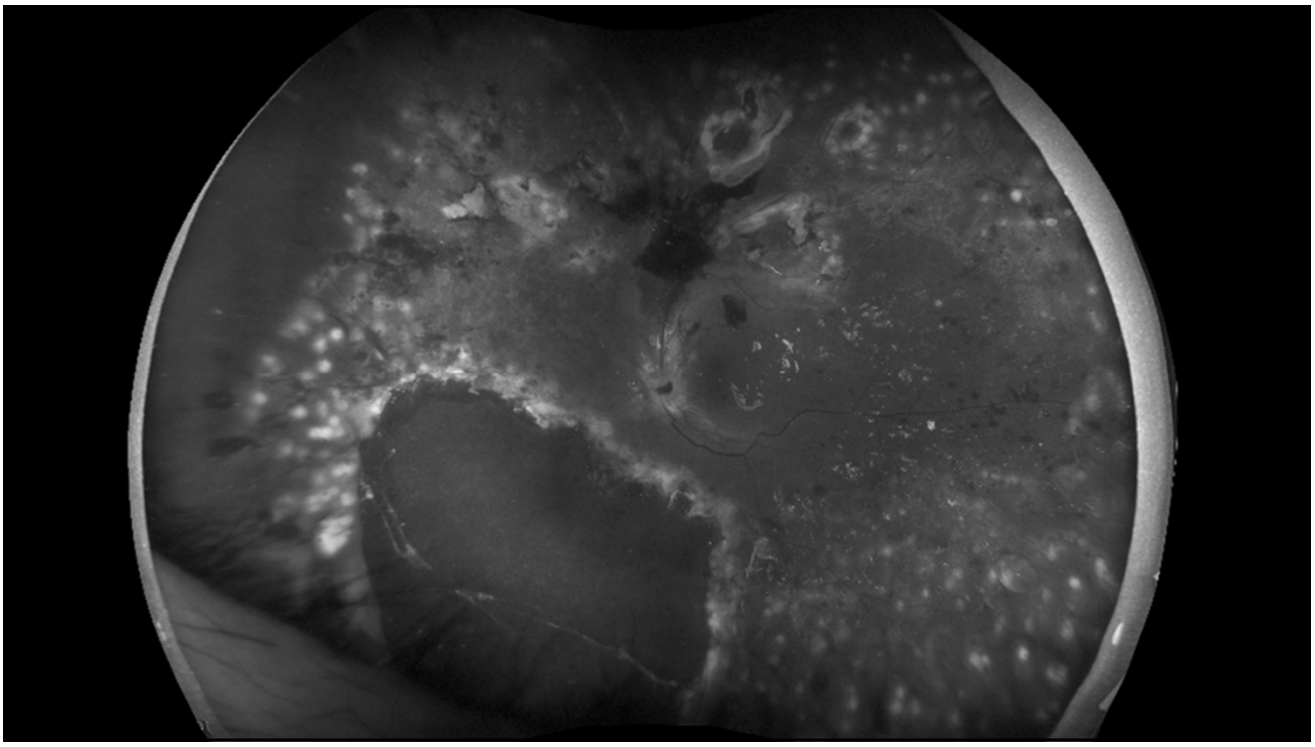
- Patient developed uncontrolled BP and proteinuria consistent with preeclampsia
- Her vitreous hemorrhage in the right eye worsened and she will require surgery post-partum to improve her vision and prevent recurrent hemorrhage in the future

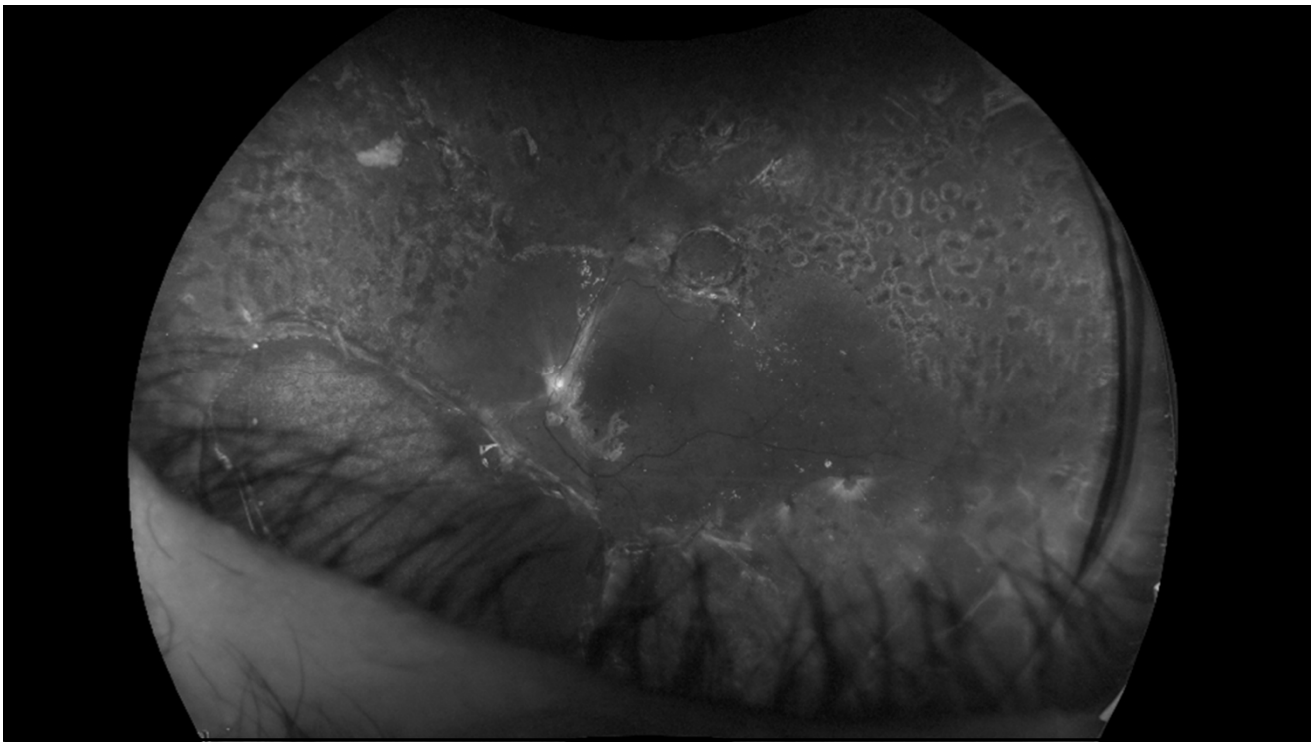
Case 2

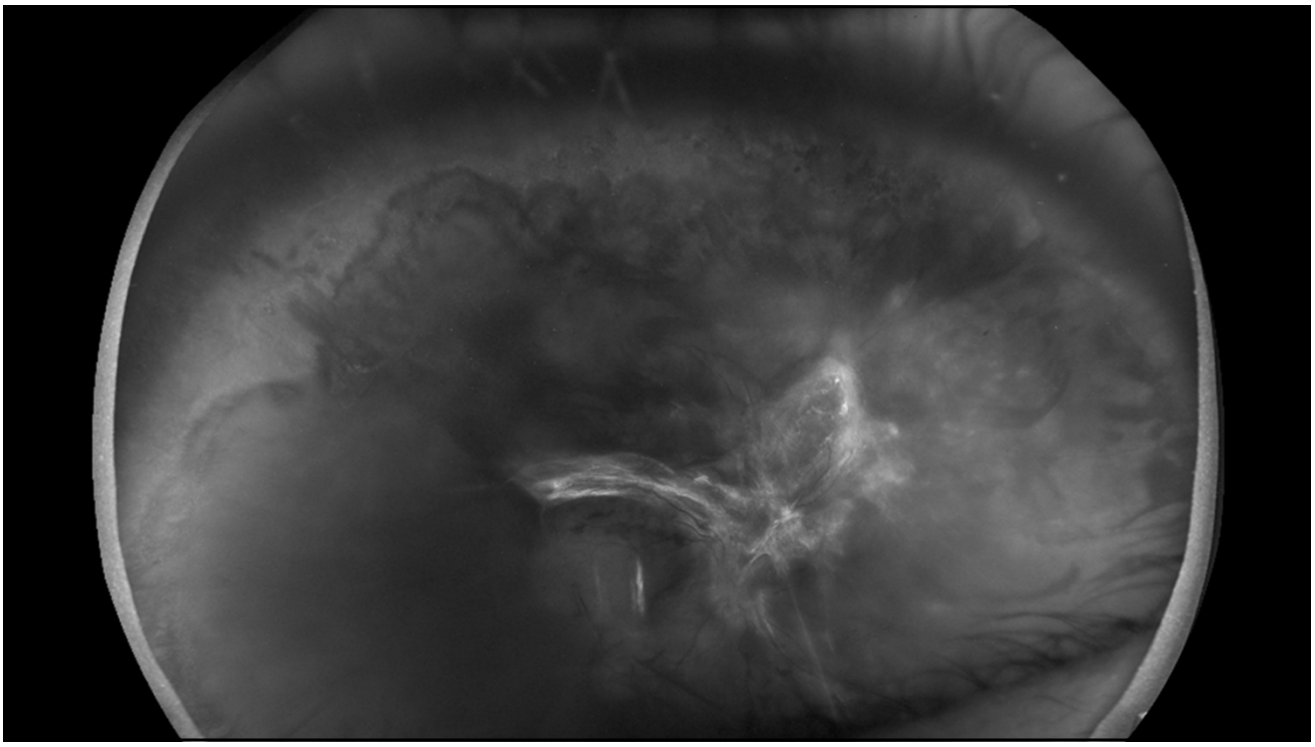
CC

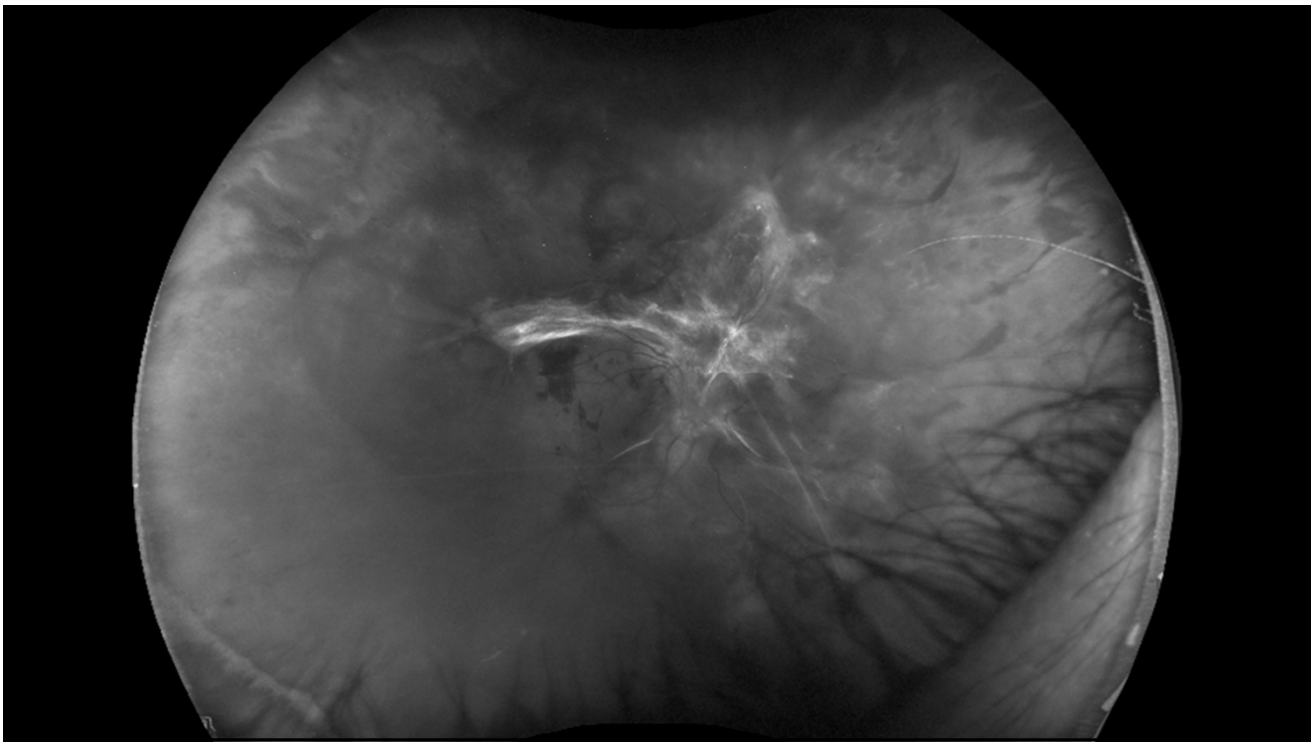
34 y/o F presenting with bilateral vision loss

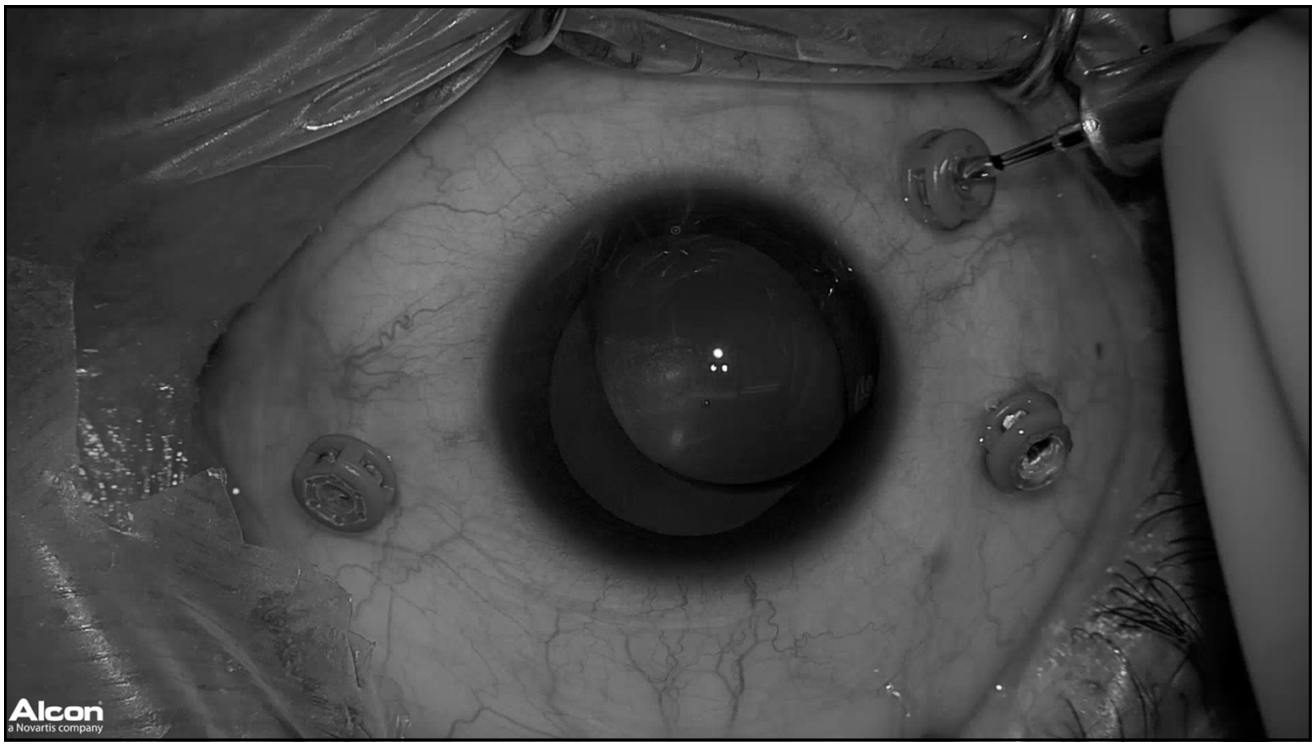


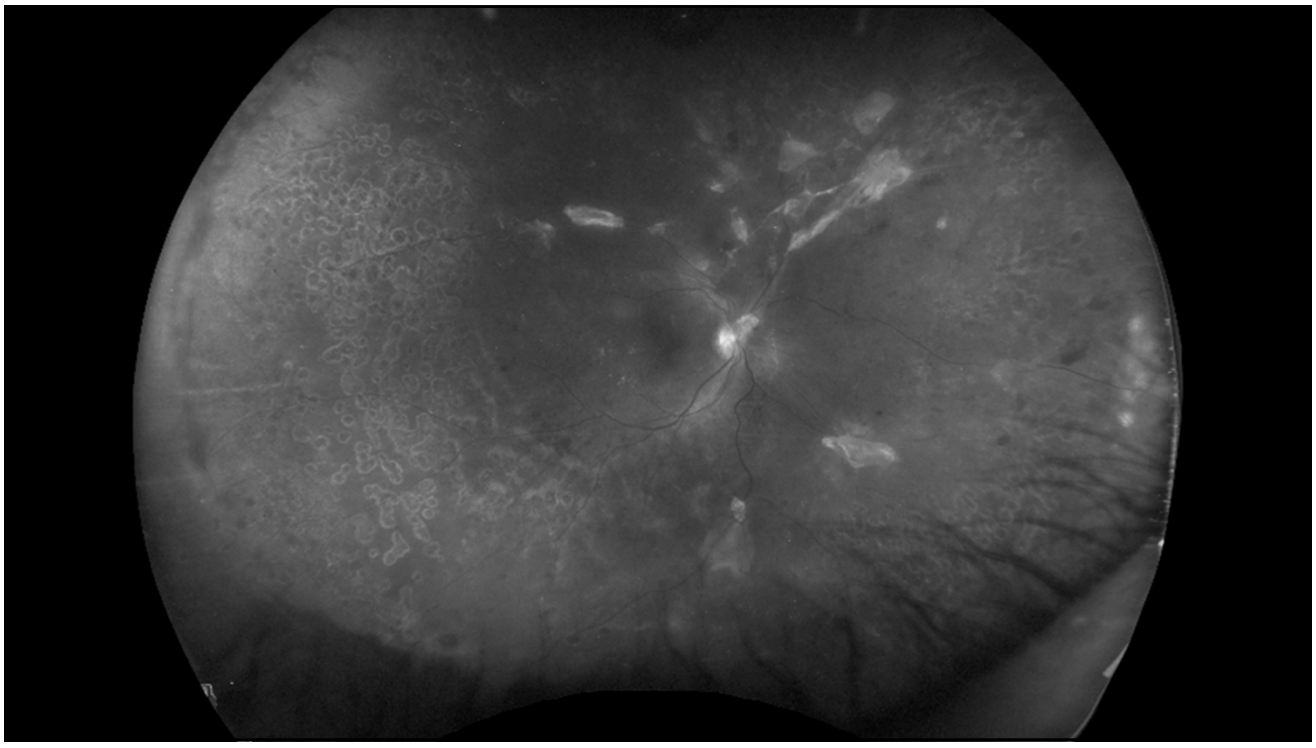









Alcon
a Novartis company



The Data

Lancet Diabetes Endocrinol. 2017 Jun;5(6):431-437. doi: 10.1016/S2213-8587(17)30104-3. Epub 2017 Mar 30.

Effects of intensive glucose control on microvascular outcomes in patients with type 2 diabetes: a meta-analysis of individual participant data from randomised controlled trials.

Zoungas S[1], Arima H[2], Gerstein HC[3], Holman RR[4], Woodward M[5], Reaven P[6], Hayward RA[7], Craven T[8], Coleman RL[4], Chalmers J[9]; Collaborators on Trials of Lowering Glucose (CONTROL) group.

⊕ Author information

Abstract

BACKGROUND: Intensive glucose control is understood to prevent complications in adults with type 2 diabetes. We aimed to more precisely estimate the effects of more intensive glucose control, compared with less intensive glucose control, on the risk of microvascular events.

METHODS: In this meta-analysis, we obtained de-identified individual participant data from large-scale randomised controlled trials assessing the effects of more intensive glucose control versus less intensive glucose control in adults with type 2 diabetes, with at least 1000 patient-years of follow-up in each treatment group and a minimum of 2 years average follow-up on randomised treatment. The prespecified and standardised primary outcomes were kidney events (a composite of end-stage kidney disease, renal death, development of an estimated glomerular filtration rate <30 mL/min per 1·73m^2, or development of overt diabetic nephropathy), eye events (a composite of requirement for retinal photocoagulation therapy or vitrectomy, development of proliferative retinopathy, or progression of diabetic retinopathy), and nerve events (a composite of new loss of vibratory sensation, ankle reflexes, or light touch). We used a random-effects model to calculate overall

The Data

Incentives in Diabetic Eye Assessment by Screening (IDEAS) trial: a three-armed randomised controlled trial of financial incentives.

Judah G[1], Darzi A[1], Vlaev I[2], Gunn L[3], King D[4], King D[1], Valabhji J[5], Bishop L[6], Brown A[7], Duncan G[6], Fogg A[6], Harris G[7], Tyacke P[6], Bicknell C[1].

Southampton (UK): NIHR Journals Library; 2017 Mar.
Health Services and Delivery Research.

⊕ Author information

Excerpt

BACKGROUND: The UK national diabetic eye screening (DES) programme invites diabetic patients aged > 12 years annually. Simple and cost-effective methods are needed to increase screening uptake. This trial tests the impact on uptake of two financial incentive schemes, based on behavioural economic principles.

OBJECTIVES: To test whether or not financial incentives encourage screening attendance. Secondarily to understand if the type of financial incentive scheme used affects screening uptake or attracts patients with a different sociodemographic status to regular attenders. If financial incentives were found to improve attendance, then a final objective was to test cost-effectiveness.

DESIGN: Three-armed randomised controlled trial.

SETTING: DES clinic within St Mary's Hospital, London, covering patients from the areas of Kensington, Chelsea and Westminster.

PARTICIPANTS: Patients aged ≥ 16 years, who had not attended their DES appointment for ≥ 2 years.

The Data

Higher levels of physical activity are independently associated with a lower incidence of diabetic retinopathy in Japanese patients with type 2 diabetes: A prospective cohort study, Diabetes Distress and Care Registry at Tenri (DDCRT15).

Kuwata H[1], Okamura S[2], Hayashino Y[2], Tsujii S[2], Ishii H[1]; Diabetes Distress and Care Registry at Tenri Study Group.

⊕ Author information

Abstract

We assessed the prospective association between baseline levels of physical activity (PA) and the incidence of newly developed diabetic retinopathy (DR) in patients with type 2 diabetes. Data from 1,814 patients with type 2 diabetes without DR were obtained from a Japanese diabetes registry at Tenri Hospital, Nara, Japan. To assess the independent correlations between baseline PA levels and newly developed DR, the participants were divided into five categories based on their PA levels. A Cox proportional hazards model with time-varying exposure information was used and adjusted for potential confounders to assess the independent correlations. At baseline, the mean age, BMI, and hemoglobin A1c levels of the patients were 65.5 years, 24.5 kg/m2, and 7.2% (54 mmol/mol), respectively. After 2 years, newly developed DR was confirmed in 184 patients (10.1%). Patients with newly developed DR had longer duration of type 2 diabetes (14.7 versus 11.0 years, $p < 0.0001$), higher systolic blood pressure (139.2 versus 135.1 mmHg, $p = 0.0012$), lower estimated glomerular filtration rate (74.0 versus 77.1 mL/min/1.73 m2, $p = 0.0382$), greater urinary albumin-creatinine ratio (4.00 versus 2.45 mg/mmol, $p < 0.0039$), and higher HbA1c levels (7.5 versus 7.2%, $p = 0.0006$) than those without newly developed DR. The multivariable-adjusted hazard ratios for DR development were 0.87 (95% CI, 0.53-1.40; $p = 0.557$), 0.83 (95% CI, 0.52-1.31; $p = 0.421$), 0.58 (95% CI, 0.35-0.94; $p = 0.027$), and 0.63 (95% CI, 0.42-0.94; p

The Data

Diabetes Care. 1995 May;18(5):631-7.

Metabolic control and progression of retinopathy. The Diabetes in Early Pregnancy Study. National Institute of Child Health and Human Development Diabetes in Early Pregnancy Study.

Chew EY[1], Mills JL, Metzger BE, Remaley NA, Jovanovic-Peterson L, Knopp RH, Conley M, Rand L, Simpson JL, Holmes LB, et al.

⊕ Author information

Abstract

OBJECTIVE: To evaluate the role of metabolic control in the progression of diabetic retinopathy during pregnancy.

RESEARCH DESIGN AND METHODS: We conducted a prospective cohort study of 155 diabetic women in the Diabetes in Early Pregnancy Study followed from the periconceptional period to 1 month postpartum. Fundus photographs were obtained shortly after conception (95% within 5 weeks of conception) and within 1 month postpartum. Glycosylated hemoglobin was measured weekly during the 1st trimester and monthly thereafter.

RESULTS: In the 140 patients who did not have proliferative retinopathy at baseline, progression of retinopathy was seen in 10.3, 21.1, 18.8, and 54.8% of patients with no retinopathy, microaneurysms only, mild nonproliferative retinopathy, and moderate-to-severe nonproliferative retinopathy at baseline, respectively. Proliferative retinopathy developed in 6.3% with mild and 29% with moderate-to-severe baseline retinopathy. Elevated glycosylated hemoglobin at baseline and the magnitude of improvement of glucose control through week 14 were associated with a higher risk of progression of retinopathy (adjusted odds ratio for progression in those with glycohemoglobin > or = 6 SD above the control mean versus those within 2 SD was 2.7; 95% confidence interval was 1.1-7.2; P = 0.039).

The Data

Cochrane Database Syst Rev. 2014 Feb 14;(2):CD009122. doi: 10.1002/14651858.CD009122.pub2.

Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus.

Fullerton B[1], Jeitler K, Seitz M, Horvath K, Berghold A, Siebenhofer A.

⊕ Author information

Abstract

BACKGROUND: Clinical guidelines differ regarding their recommended blood glucose targets for patients with type 1 diabetes and recent studies on patients with type 2 diabetes suggest that aiming at very low targets can increase the risk of mortality.

OBJECTIVES: To assess the effects of intensive versus conventional glycaemic targets in patients with type 1 diabetes in terms of long-term complications and determine whether very low, near normoglycaemic values are of additional benefit.

SEARCH METHODS: A systematic literature search was performed in the databases The Cochrane Library, MEDLINE and EMBASE. The date of the last search was December 2012 for all databases.

SELECTION CRITERIA: We included all randomised controlled trials (RCTs) that had defined different glycaemic targets in the treatment arms, studied patients with type 1 diabetes, and had a follow-up duration of at least one year.

DATA COLLECTION AND ANALYSIS: Two review authors independently extracted data, assessed studies for risk of bias, with differences resolved by consensus. Overall study quality was evaluated by the 'Grading of Recommendations Assessment, Development, and Evaluation' (GRADE) system. Random-effects models were used for the main analyses and the results are presented as risk ratios (RR) with 95% confidence intervals (CI) for dichotomous outcomes.

The Data

Kidney Int. 2004 Sep;66(3):1173-9.

Risk factors for renal replacement therapy in the Early Treatment Diabetic Retinopathy Study (ETDRS), Early Treatment Diabetic Retinopathy Study Report No. 26.

Cusick M[1], Chew EY, Hoogwerf B, Agrón E, Wu L, Lindley A, Ferris FL 3rd; Early Treatment Diabetic Retinopathy Study Research Group.

⊕ Author information

Abstract

BACKGROUND: Diabetes is a leading cause of end-stage renal disease (ESRD). The purpose of this study is to assess the risk factors for renal replacement therapy (RRT) in the Early Treatment Diabetic Retinopathy Study (ETDRS).

METHODS: We examined demographic, clinical, and laboratory characteristics of the 2226 subjects with complete laboratory data enrolled in the ETDRS. The primary renal variable evaluated was the time to development of renal replacement therapy, defined as the need for dialysis or transplantation. Multivariable Cox proportional hazards regression was used to assess risk factors for type 1 and type 2 diabetes separately.

RESULTS: The 5-year estimated incidence of RRT in the entire ETDRS population was 10.2% and 9.8% for patients with type 1 and type 2 diabetes, respectively. Of those patients with complete data, 127 of 934 (14%) of patients with type 1 diabetes, and 150 of 1292 (12%) patients with type 2 diabetes required RRT during the study. Baseline risk factors common to type 1 and type 2 diabetes included elevated total cholesterol, and serum creatinine; and low serum albumin and anemia. Other risk factors significant in type 1 diabetes included body mass index (BMI), shorter duration of diabetes, elevated hemoglobin A(1c) (HbA(1c)), elevated systolic blood pressure, and the development

Questions?

Thank you!