Diabetic Retinopathy

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Financial disclosures

- None

Learning Objectives

- Understand the epidemiology and pathogenesis of diabetic retinopathy
- Discuss diabetic retinopathy disease as an serious public health problem
- Identify the risk factors for diabetic retinopathy
- Describe diabetic retinopathy classification
- Discuss the medical and surgical treatment of diabetic retinopathy
- Describe how vision loss can be prevented

Diabetic retinopathy: Why does it matter?

- Leading cause of blindness in patients aged 20-64 years old
- Microvascular end-organ damage to the eye
- Prevalence increases with the duration of diabetes and patient age

The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR)

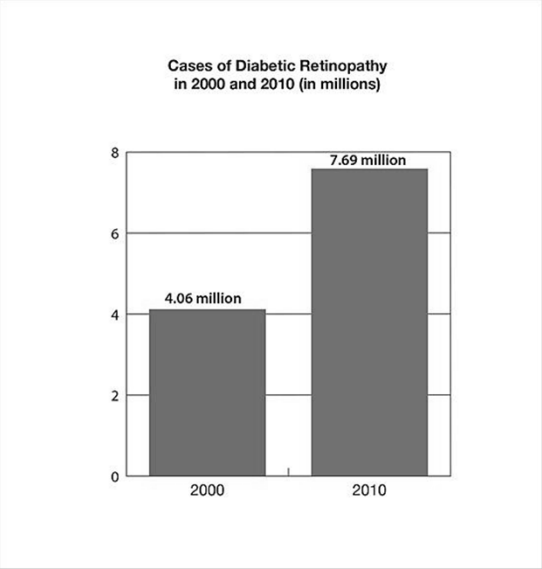
- 99% Type 1 DM – some degree of retinopathy
- 60% Type 2 DM
- Legal blindness
  - 86% younger-onset DM
  - 33% older-onset DM

Diabetes Mellitus: Epidemiology

- CDC estimates that 37.3 million Americans have diabetes
  - 20% are yet to be diagnosed
- Type II accounts for 95%, affecting 10 % of population
- Prevalence is constantly increasing

Source: https://www.cdc.gov/diabetes/basics/diabetes.html

Projections for Diabetic Retinopathy



- Projections for Diabetic Retinopathy
- From 2010 to 2050 the number is projected to double
- 7.7 million to 14.6 million
- Leading cause of blindness in working-age Americans

Source: https://www.nei.nih.gov/learn-about-eye-health/outreach-campaigns-and-resources/eye-health-data-and-statistics/diabetic-retinopathy-data-and-statistics

Recommended Eye Exam Schedules

Table 2 – Recommended Eye Examinations For Patients with Diabetes Mellitus of No Diabetic Retinopathy

Diabetes Type	Recommendation Initial Evaluation	Recommended Follow-up*
Type 1’	5 years after diagnosis[34]	Yearly[34]
Type 2’	At time of diagnosisYearly[40,122]	Yearly[40,122]
Pregnancy (type 1 or type 2)	Soon after conception and early in the first trimester[123-125]	• No retinopathy to mild or moderate NPDR: every 3-12 months[123-125] • • Severe NPDR or worse every 1-3 months[123-125]

Modified from American Academy of Ophthalmology: 2019 Preferred Practice Patterns, *Diabetic retinopathy*

NPDR = nonproliferative diabetic retinopathy

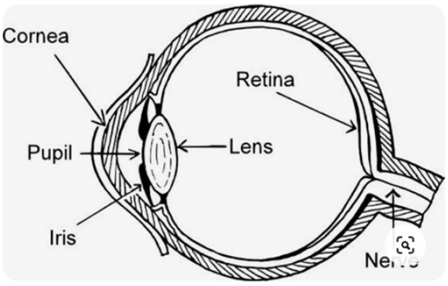
*Abnormal findings may dictate frequent follow-up examinations

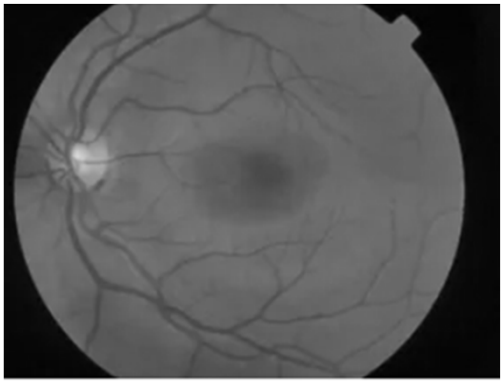
‘Pubertal patients require increased vigilance due to increased risk of progression

Women who develop gestational diabetes do not require an eye examination during pregnancy and do not appear to be at increased risk for diabetic retinopathy during pregnancy.

Source: https://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp

Normal Eye





www.aao.org

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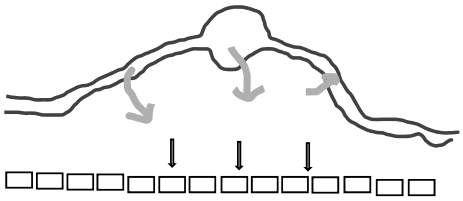
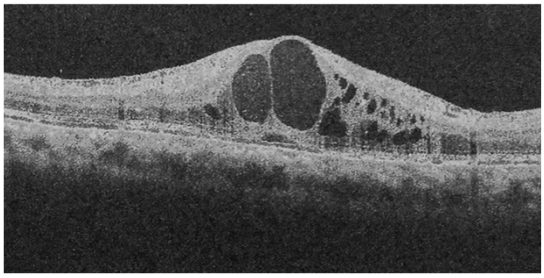
Pathogenesis: capillary leak

- hyperglycemia → endothelial damage





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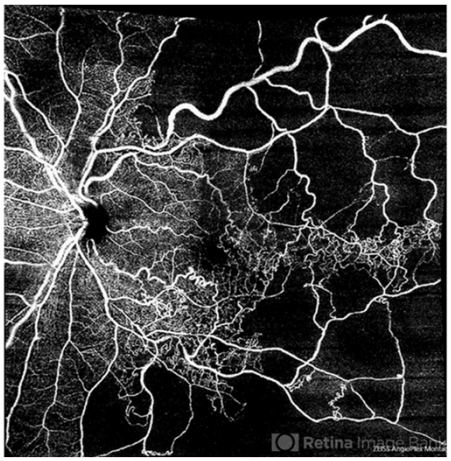
Pathogenesis: capillary occlusion

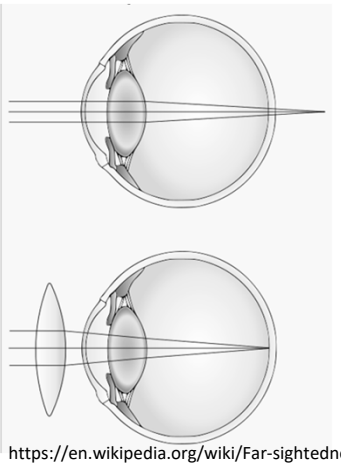
- Selective loss of pericytes and basement membrane thickening → capillary occlusion and retinal non-perfusion
- Progression from mild to advanced: blood pressure, lipid profile, blood sugar levels



By JEFFERSON R SOUSA, Tecg.º (Biomedical Systems Technology)
Institute Suel Abujamra

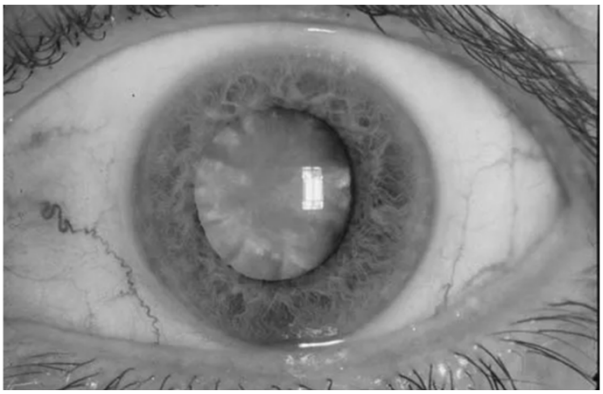
Blurred vision without retinopathy…

Acquired hyperopia



https://en.wikipedia.org/wiki/Far-sightedness

Cataracts



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Diabetic retinopathy classification

Non-proliferative (NPDR)

- Mild
- Moderate
- Severe

Proliferative (PDR)

- Early
- High-risk
- Advanced

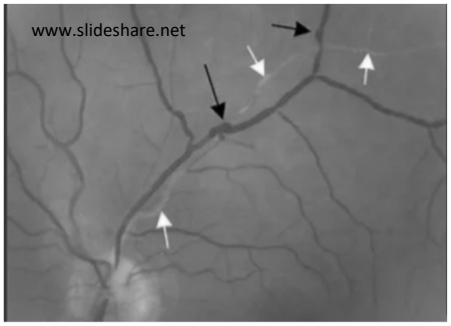
Clinical findings in NPDR

- Microaneurysms
- Nerve fiber layer infarcts (“cotton wool spots”)
- Intraretinal microvascular abnormalities (IRMAs)
- Intraretinal hemorrhages (“dot-and-blot”)

This image was originally published in the Retina Image Bank. Henry J. Kaplan, MD. Niloofar Piri, MD. Diabetes NPDR. Retina Image Bank. 2013; 5362 © the American Society of Retina Specialists.

Other findings

- Capillary non-perfusion
- Dilation and beading of retinal veins

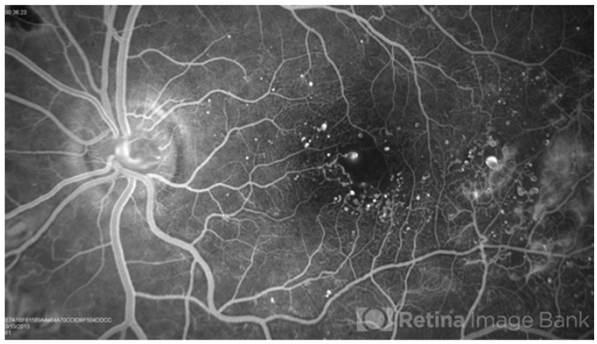


- Macular edema
- Hard exudates

This image was originally published in the Retina Image Bank. Mallika Goyal, MD. Diabetic macular edema. Retina Image Bank. Oct 26, 2012; 1837. © the American Society of Retina Specialists.

Diabetic macular edema

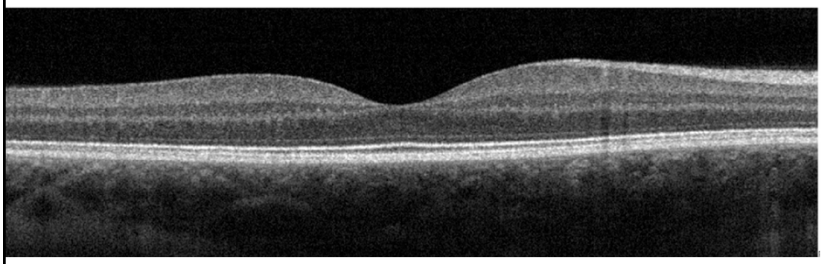
- Retinal edema involving or threatening fovea → vision loss
- Abnormal retinal vascular permeability
- Diagnosis predominantly using optic coherence tomography (OCT)



This image was originally published in the Retina Image Bank. Pamela A Weber, MD. James B. Soque, CRA, OCT-C, COA, FOPS. Diabetic Macular Edema, Proliferative Diabetic retinopathy, Neovascularization elsewhere. Retina Image Bank. Apr 1, 2013; 5480. © the American Society of Retina Specialists.

Optical Coherence Tomography (OCT)

- imaging technique common in retina
- uses low-coherence light to capture micrometer-resolution



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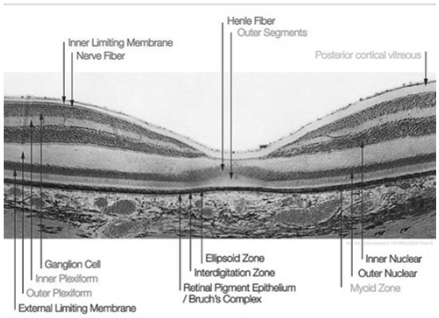


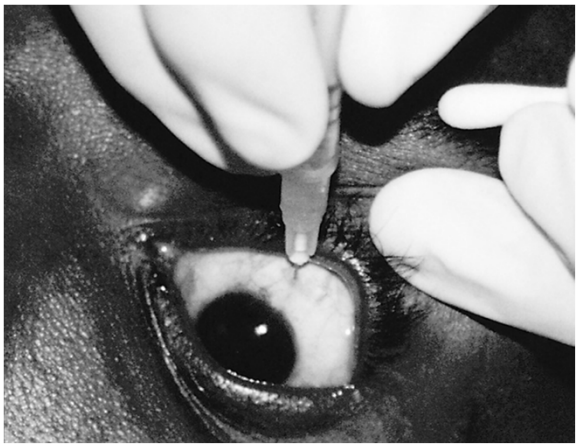
Treatment of DME: the beginning

Pxhere.com

- Lifestyle modifications – diet, exercise, smoking cessation
- Optimization of blood sugar, lipid levels, BMI

Escalating treatment

- Injection of corticosteroid (intravitreal)
- Injection of anti-VEGF (intravitreal)
- Focal laser photocoagulation



Linda Visser. Published in: *Community Eye Health Journal* Vol. 16 No. 47 2003

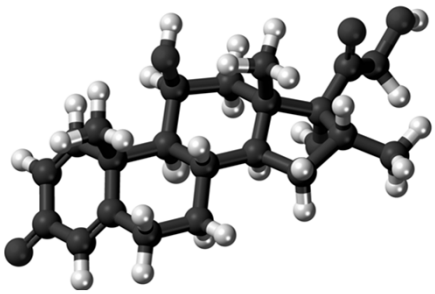
Intravitreal Anti-VEGF

- Blocks angiogenesis and decreases capillary "leak"
- Avastin was first anti-VEGF medication: used to treat colon cancer
- Ranibizumab (Lucentis), bevacizumab (Avastin), and aflibercept (Eylea)

Wanjiku Mathenge.
Published in: Community Eye Health Journal Vol. 27 No. 87 2014

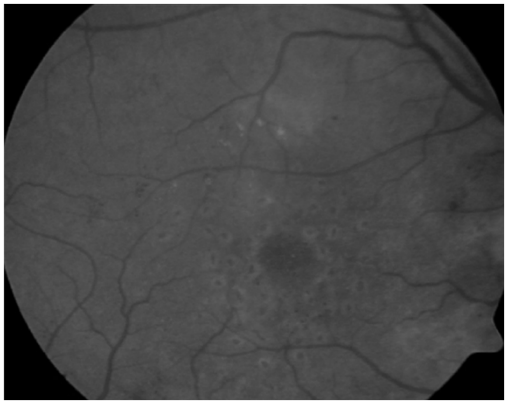
Intravitreal corticosteroid

- Triamcinolone (Triesence)- 1 month
- Dexamethasone (Ozurdex) – 3 months
- Fluocinolone acetonide (Iluvien) – 36 months!



Focal laser photocoagulation

- Laser treats small leaking microaneurysms in the macula



Nicholas Beare
Published in: RSOC Vol. 13 No. 17 2016. Published online 31 March 2017

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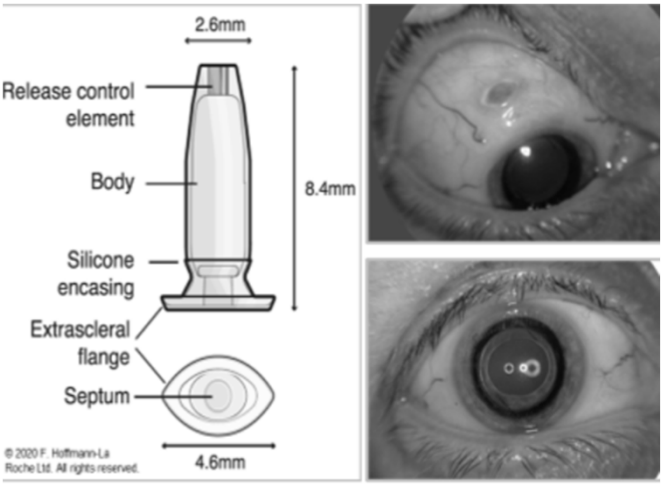
New FDA approved therapies

- Faricimab (Vabysmo) : angiopoietin-2 and VEGF-A targets
- Brolicizumab (Beovu): anti-VEGF

- Both medications thought to decrease treatment burden
- Beovu used with caution

In clinical trials…

- Port delivery system – Ranibizumab (Susvimo)
- Silicone reservoir surgically implanted
- Can hold 20 uL (very concentrated Ranibizumab)
- Refillable in clinic via self-sealing septum every 6 months



Exam Schedule Based on DR Severity

Table 5 – Initial Management Recommendations For Patients with Diabetes

Severity of Retinopathy	Presence of Macular Edema	Follow-up (Months)	Panretinal Photocoagulation (Scatter) Laser	Focal and/or Grid Laser*	Intravitreal Anti-VEGF Therapy
Normal or minimal NPDR	No	12	No	No	No
Mild NPDR	No NCI-DME CI-DME	12 3-6 1*	No No No	No Sometimes Rarely	No No Usually
Moderate NPDR	No NCI-DME CI-DME	6-12 3-6 1*	No No No	No Sometimes Rarely	No Rarely Usually

Modified from American Academy of Ophthalmology: 2019 Preferred Practice Patterns, *Diabetic retinopathy*

Source: https://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp

Exam Schedule Based on DR Severity

Table 5 – Initial Management Recommendations For Patients with Diabetes

Severity of Retinopathy	Presence of Macular Edema	Follow-up (Months)	Panretinal Photocoagulation (Scatter) Laser	Focal and/or Grid Laser*	Intravitreal Anti-VEGF Therapy
Severe NPDR	No NCI-DME CI-DME	3-4 2-4 1*	Sometimes Sometimes Sometimes	No Sometimes Rarely	Sometimes Sometimes Usually
Non-high-risk PDR	No NCI-DME CI-DME	3-4 2-4 1*	Sometimes Sometimes Sometimes	No Sometimes Sometimes	Sometimes Sometimes Usually
High-risk PDR	No NCI-DME CI-DME	2-4 2-4 1*	Recommended Recommended Recommended	No Sometimes Sometimes	Sometimes Sometimes Usually

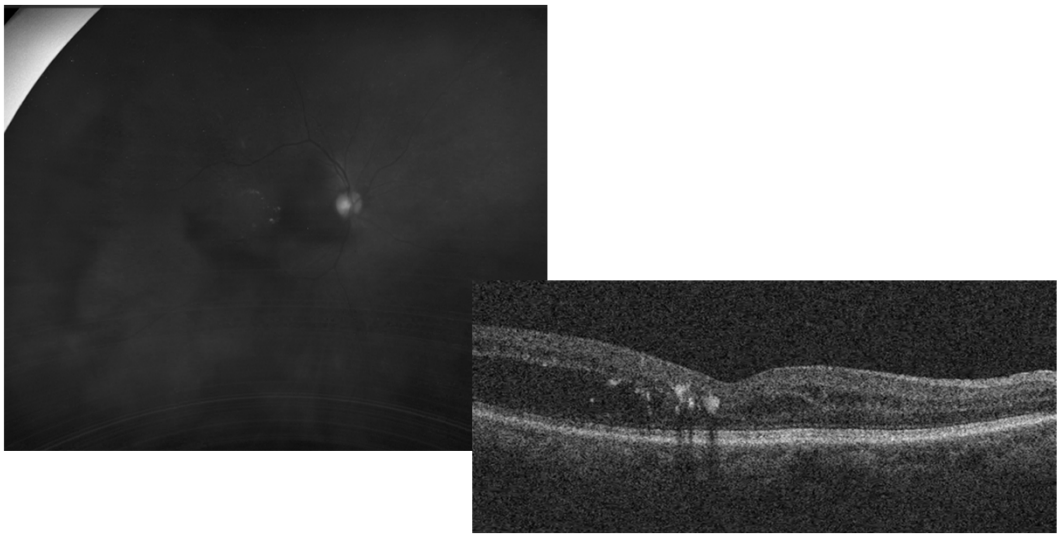
Modified from American Academy of Ophthalmology: 2019 Preferred Practice Patterns, *Diabetic retinopathy*

Source: https://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp

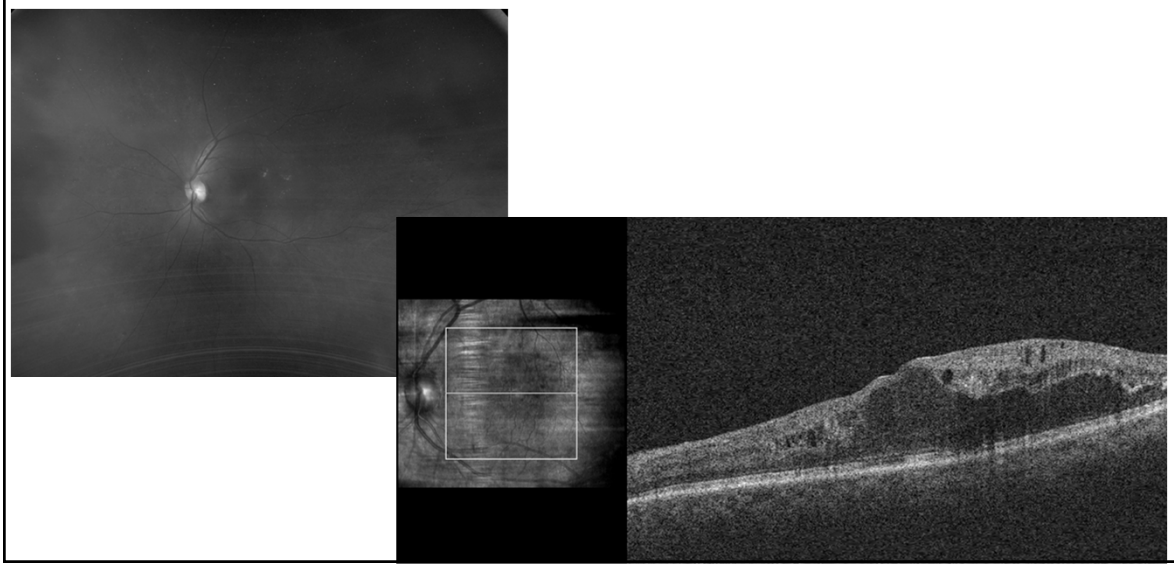
Case #1

- 72 yo AAF with Type 2 DM
- Blurred vision for past couple years
- VA 20/30 in right eye, 20/50 in left eye
- Last A1C 7.1% - had been “much higher” (around 11) couple years ago

Right eye



Left eye

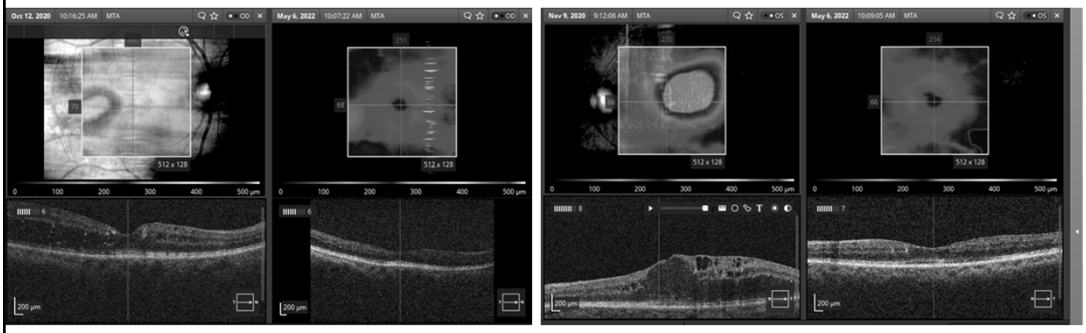


Treatment course

- Started on q4 weeks bilateral Avastin injections
- Switched to Eylea injections after few months (Protocol T)
- “treat-and-extend” – currently q 8 week injections

Then…and now

Right eye – 20/25 **Left eye – 20/25**



Diabetic Retinopathy

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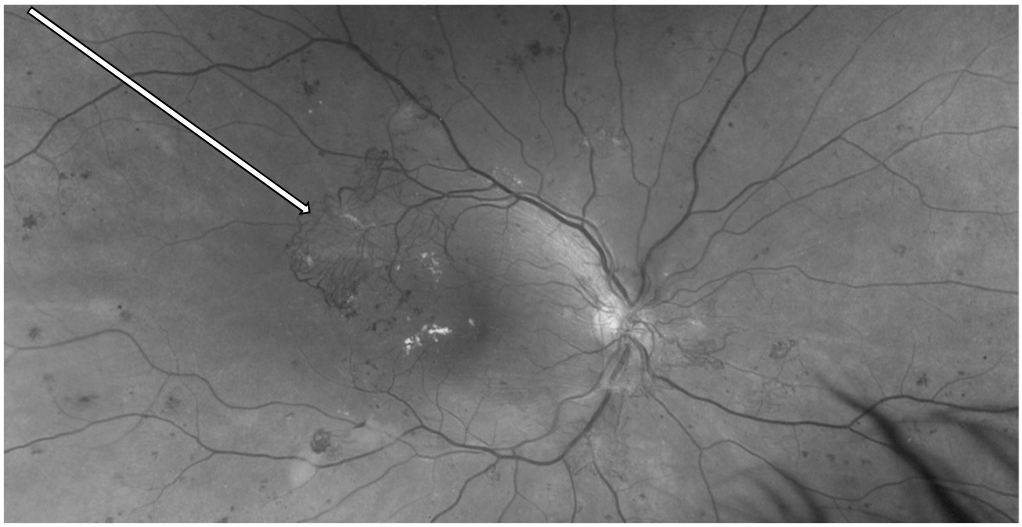
Proliferative Diabetic Retinopathy (PDR)

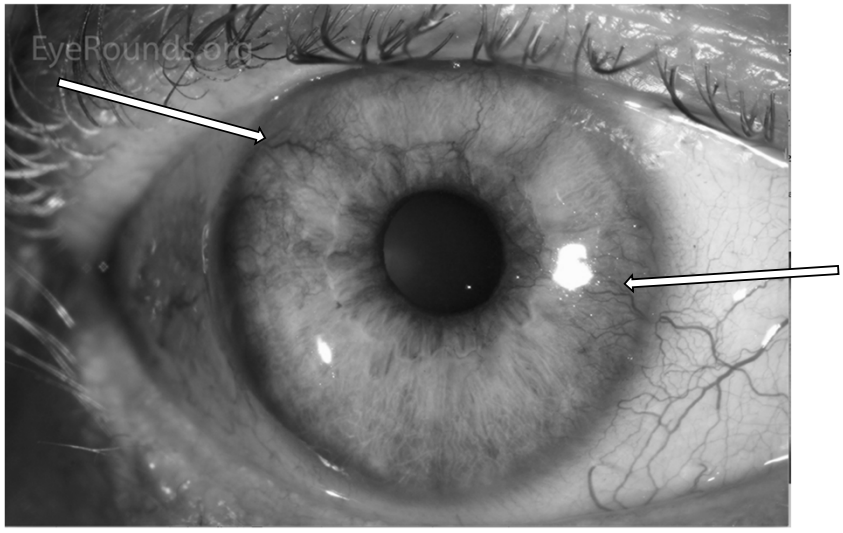
- Most severe stage of diabetic retinopathy
- Ischemia leads to angiogenesis i.e. neovascularization
- Can develop on the optic nerve, iris or retina
- Fragile disorganized vessels, prone to hemorrhage and fibrosis

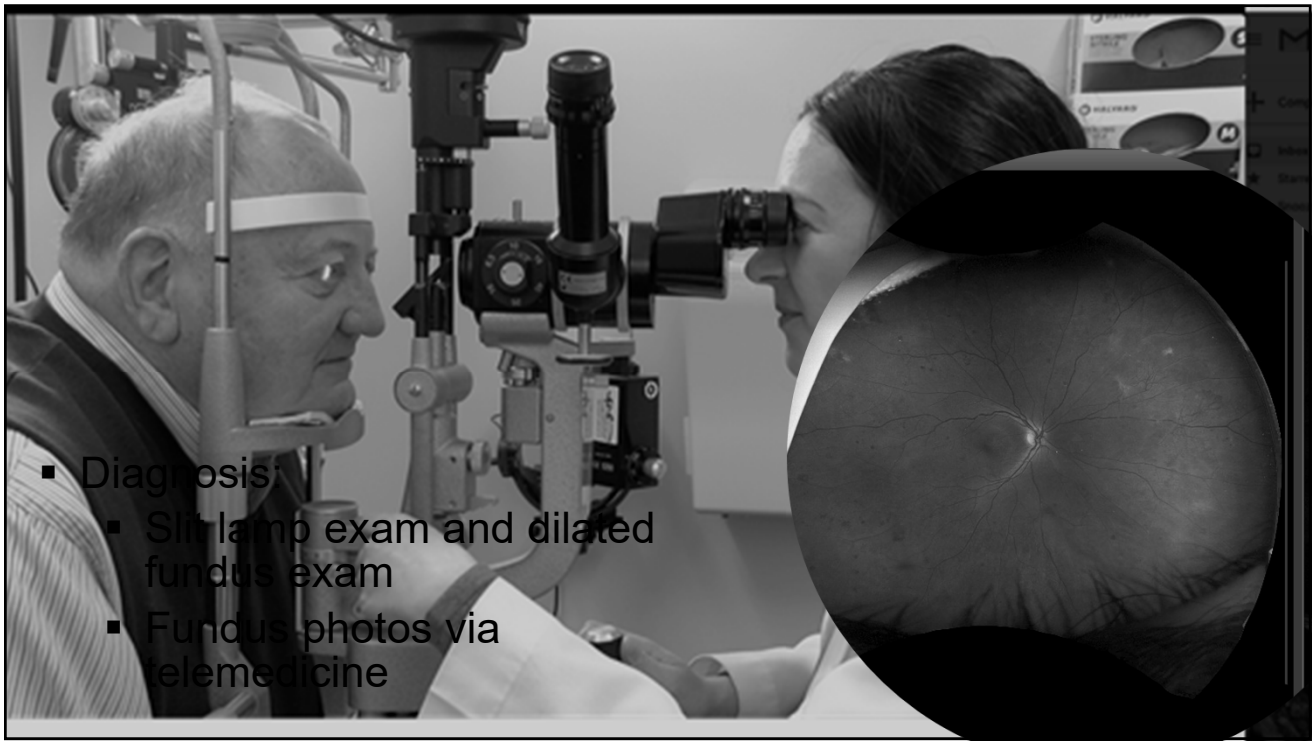
Neovascularization at Optic Nerve Head (NVD)

Neovascularization Elsewhere (NVE)



Neovascular on the Iris (NVI)

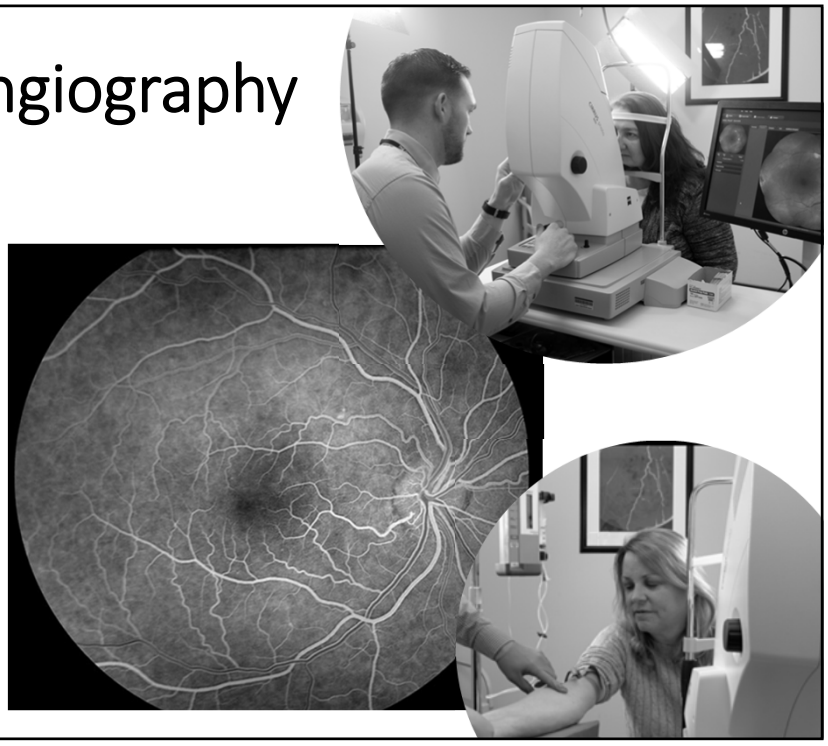




- Diagnosis:
  - Slit lamp exam and dilated fundus exam
  - Fundus photos via telemedicine

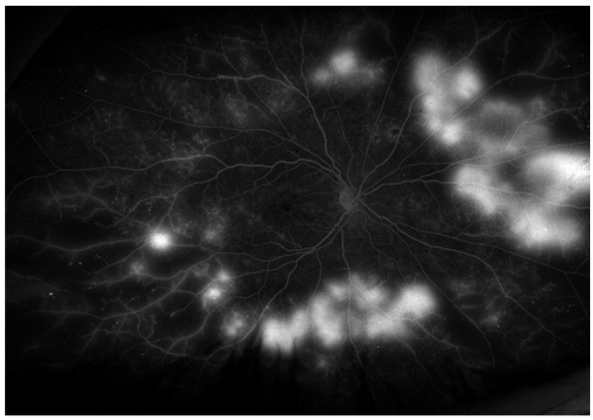
Fluorescein Angiography

- Sodium fluorescein dye
- Intravenous injections



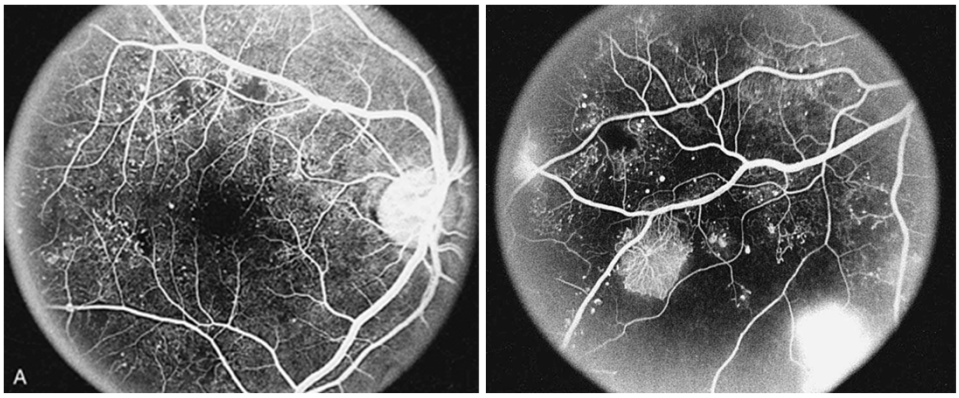
Fluorescein Angiography

Hyperfluorescence – leakage



Fluorescein Angiography

Hypofluorescence – non-perfusion

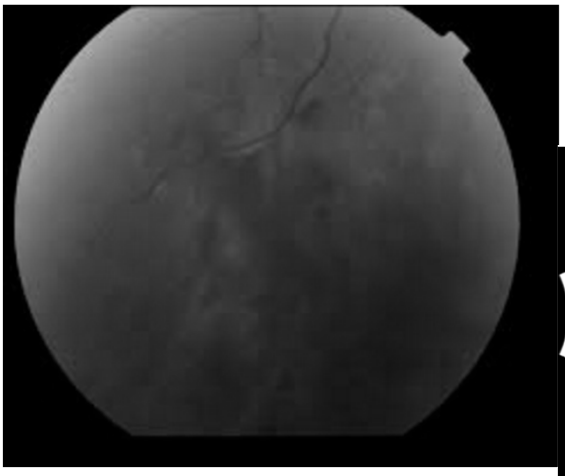


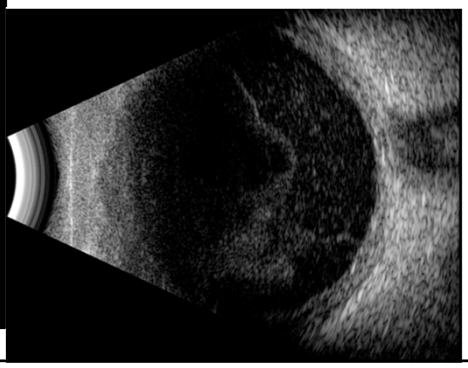
Presentation

- Asymptomatic
- Vision loss
  - Vitreous hemorrhage
  - Tractional retinal detachment
  - Neovascular glaucoma
  - Macula ischemia
  - Macula edema

I. Vitreous Hemorrhage

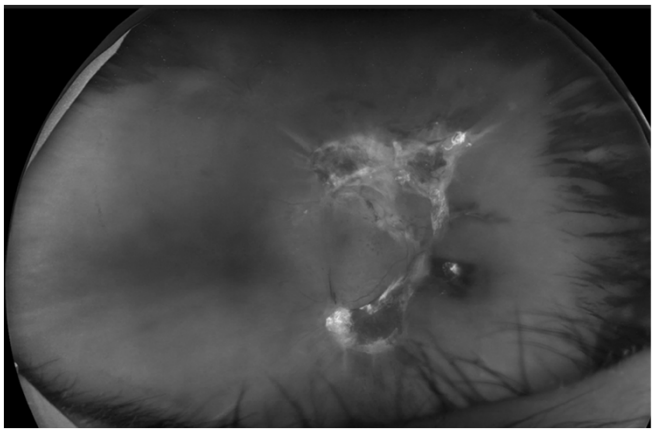
- Hemorrhage from neovascularization
- Sudden blurred or decrease of vision
- Black floaters



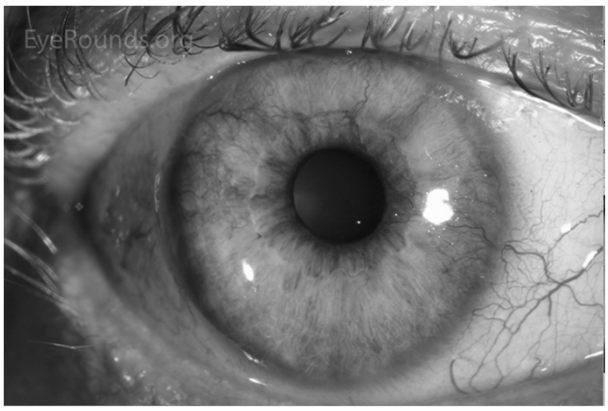


II- Tractional Retinal Detachment

- Neovascularization is fibrovascular process
- Tissue contracts over time and pulls up on the retina, often causing it to detach
- Asymptomatic or slow progressive vision loss
- Treatment is surgical
- Prognosis is typically poor, but with new microsurgical tools and techniques, outcomes have improved significantly



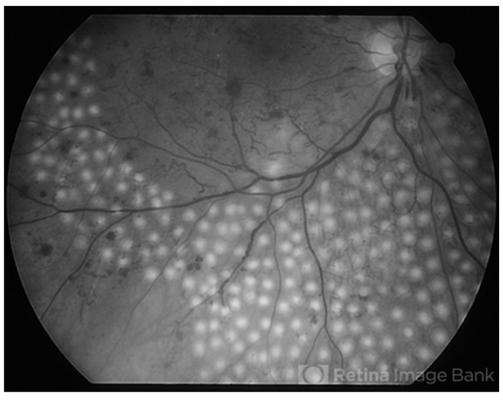
III- Neovascular Glaucoma



- Neovascular membranes occlude the trabecular meshwork
- Severe elevation in the intraocular pressure
- Eye pain and headache
- True emergency
- Can rapidly lead to severe and irreversible blindness

Management of PDR

- The goal is to decrease the ischemic drive to allow the neovascularization to regress
- Pan-retinal laser photocoagulation (PRP)
  - The standard for care for decades
- Intravitreal anti-VEGF injections
  - Fast acting
  - Requires frequent injections
- Combo treatment is often needed



"This image was originally published in the Retina Image Bank. Henry J. Kaplan, MD Niloofar Piri, MD. University of LouisvillePan photocoagulation laser retina image back. Retina Image Bank. 2013; 5338. © the American Society of Retina Specialists."

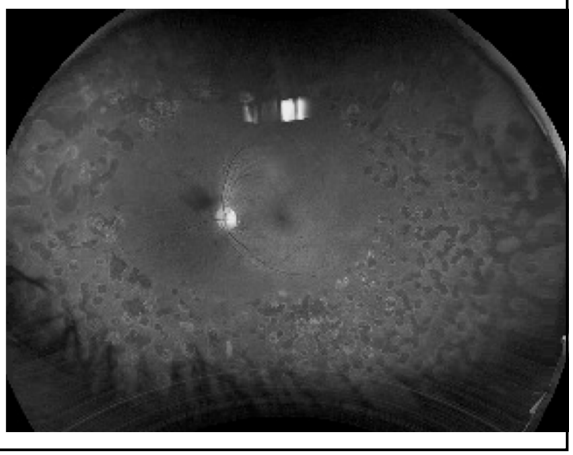
Mechanisms of Laser Photocoagulation

Laser destroys the peripheral retina

→Decreases retina oxygen consumption of the retina

→ decreases ischemic drive

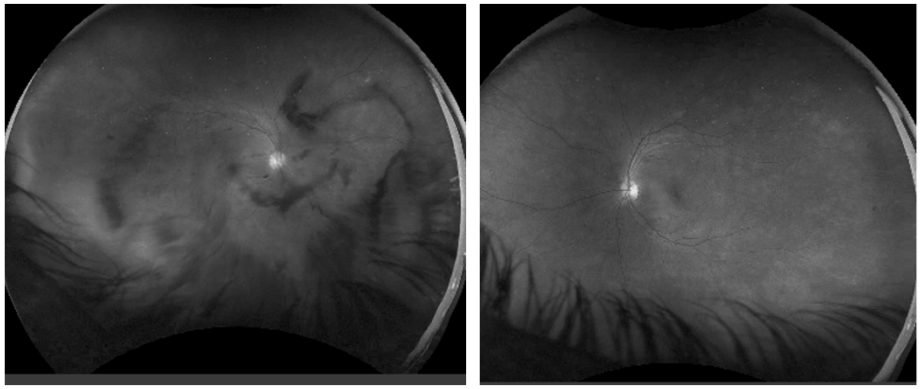
→ regression of NV



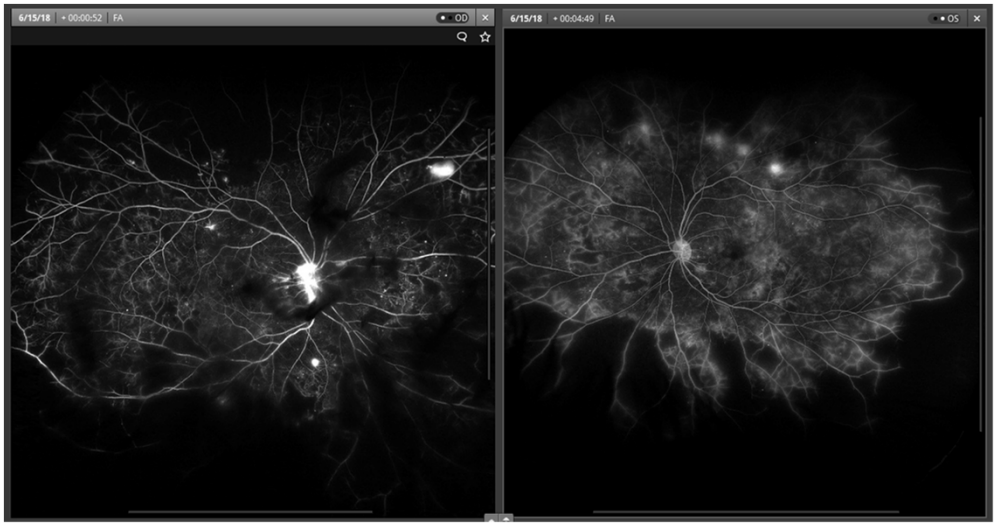
Case #1

- 46 yo male with type 2 DM for 11 years with an HgA1C 11.8 %
- Blurred vision in right eye for 2 days
- VA 20/200 in right eye, 20/ 25 in left eye

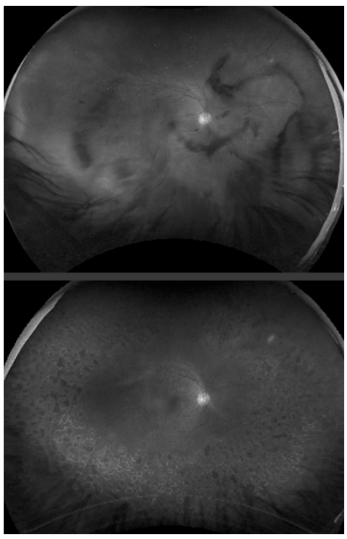
Fundus photos

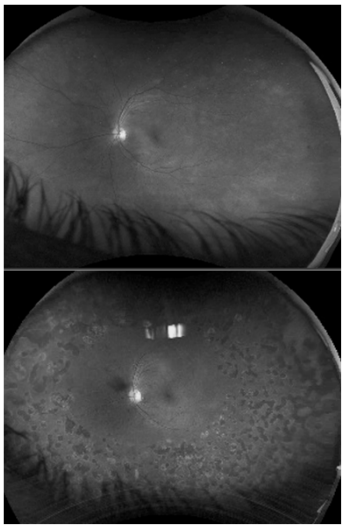


Fluorescein angiography



s/p Laser photocoagulation in both eyes

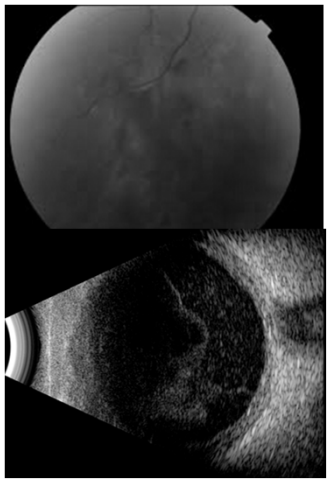




4 years f/u:
- HgA1C 6.2
- vision: 20/25 in both eyes

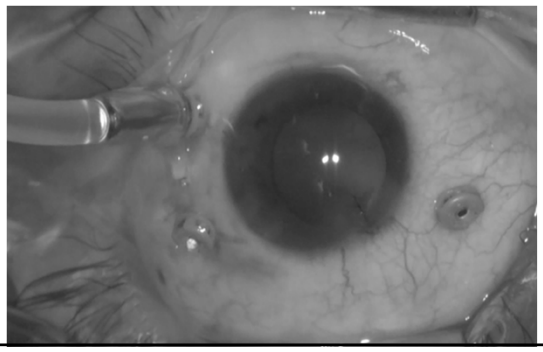
Management of Vitreous hemorrhage

- Vitreous hemorrhage
  - Can re-absorb over time
  - Intravitreal anti-VEGF injection
  - Laser photocoagulation
  - Pars plana Vitrectomy



Surgical management of PDR

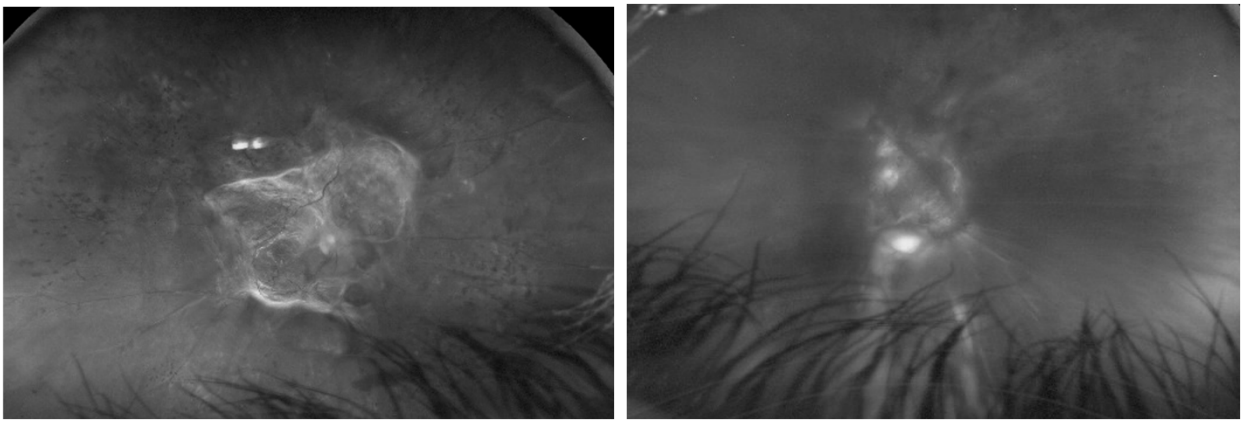
- Usually in setting of non-clearing vitreous hemorrhage or tractional retinal detachment
- Pars plana vitrectomy
  - Small incision (23, 25, 27 G) – 3 “ports”
  - Involves removing vitreous gel
  - Segmenting/peeling tractional membranes as needed
  - Endolaser (surgical PRP)



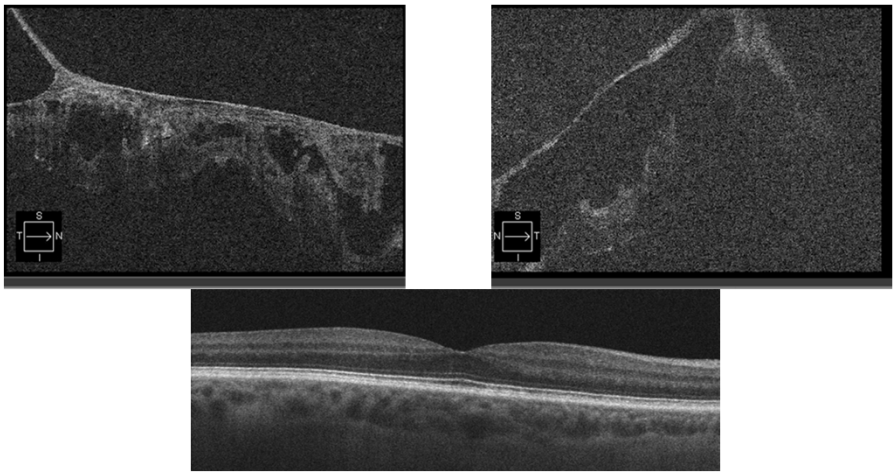
Case #2

- 33 yo female with type 2 DM for 9 years with an HgA1C 12.1%
- Blurred vision in both eyes for 7 months
- VA 20/400 in right eye, CF in left eye

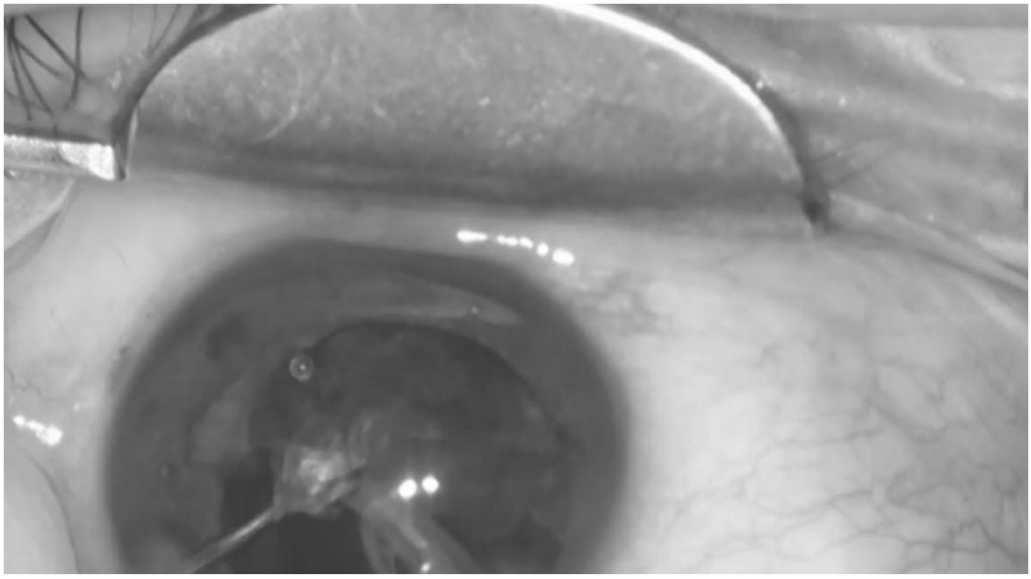
Fundus Photo



OCT Macula



Video of TRD Repair Combined with Cataract Surgery

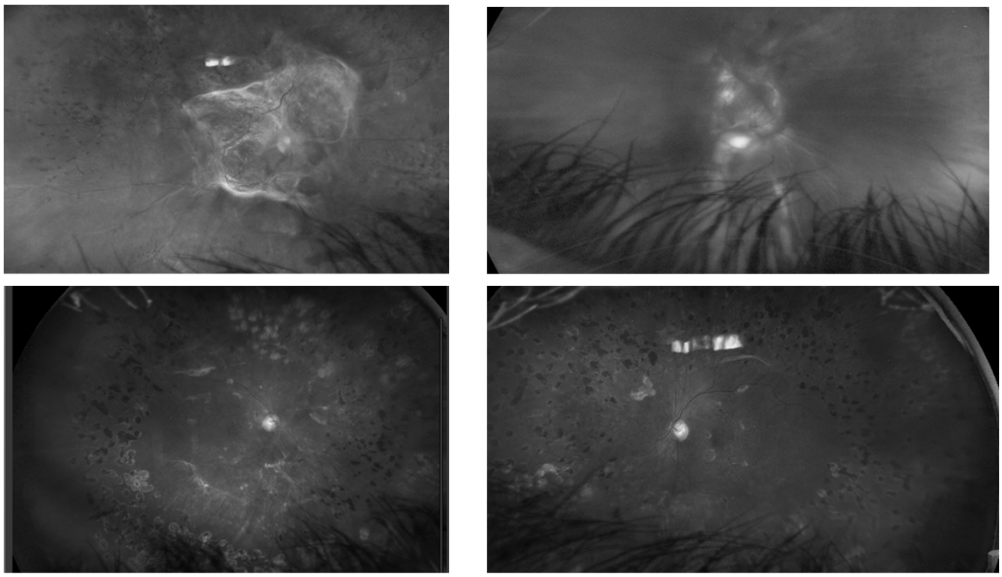


TRD repair, both eyes

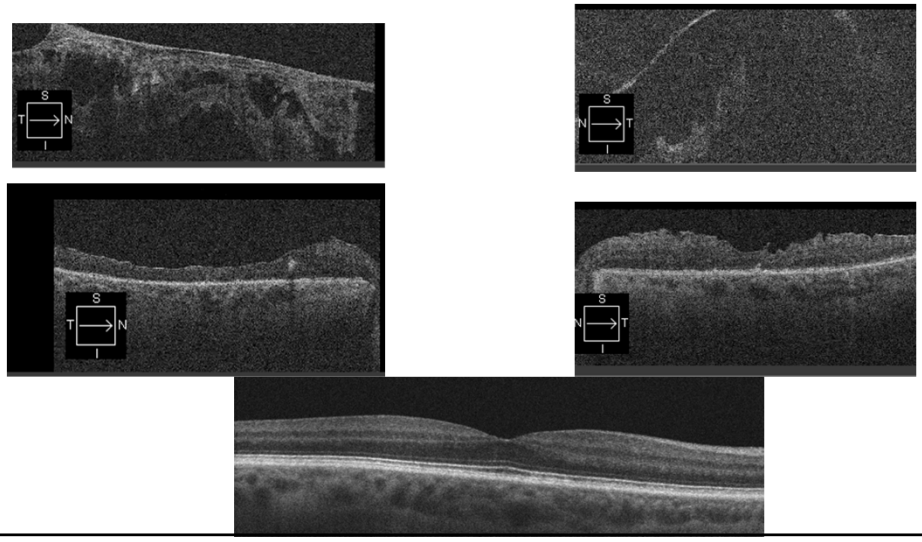
Before: 20/400 and CF

After: 20/60

And 20/30



OCT Before and after surgery



PREVENTION

- 90 percent of vision loss due to diabetic eye disease can be prevented
- Primary prevention
  - Strict glycemic control
  - Blood pressure control
- Secondary prevention
  - Annual eye exams
- Tertiary prevention
  - Retinal Laser photocoagulation
  - Intravitreal injection
  - Vitrectomy

http://www.aao.org/newsroom/release/20091030.cfm

Systemic Medical Management

- Most important: good glycemic control
- 2 clinical trials: intensive glycemic control reduces risk of developing diabetic retinopathy and reduces progression of existing retinopathy
  - DCCT (Diabetes Control and Complications Trial) – Type I
  - UKPDS (United Kingdom Prospective Diabetes Study) – Type II

DCCT and EDIC

- The Diabetes Control and Complications Trial (DCCT, 1982-93) multicenter randomized clinic trial that enrolled 1441 patients with Type 1 diabetes with no retinopathy or mild to moderate diabetic retinopathy

Study Groups:

Intensive control of blood sugar vs conventional management

Outcome variables:

Development and progression of the early vascular (including diabetic retinopathy) and neurologic complications of type 1 diabetes

DCCT and EDIC

- Epidemiology of Diabetes Interventions and Complications (EDIC, 1994-2006)
- A follow-up study that examined the longer term effects on complications, such as cardiovascular and more advanced stages of retinal and renal disease
- Intensive therapy reduces the development and progression of all diabetes-specific complications by as much as 76%
- Diabetic retinopathy
  - PDR 63% DDCT 76% EDIC
  - DME 26% DDCT 77% EDIC
  - Laser therapy 51%DDCT 77% EDIC

DCCT and EDIC

- Intensive intervention is most effective when implemented early in the course of diabetes
- Chronic glycemia and duration of diabetes are the major factors in the pathogenesis of microvascular complications

UKPDS

- UK Prospective Diabetes Study (UKPDS) multicenter randomized clinic trial that enrolled 5,102 patients for 1977 to 1997
- Study group
  - Intensive control of blood sugar vs conventional management

Study questions:

Will intensive **blood sugar** control in Type II DM, reduce DR progression?

2. Will intensive **blood pressure** control in Type II DM, reduce DR progression?

Results:

Intensive blood sugar AND blood pressure control slowed progression of retinopathy and reduced the risk of other microvascular complications of DM

Conclusion

- Diabetic retinopathy is a serous public health problem and is the leading cause of blindness in working age Americans
- The stages of diabetic retinopathy
- Medical and surgical management of diabetic retinopathy
- Vision loss can be prevented through glycemic control, annual eye exams and retinal therapeutic interventions