

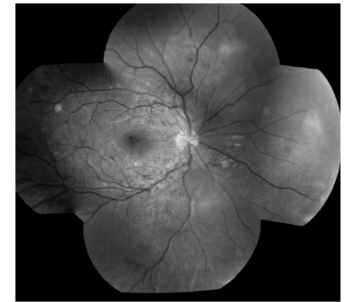
Preventing & Treating Diabetes-Related Blindness

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Everything You Wanted to Know About Diabetic Retinopathy

And then some...



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Prevalence of Diabetes



World wide impact of diabetes

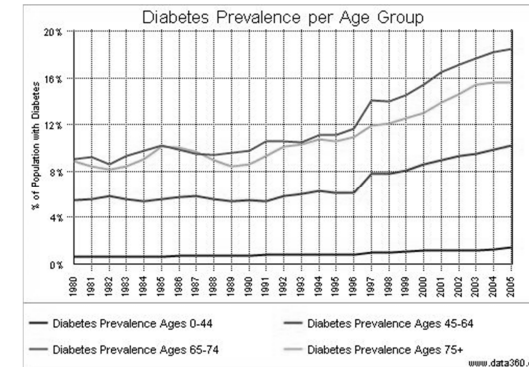
Prevalence estimates of diabetes, 2025



SOURCE: DIABETES ATLAS THIRD EDITION, © INTERNATIONAL DIABETES FEDERATION, 2006

Diabetes Facts

- Diabetes affects 25.8 million people of all ages in the US
 - This is 8.3% of the population
- Among people 65 years and older, 26.9% have diabetes
 - 50% are considered pre-diabetic



<http://diabetes.niddk.nih.gov/dm/pubs/statistics/>



Age-adjusted prevalence of diagnosed diabetes in US adults^{1,2}



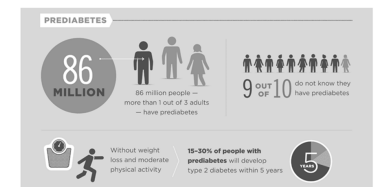
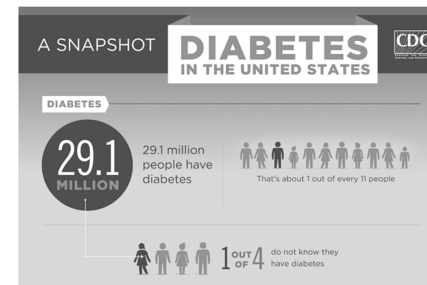
How common is diabetes?

1994 > 1998 > 2003 > 2008 > 2014

1. Centers for Disease Control and Prevention. http://www.cdc.gov/diabetes/statistics/slides/maps_diabetes_trends.pptx. Accessed March 8, 2016.
 2. Centers for Disease Control and Prevention. <http://gis.cdc.gov/grasp/diabetes/DiabetesAtlas.html>. Accessed March 29, 2016.

Staggering Numbers – thanks Apple, Pepsi, Chipotle!

- 29 MILLION in USA have Diabetes
- 86 MILLION in USA have Pre-Diabetes !!!
- 1 in 4 Don't KNOW they have it !
- 250 BILLION DOLLARS annual healthcare costs



CDC Centers for Disease Control and Prevention
 CDC 24/7: Saving Lives. Protecting People™

The Burden of Diabetes in Colorado



Diabetes is growing at an epidemic rate in the United States. According to the Centers for Disease Control and Prevention (CDC), nearly 30 million Americans have diabetes and face its devastating consequences. What's true nationwide is also true in Colorado.

Colorado's diabetes epidemic:

Approximately **416,301 people in Colorado**, or 9.8% of the adult population, have diabetes.

- Of these, an estimated **118,000 have diabetes but don't know it**, greatly increasing their health risk.
- In addition, **1,342,000 people in Colorado**, 34.8% of the adult population, have **prediabetes** with blood glucose levels higher than normal but not yet high enough to be diagnosed as diabetes.

Diabetes costs an estimated **\$3.6 billion** in Colorado each year.

The serious complications include heart disease, stroke, amputation, end-stage kidney disease, blindness – and death.

44% of Coloradans are Diabetic or Pre-Diabetic



Diabetes is Associated with Serious Systemic Comorbidities

Diabetic Retinopathy

28.5% of adults with diabetes ≥ 40 years of age have DR¹

~13% of DR patients have DME²

Diabetic Nephropathy

~33% of self-reported diabetics have chronic renal disease³

Diabetic Neuropathy

60%-70% of people with diabetes have some form of nervous system damage¹

Whatever is observed in the retinal blood vessels, is also taking place in all of the other major organs- brain, heart, kidneys.

stroke
DME patients are ~2 times more likely to have a stroke compared with diabetes patients without DME⁴

Coronary Heart Disease
DME patients are 2.5 times more likely to have a heart attack compared with diabetes patients without DME⁴

Prevalence of Microvascular and Macrovascular Complications in Patients With Diabetes and DME

1. National Diabetes Fact Sheet, 2011. <http://apps.nccd.cdc.gov/DDTSTRS/FactSheet.aspx>; 2. NHANES database search by Genentech, data on file; 3. US Renal Data System. <http://www.usrds.org/atlas.aspx>; 4. Nguyen-Khoa et al. *BMC Ophthalmology*; 2012;12:11.

NPDR & PDR

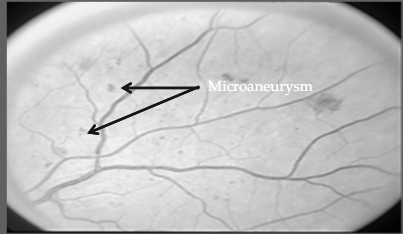
- nonproliferative & proliferative diabetic retinopathy



Diabetic Retinopathy

DR

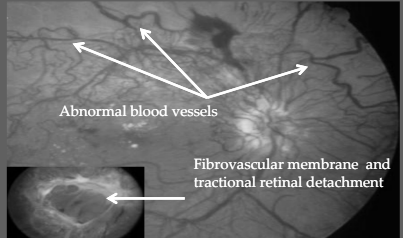
Nonproliferative DR (NPDR)



Microaneurysm

- Chronic, occurring over years
- Typically no significant vision loss, but can progress to DME and/or PDR
- Similar damage occurs in other end-organ vascular beds

Proliferative DR (PDR)



Abnormal blood vessels

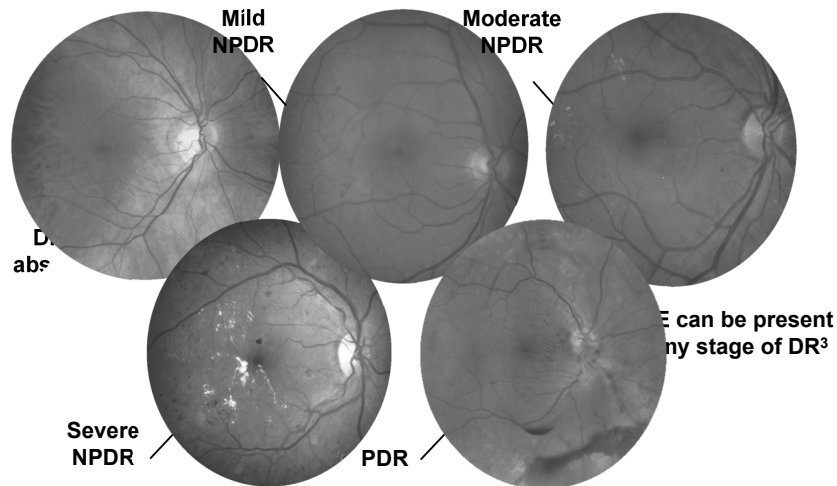
Fibrovascular membrane and tractional retinal detachment

- Neovascularization of retina
- High risk of severe visual loss

1. NHANES database search by Genentech, data on file.

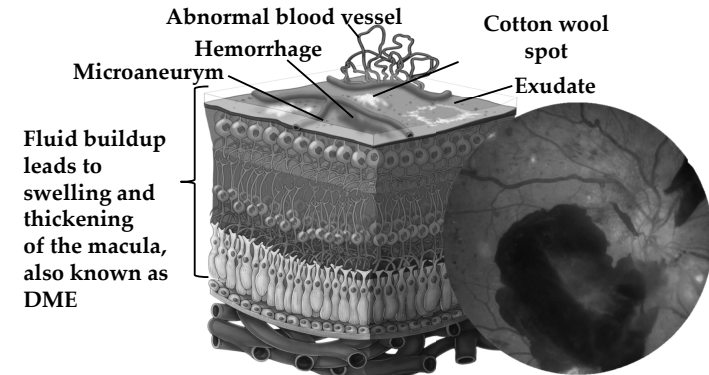


What are the different stages of diabetic retinopathy?^{1,2}



1. Ip et al. *Arch Ophthalmol*. 2012;130:1145. 2. American Academy of Ophthalmology. <http://www.iooph.org/resources/45/International-Clinical-Diabetic-Retinopathy-Disease-Severity-Scale-Detailed-Table-.html>. Accessed April 27, 2016. 3. American Academy of Ophthalmology Retina/Vitreous Panel. <http://www.aao.org/ppp>. Accessed April 27, 2016.

DR is a complication of diabetes that causes damage to retinal blood vessels¹

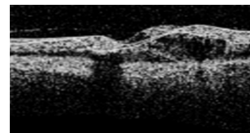
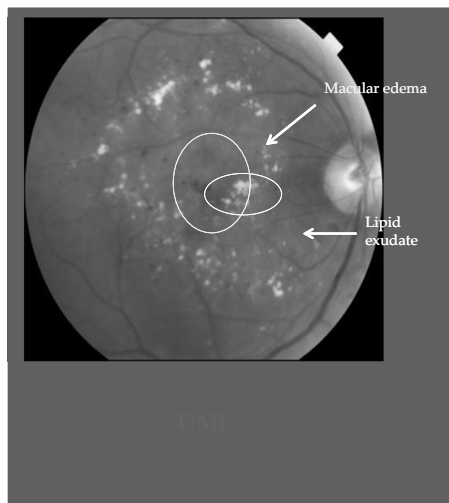


What are Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME)?

1. The American Society of Retina Specialists. <https://www.asrs.org/patients/retinal-diseases/3/diabetic-retinopathy>. Accessed February 2016.



Diabetic Macular Edema Is a Major Cause of Vision Loss



Risk Factors for DME¹⁻⁴

Medical Conditions

Duration of diabetes

- Patients who have had diabetes for ≥ 10 years are 11 times more likely to have DME¹

Elevated hemoglobin A_{1c} (HbA_{1c})¹⁻³

- Every 1% increase in HbA_{1c} levels corresponds to a 50% increased risk of DME¹

Uncontrolled hypertension¹

Hyperlipidemia³

1. NHANES database search by Genentech, data on file
 2. Klein et al. *Ophthalmology*. 2009;116:497.
 3. Bhagat et al. *Surv Ophthalmol*. 2009;54:1.

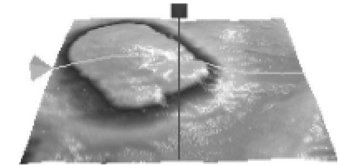
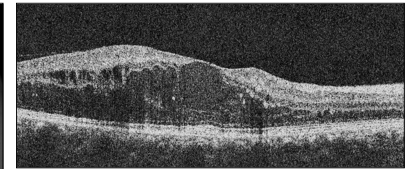
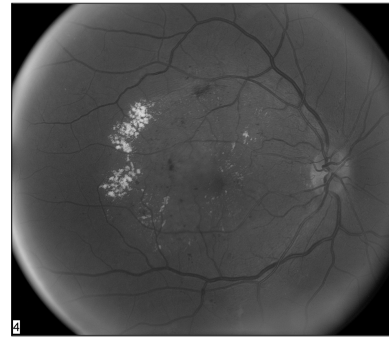


■ DME

- OCT (Optical coherence tomography)
- Fluorescein Angiography
- OCT A



OCT- DME

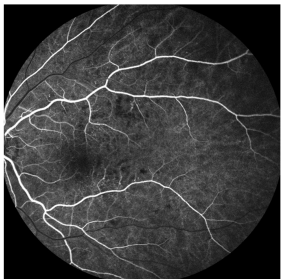
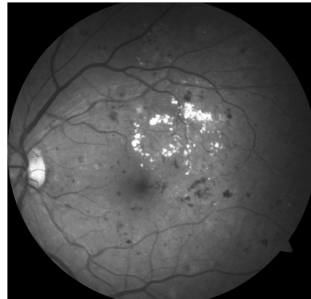


VA 20/60

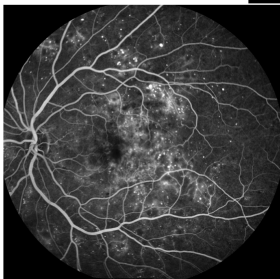


FA- NPDR with DME

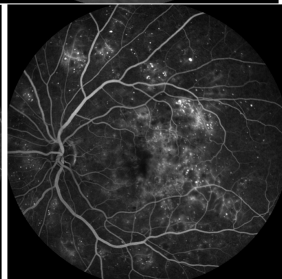
NPDR with DME



Early FA



Mid FA

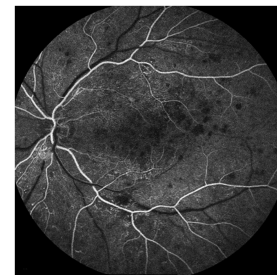
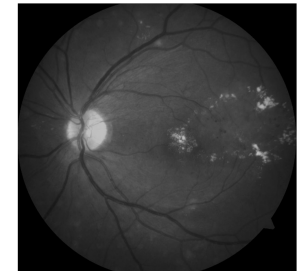


Late FA

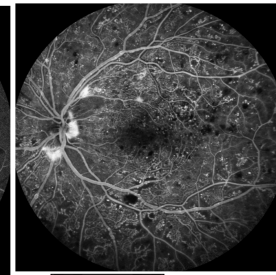
FA- PDR with DME

PDR with DME

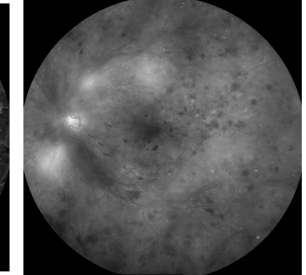
TX: Anti VEGF to reduce DME then PRP in 2 sessions



Early FA



Mid FA

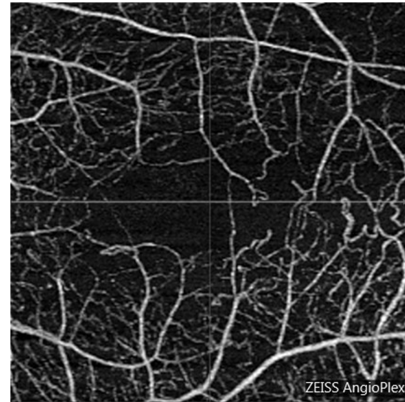


Late FA

OCT A- DR



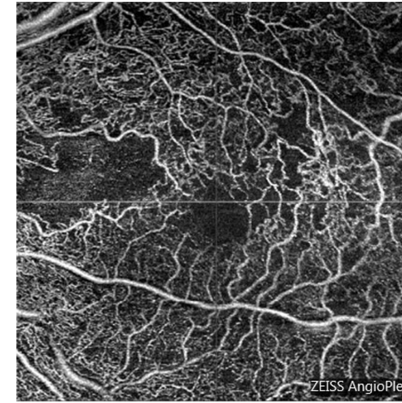
superficial



deep



OCT- DR with nonperfusion



OCT-A



FA



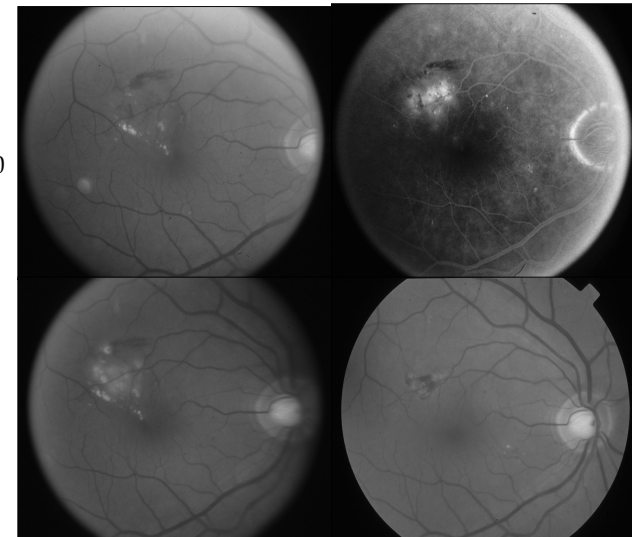
Macular edema treatment

1. Laser
 - Formerly the gold standard
2. Injections of steroid
 - SubTenons kenalog
 - Intravitreal triamcinolone
 - Ozurdex
3. Anti VEGF treatment
 - Avastin (Bevacizumab)
 - Lucentis (Ranibizumab)
 - Eylea (Aflibercept)



Clinically Significant Macular Edema

VA
20/20



VA
20/20



ETDRS Focal/Grid Laser Shortcomings

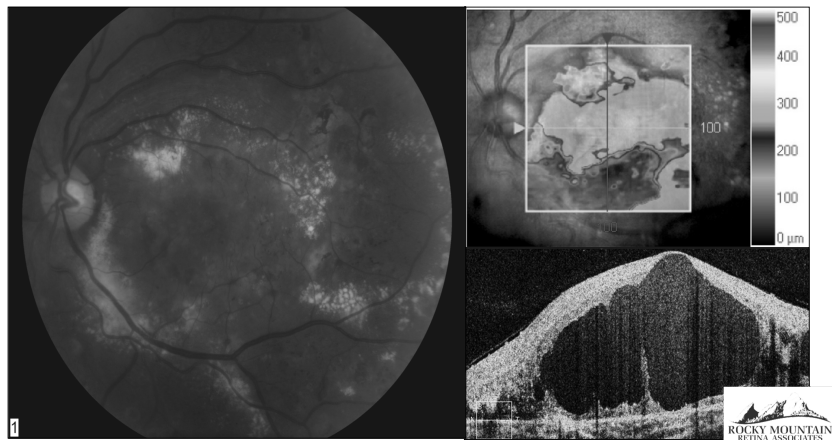
1. Relatively heavy treatment
 - Blind spots
 - Aggravate macular edema
2. Goal: stable vision
 - Only modest visual gains
 - Less effect with diffuse edema
 - More commonly used with focal edema
 - Less effect with advanced diabetic retinopathy



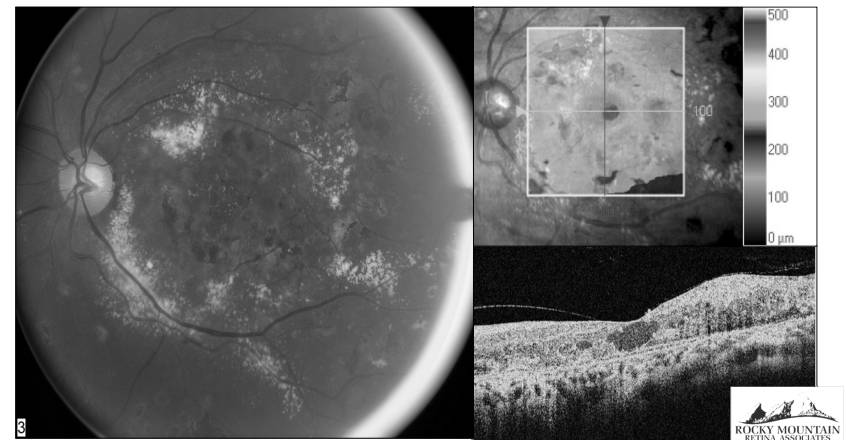
- Triamcinolone
- Ozurdex (dexamethasone implant)

Steroids for DME

43 yo man with DME
VA 20/400



43 yo man with DME
6 weeks s/p Ozurdex VA 20/200



Steroid Injection Shortcomings

1. Side effect profile
 - Cataract formation
 - Possible IOP rise
2. Limited Response
 - No difference noted in DRCR protocols when compared to laser
 - Often need repeat therapy



Anti VEGF (vascular endothelial growth factor)

Treatment for DME

- Avastin
- Lucentis
- Eylea



Anti VEGF Injection for DME Shortcomings

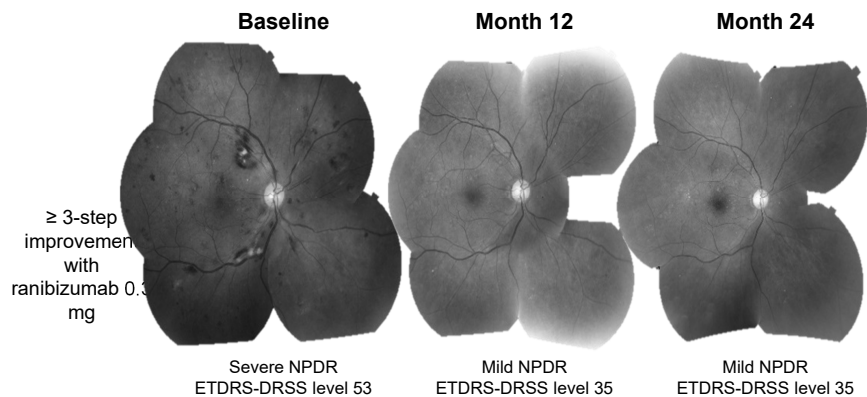
1. Need for continuous therapy
 - Not a cure
 - May be able to increase interval between injections after one year but still uncertain
 - DME will typically return if untreated
2. Financial Impact
 - Less cost effective than laser
 - Burden of need to return for office visits



Treating Diabetic Retinopathy without DME present

- Unless DME is present, the vision is NOT affected.
- Crucial to be checked annually because DR can be very advanced even though the vision is not affected.

RIDE/RISE: DR Improvement With Ranibizumab



Wykoff et al. *Ophthalmol Retina*. 2018 (Publication Pending)
ETDRS-DRSS, Early Treatment Diabetic Retinopathy Study Diabetic Retinopathy Severity Scale; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.



3
3

Should we treat?

Anti VEGF Injection for Diabetic Retinopathy Shortcomings

1. Causes regression of the disease process
 - Patients need to understand the limitations of treatment
2. Need For continuous therapy
 - Not a cure
 - May be able to increase interval between injections after one year but still uncertain
 - Patients need to understand the pathology and their risk of recurrence without treatment
3. Financial Impact
 - Cost effective than laser
 - Burden of need to return for office visits



PDR



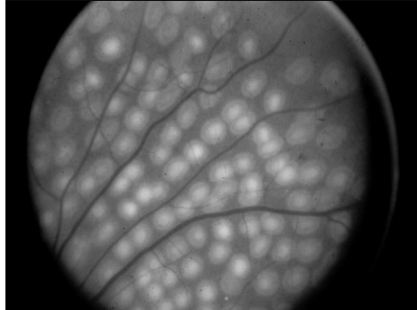
Panretinal Photocoagulation Standard Technique (DRS/ETDRS):

Spot size: 500 micron
(varies with contact lens)

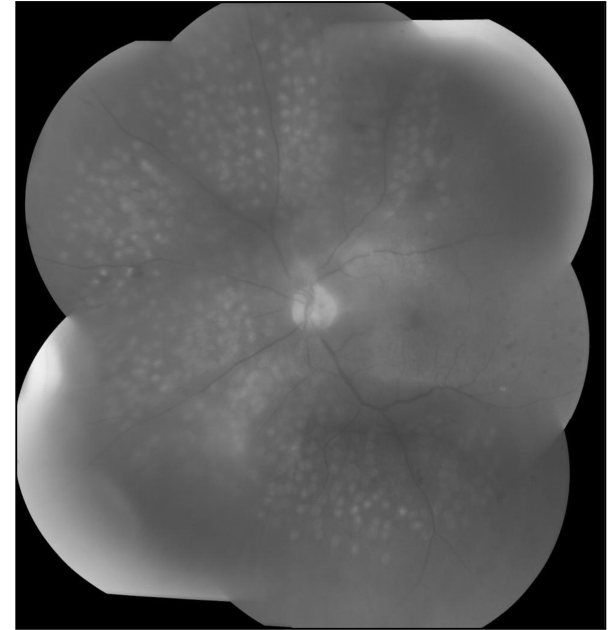
Duration: 0.05 to 0.1
seconds

Power: 200-700
milliwatts

Intensity: Yellow-white
moderate burns

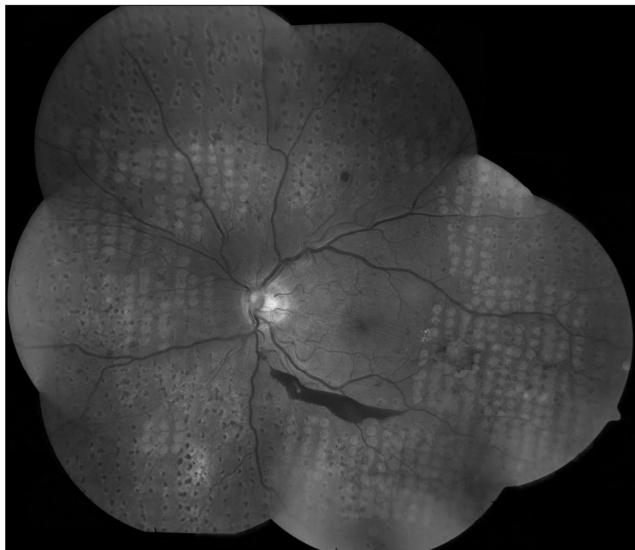


Laser Applied



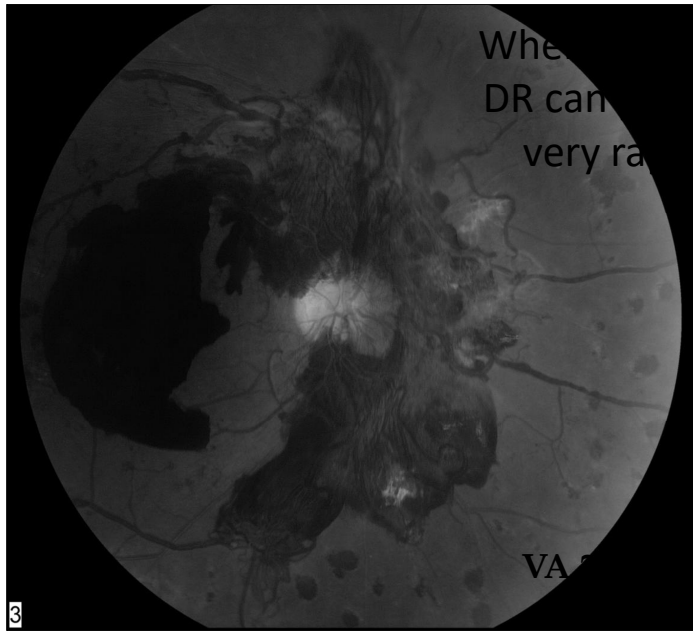
s/p laser

Laser is applied
to prevent
further growth
of new blood
vessels and
retinal
detachment,
NOT to improve
vision.



Anti VEGF therapy for PDR

- Can regress disease significantly
- Reduces loss of VF and night vision induced by panretinal photocoagulation (PRP)
- High risk of progression in noncompliant patients
 - Need to assess patient understanding of the disease
 - Consider for 'early' PDR patients



When... ated,
DR can... gress
very rapidly.

VA

3

Reasons for surgery for PDR

- Bleeding in the retina prevents laser application
- Traction from fibrosis is causing a retinal detachment
- Surgery involves removing blood/fibrosis and applying laser
- Sometimes the retina needs additional help remaining flat, so gas or silicone oil may be placed to keep the retina flat



The best treatment for diabetic retinopathy?

Routine eye evaluations to ensure that it is caught early

Prevention is key

Thank You!



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