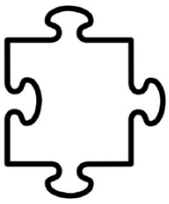
Diabetes Cases & Conundrums



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Disclosures

- Dr. Gerson is a paid speaker or consultant for Allergan, Asta Real, Bausch & Lomb, Essilor, Genentech, Luneau Technology, Maculogix, Notal, Optos, Regeneron, VSP, ZeaVision
- Dr. Chous is a paid speaker or consultant for American Diabetes Association, AI Optics, EyeNUK, LKC, Macular Degeneration Association, Notal, OcuTerra, Regeneron, VSP, ZeaVision

Increasing Prevalence of DM

37.3 million Americans now have **diabetes**

2018 *incidence rate* was 1.5 million

> 96 million Americans have **prediabetes**

- NHANES analysis (2012) suggested ≥*50% of American adults had diabetes or prediabetes*
- Up to 100 million have NAFLD (largely associated with insulin resistance)

You won't lose vision to DR if you don't develop diabetes

DM = diabetes mellitus; NHANES = National Health and Nutrition Examination Survey; NAFLD = non-alcoholic fatty liver disease; DR = diabetic retinopathy.

Centers for Disease Control and Prevention (CDC). Diabetes statistics—2020 [www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf]. Accessed 6/15/2020. Wanko A, et al. JAMA. 2019;314:1021-1029. Le MH, et al. PLoS Dev. 2017; 13: e0173499. Therapeutic Research – Pharmacist's Letter-Optimize meds for comorbidities in non-alcoholic fatty liver disease – 2017 [https://pharmacist.therapeuticresearch.com/Content/Articles/PL/2017/Aug/Optimize-Rxs-for-Comorbidities-in-Nonalcoholic-Fatty-Liver-Disease]. Accessed June 16, 2020.

It's a little late….

- **Up to 60% of pancreatic beta cells are non-functional AT Dx of T2DM** *Diabetologia* 2001;**44**:929–945
- **Estimated duration of T2DM AT Dx is a mean of 6.2 YEARS!** Diabetes Care. 2014 Jun;37(6):1668-74
- **1 in 5 patients with newly Dx T2DM has DR/DME! (3% have CSME) and both entities are associated with increased CV mortality**

Circ Cardiovasc Qual Outcomes. 2015 May;8(3):260-7

Some Staggering Numbers

- **Seventeen people on our planet develop diabetes every minute**
  - **3 people every minute in the US**
- **580,000,000 people have diabetes today (projected 1 billion by 2050)**
  - **> 40 million Americans have diabetes in 2022**
- **Diabetes costs the World economy $2.5 trillion annually**
  - **The US spent $327 billion on diabetes in 2017**
- **A child born in 2020 has a 40% chance of developing diabetes in her/his lifetime**

International Diabetes Federation, 2020; www.diabetesatlas.org

Why Is This Happening? food

Diabetes Complications

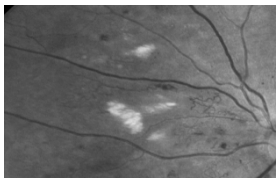
- Only occur in tissues containing:

- **Blood Vessels**
- **Nerves**
- **Proteins**……..

When to Worry About NPDR

- **When there is associated DME**
- **When it qualifies as Severe NPDR**
  - **The 4-2-1 Rule (Hmg/MA; Venous Beading; IRMA)**
  - **15% to PDR in 1 yr**
  - **45% to PDR in 1 yr if 2 of 3 findings**
  - **60-75% to high-risk PDR in 5 yrs**

Per ETDRS



When to worry…

- Do we need to worry even before somebody has diabetes?
  - Doing better doesn't always mean doing better
  - DPP/DPPOS after 20 yrs, no difference in devel of DR if in metformin vs lifestyle vs standard
  - Even though we can delay DM, may not prevent DR…….UNLESS WE PREVENT DM!

The Effect of Interventions to Prevent T2DM on DR: The DPP/DPPOS Experience. *Diabetes Care 2022 May 25; [EPub Ahead of Print], NH White et al.*

Who Would Benefit From Earlier Referral to a Retinal Specialist?

- **Studies show that ODs, general ophthalmologists & even RS tend to under-grade severity of DR compared with image reading centers**

Retina. 2008 Jan; 28(1): 36–40.
PLoS One. 2016; 11(9): e0163108

- **Recent evidence shows that anti-VEGF therapy (aflibercept or ranibizumab) can significantly improve DR severity, especially when ETDRS level 47 (moderately severe NPDR) or worse**

Ophthalmology. 2015 Feb;122(2):367-74
Ophthalmol Retina. 2018 Oct;2(10):988-996
Wykoff CC. Intravitreal Aflibercept for Moderately Severe to Severe Non-Proliferative Diabetic Retinopathy (NPDR): 2-Year Outcomes of the Phase 3 PANORAMA Study. Data presented at Angiogenesis, Exudation and Degeneration Annual Meeting; February 8, 2020; Miami, FL.

When SHOULD We Refer?

- When patients have or may have DR/DME requiring treatment
- When we are unsure of disease severity
- When patients have chronically suboptimal metabolic control or are receiving suboptimal care
- When the eye exam suggests undiagnosed diabetes

REAL WORLD DIABETES CONTROL

The Vast Majority of T2DM Patients with HbA1c > 8% and initiating add-on Tx Don't Achieve Metabolic Targets within 5 YEARS of Diagnosis (*DISCOVER* Trial of 16K T2DM Subjects Worldwide: 38 Nations)

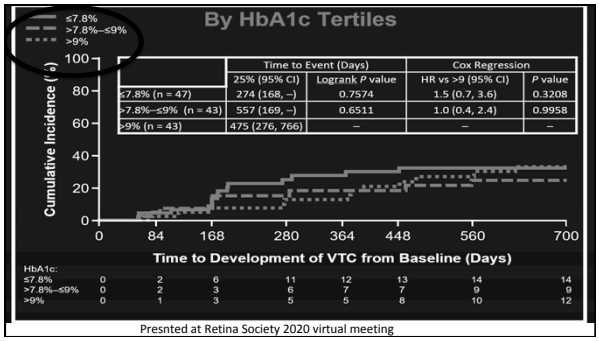
- After 5 years Dx with T2DM:
  - Mean A1c = 8.3% (Europe = 8.1%; US = 8.6%)
  - Mean Age at Dx = 51.6 years (EU = 61.9; US = 58.3)
  - **Only 17.6% with HbA1c ≤ 7% (18.7% EU; US = 17.1%)**
  - **Only 49.2% with HbA1c ≤ 8% (53.9% EU; 47.1% US)**
  - Microvasccular Dz = 18.9% CAD/Stroke = 12.9%
  - Metformin alone = 55.6% met + SFU = 20.9%
  - Metformin + DPP4 inhibitor (Januvia) = 23.5%

Diabetes Res Clin Pract. 2019;151:20-32.

Metabolic Memory

- Patients with tight glucose control within 1-8 years of Dx are significantly less likely to develop severe DR despite worsening glucose control over time
- Patients with poor glucose control within 1-8 years of Dx are significantly more likely to devlop severe DR despite improved glucose control over time
- **Tight glucose control is WORTHLESS for protection against PDR/ CI-DME once NPDR becomes moderately severe or severe (post-hoc analysis of the PANORAMA trial)**

Kowluru RA. Diabetic retinopathy, metabolic memory and epigenetic modifications. Vision Res. 2017 Oct; 139:30-38. JAMA Ophthalmol. 2021 Sep 1;139(9):946-955.



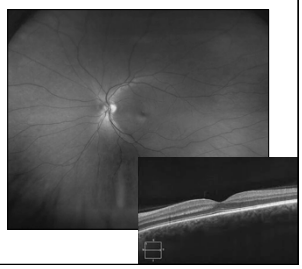
	Time to Event (Days)		Cox Regression	
	25% (95% CI)	Logrank *P* value	HR vs >9 (95% CI)	*P* value
≤7.8% (n = 47)	274 (168, –)	0.7574	1.5 (0.7, 3.6)	0.3208
>7.8%–≤9% (n = 43)	557 (169, –)	0.6511	1.0 (0.4, 2.4)	0.9958
>9% (n = 43)	475 (276, 766)	–	–	–

Presnted at Retina Society 2020 virtual meeting

It's IMPERATIVE to Get Good Blood Glucose Control As SOON After Diabetes Diagnosis as is Possible!

Most common patient

- 52yo male w type 2 DM x 3 years
- A1c was difficult to control for first 2 years, but 6.2 for last year
- DM meds include metformin and Ozempic
- HTN moderately controlled
- BMI 30
- In for exam because "my doctor made me"



What do we discuss with this patient?

We could discuss this for the rest of the 2 hour course

But…we need to have a few sentences to give our patients that come in every day

58 yo male

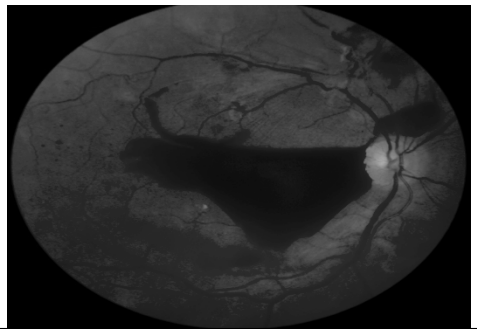
- Just saw PCP and HbA1c = 10.4%
  - T2DM x 5 years with A1c > 8% throughout
  - No DR YET
- Patient still on metformin alone
  - No terminal illness
  - Had an MI at age 53

Why and to Whom should this patient be referred?

A Few More Good Cases…..

Patient RC: Short & Sweet

- **21 yo male with T1DM x 12 years**
- **Recent HbA1c = 7% but pt reports had been as high as 13% for 'many years'**
- **Saw OMD 14 months earlier and was told he had "some early changes" but could be seen Q2 years if he kept his A1c in range**
- **Complaining of reduced vision in the right eye for a few days**
- **20/400 and 20/20 NI with pinhole**



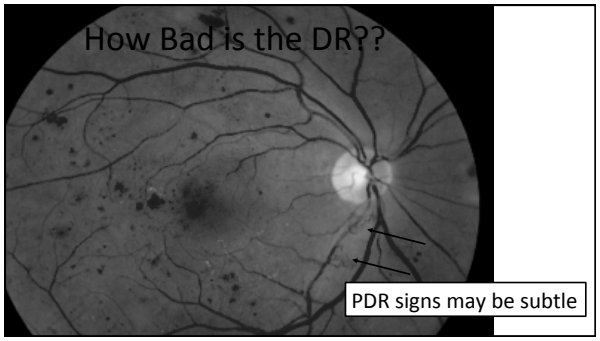
Patient RC

- **Referred to retinal specialty**
- **Consult letter reports PRP and ranibizumab (Lucentis®) delivered at 1st/2nd visits**
  - **REMEMBER, Good A1c doesn't protect from VTC once NPDR is > moderate (>DRSS Level 43)**
- **This patient represents a strong argument AGAINST less frequent eye examination intervals for higher risk patients**
  - **Young males, T1DM, Hx of initial, chronic, poor control, diabetes duration > 10 years**

Patient JF

- T2DM x 6 years
- HbA1c = 7.2% (had been as high as 9%)
- metformin + basal/bolus insulin (Lantus + Novolog) → 190 total units/d
- CABG

Case & Images courtesy of Diana Shechtman, OD, FAAO



PDR 5 Years After Dx of T2DM

- 71K patients
  - 1.74% (1,249 of 71,817) developed PDR, 0.25% TRD, and 0.14% NVG.
- Any insulin use was greatest risk factor for PDR at 3.6x risk
- A1c over 9.0 was 2.1x risk
- Protective factors appeared to be
- Young age (age 18–23)(OR 0.46), Medicare insurance (OR 0.60), ***morbid obesity (OR 0.72), and smoking (OR 0.84)***

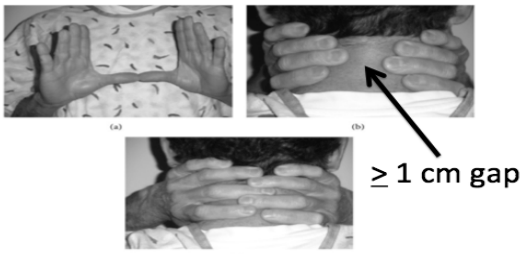
Diabetes Care. 2021 Nov;44(11):2518-2526.

Patient MLH – "Routine Exam"

- "I was told I might have prediabetes"
  - He has not visited a physician in > 5 years
  - Recently gained 20 pounds during pandemic
- Meds: none
- Physical exam:
  - BP 152/95
  - Height 5'-9"
  - Weight 226 Lbs.
  - BMI 33 & Waist 40"
  - Reports being tired all the time → + ESAP

Ocular Dx:
1+ NS
Presbyopia
20/20 OD/OS
Retina appears normal
IOP = 17/16

+ ESAP = Easy Sleep Apnea Predictor



Neck Grasp Predicts Obstructive Sleep Apnea in Type 2 Diabetes Mellitus. Sleep Disord. 2019 Jul 1;2019

In-office Random Blood Glucose =212 mg/dl

→ Refer to primary care physician

Lab Results: What do they mean?

- **Fasting glucose 165 mg/dl (65-99 mg/dl)**
- **AST 42 IU/L (0-40 IU/L)**
- **ALT 54 IU/L (0-44 IU/L)**
- ALK PHOS 110 IU/L (39-117 IU/L)
- BUN 18 mg/dl (6-24 mg/dl)
- Cr 1.2 mg/dl (.76 – 1.27 mg/dl)
- **Total Chol 232 mg/dl (100-199 mg/dl)**
- **Trig 302 mg/dl (0-149 mg/dl)**
- HDL 30 mg/dl (>39 mg/dl)
- **LDL 164 mg/dl (0-99 mg/dl)**
- **Urine Albumin / Creatine 110 mcg/mg (<30 mcg/mg)**

HbA1c of 8.2%

Diagnoses:
Elevated LFTs
→ ?NAFLD

Metabolic Syndrome
High TG/Low HDL
HTN (>130/85)
FBG ≥ 100
waist ≥ 40 inches

Diabetes mellitus
DKD

→ Referred for Sleep Study by PCP

- In-home polysomnography (PSG)

– Apnea-Hypopnea Index: 32 events/hour

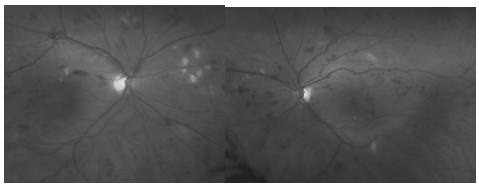
Severe OSAS

Mild = 5-15
Moderate = 15-30
Severe > 30

What You Gonna Do?

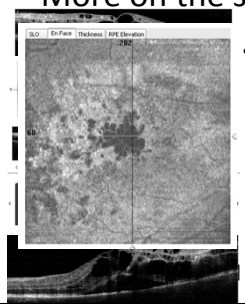
- Pharmacotherapy for hyperglycemia/HTN/lipids
  - Why? Prevent MACE, ESRD and eye disease
  - Probable: metformin, lisinopril, high potency statin
- Sleep therapy
  - Why? Increased risk of CV events and DR/DME
  - Weight loss, CPAP+
- Weight loss
  - Why? Improves all metabolic markers of DM
  - Not a candidate for bariatric surgery (BMI ≥ 35 w DM)
  - Discuss Fasting Regimes
  - Drug therapy – unimpressive until NOW

New Dx Diabetes

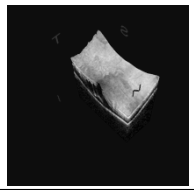


- New Diagnosis of DM: 2 wks ago
- Vision 20/60 OU

More on the same patient



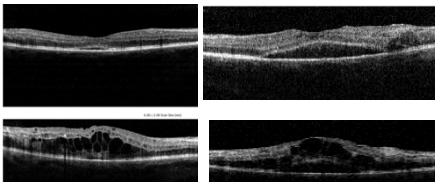
- You won't believe the story…



Avastin Tx to 20/25

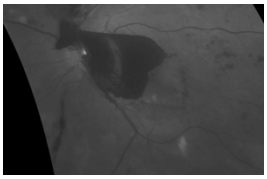
OD 10 days after Avastin
From 20/60 to 20/25

OS 2 days after Avastin
From 20/60 to 20/25



From great to…..

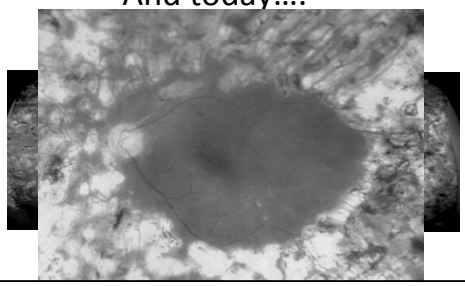
- Vision dropped to 20/60
- Sent back to MD for eval
- Tx
- Now…..
- 10 yrs later: Multiple injections and PPVs



What does this patient need?

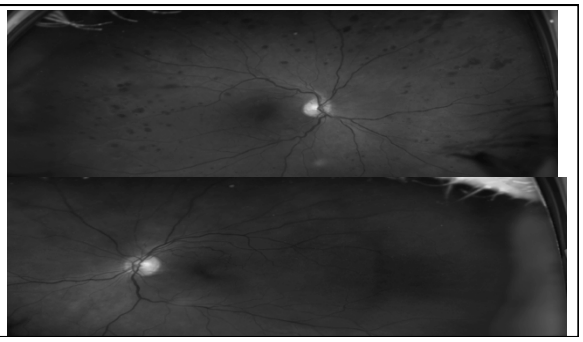
- Another Vitrectomy to try to salvage vision?
- Systemic help! She has completely uncontrolled metabolic syndrome with diabetes
- Recmd. Consult diabetic educator and consult dietitian

And today….



Patient JQ

- **T2DM x 8 years; 72 yo Latino male**
- **A1c 6% on insulin (Novolog + Lantus)**
- **Asymmetric NPDR without DME**
- **Emmetropia *IOP 17/17 mmHg**
- **Review of medical record shows A1c 11.3% at diagnosis and not reduced < 8% until year 5 when PCP referred to endocrinology**

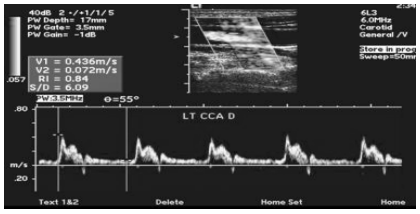


Asymmetric NPDR

- **Associated with carotid artery stenosis both ipsilateral and contralateral to the eye with worse DR** Ophthalmology 1990; 97(7):869-74
- **Eyes with lower IOP may have increased risk of sight-threatening DR due to increased blood flow in compromised retinal capillary bed** Brit J Diab Vasc Dis 2001; 1(1):80-87
- **Protection also associated with prior chorioretinal scarring and high myopia** Retina. 2017 Jul;37(7):1270-1276

No bruit was detected……..But

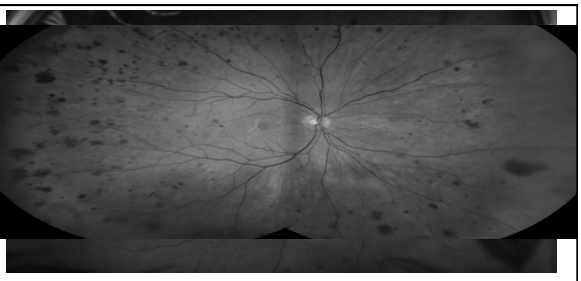
- Referred for carotid ultrasound



- 90% stenosis of the left common carotid artery

For Patients with Asymmetric DR

- **In the absence of <u>HIGH</u> IOP, high myopia and/or chorioretinal scarring in the eye with less severe DR…**
- **It is prudent to rule out**
  - **Carotid artery stenosis**
  - **Venous Stasis Retinopathy or Ocular Ischemic Syndrome**



What Else Is of Concern in this Eye?

What Else?

- **Over 4 years, eyes with predominantly peripheral DR lesions (PPL) were**
  - 3.2 X more likely to have a 2-step ETDRS severity progression
  - **4.7 X more likely to develop PDR**

  n = 200 eyes
  p = 0.005
  - PPL are associated with non-perfusion on ultrawide field fluorescein angiography

Ophthalmology. 2015 Feb 19.
Ophthalmology. 2015 Sep 6.

Protocol AA Calls BS!

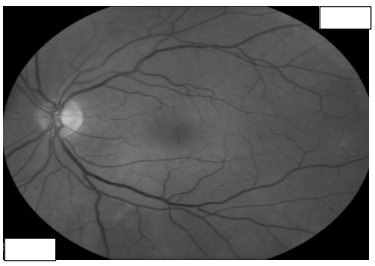
BUT

evaluation of periphery in this case does reveal very severe NPDR
So this patient deserves referral for FA

JAMA Ophthalmol. 2022;140(10):946-954.

GN - Simple Stuff that Matters

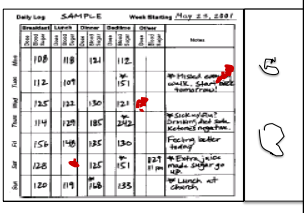
- 68 yo man with T2DM x 15 years; CHF
- 250 units of insulin daily (Levemir + Novolog)
- A1c has not been below 8% since starting insulin
- Patient and his endocrinologist are frustrated with each other
- **Fasting glucose is never > 150 (log book) <u>BUT</u>**
- **2-4 hour post-prandial glucoses are always > 200**



Mild NPDR without macular edema

The Glucose Log Book

- **Pre-prandial numbers 110-150 mg/dl**
- **Post-prandial numbers 250-350 mg/dl**



A Simple Question

- **When are you taking your Novolog insulin?**

Answer:

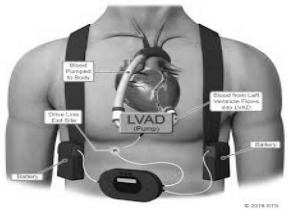
- **"About an hour after I eat…….Why? Is that important?"**

Outcome for GN

- **HbA1c dropped from 8.7% to 6.9% within 3 months**
- **Insulin dosage reduced from 250 to 150 units**
- **Diabetic retinopathy stable x 12 years → worsening CHF → LVAD**

LVAD for end-stage CHF

(left-ventricular assist device)



When Should Patients See an Endo?

- **Sub-optimal glycemic control with progressive DR despite current therapy**
- **Children with newly Dx T1DM**
- **Patients with frequent hypoglycemia**
- **Any patient < 60 years of age put on a sulfonylurea as first-line therapy for T2DM**

Patient - ML

- **18 yo with T1DM x 6 yrs in with her parents, who are very concerned**
- **HbA1c = 9.2% on insulin pump**
  - **A1c always < 7% under care of pediatric endocrinologist**
  - **Plays collegiate volleyball**
- **No DR or DME**

ML gets hypoglycemic in the exam room (random glucose = 47)

"I feel lousy when my blood sugar is < 150, and I can't afford to get low in class or on the court"

Mom & Dad are worried – ML dislikes their 'over-protective' instincts

A Reality Check

Hypoglycemia is disabling & can quickly incapacitate (even kill) patients

Many patients opt for chronic hyperglycemia because it has far less impact on function, and the consequences are distant in time

Treatment Plan

- Patient education about HbA1c and risk of retinopathy during exam & while she dilates – demonstrated DR risk calculator
  www.RetinaRisk.com
- We looked at retinal images eyes and thos
- Recommend CGMS & tabs

4g glucose

FAMILY talk

Parents advised that Emily's preference for hyperglycemia is b/c her glucose thermostat is set too high – will 'reset thermostat' if we gradually lower A1c

Discuss carb intake, demonstrate CGMS

Discuss the Joslin "Gold Medalist" Study, metabolic memory & DiVFuSS formula

Letter to Endo and family

Gold Medalists

- Time may not always be the enemy…
- "Medalists": h/o T1DM x 50+yrs
- 42.6% did not have PDR, and those without had little progression of DR after first 18 yrs
  - With little to no correspondence to A1c

"This population may be enriched for protective factors….."

Diabetes Care. 2011 Apr;34(4):968-74

ML 6 Mos Later

- **A1c reduced to 7.2% by next visit – still no DR**
- **Wearing DexCom G6 CGM device and she reports much better confidence dealing with low blood sugars**
- **ML tells me she wants to be an optometrist**

KW - Simple Stuff that MATTERS

- 36 yo with T1DM x 25 years
- Basal-Bolus MDDI therapy (Humalog + Lantus)
- Mild NPDR (a few microaneurysms)
- Excellent glycemic control x 15 years (HbA1c ranging 6.5%-7%)
- **A1c has increased x 1 year from 7.2% to 8.5%**
- **Last HbA1c = 9.1%**

KW – What Happened?

- **Total daily insulin dose has increased from 50 units to 190 units but "I'm always high"**
- **Patient swears no change in diet, exercise or adherence to insulin; glucose log shows no pre- or post-prandial patterns**
- **(Excellent & famous) endocrinologist is unhappy**
- **What Happened?**

Questions

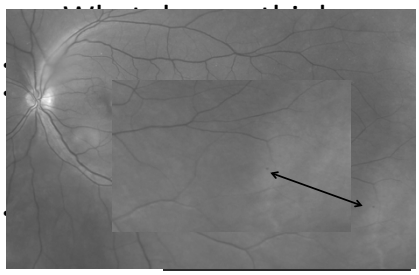
- **Where do you inject?**
- **"The left side of my stomach because I'm right handed and always driving"**
- **May I take a look at where you inject?????**

Injection Site Lipohypertrophy

With Rotation of Injection sites:

- **A1c dropped to 6.4% within 3 months**
- **Insulin dosage dropped from 190 units/day to 50 units/day**

"The patient's optometrist noted injection site lipohypertrophy, recommended site rotation and the glucoses have improved appreciably"



Now what do you want to know?

- In office RBG 463
- In office A1c: >13
- Unable to go to PCP today or tomorrow due work schedule
- Went to PCP 2 days later and started on Janumet
- I always try to f/u on this type of pt…

3 months later….

- Came in for "retinal f/u"
- Retina unchanged
- Now on 2 meds for T2DM w dramatically changed outlook on disease

EYE EXAM MADE THE DIFFERENCE (as happens hundreds of thousands of times a year!)

GF – Too Low – Disaster Averted

- 72 yo with T2DM x 15 years
- No DR or DME
- CVD s/p CABG
- Meds include Toprol, lisinopril, metformin, ASA, **Lantus (50 units BID) * No CGM**
- GF gets a little confused during the eye exam
- **In-office blood sugar measures 52 mg/dl**

GF

50 ≠ 15

- *Q: Do you get a lot of low blood sugars?*
- *A: Ever since I started taking insulin*

- In-office A1c = 4.2% (mean glucose = 72 mg/dl)
- Phone Call to PCP: "GF's last A1c was 8%, so I put him on Lantus"

- What Dose: "15 units morning & night"

GF- conclusions

- Measuring GF's A1c allowed us to immediately adjust his insulin dose
- It may have saved his life
- A single episode of acute hypoglycemia in a susceptible patient with heart disease can be fatal

Symptoms of Acute Hypoglycemia

- **Perspiration (diaphoresis)**
- **Confusion**
- **Tremor**

Who Gets:

Patients on insulin

Or

Sulfonylureas (Glipizide, Glyburide, Glimepreride)

Hypoglycemia

•Always have a rapid-acting carbohydrate in the office (juice, sugared soda, glucose gel)

15gm CHO will ↑ ~ 30-40 mg/dl (1.7-2.2 mmol/L)

Hypoglycemia WORSENS DR!

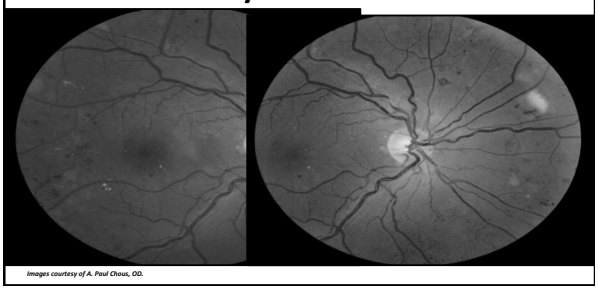
- **Episodic or chronic hypoglycemia ↑ GLUT1 & HIF-1 in Müller Cells leading to massive ↑ VEGF**
- **Hospitalization for severe hypoglycemia was the single best predictor of 2+ lines of VISION LOSS due to diabetes in the Freemantle Diabetes Study (5.6X)**

Cell Rep. 2023 Jan 31;42(1):111976.
J Diabetes Complications. 2020 Jun;34(6):107560.

RL - Why Do I Need Treatment?

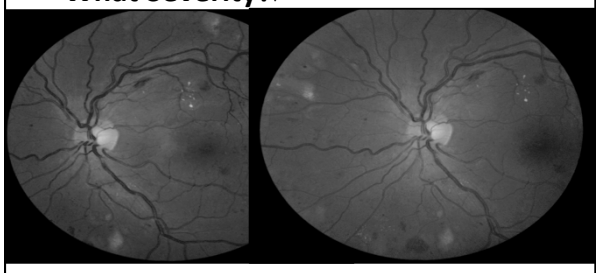
- 33-year-old male with T1DM x 19 years
- Referred by endocrinology
- Last eye exam was 5 years ago
- Last HbA1C: 7.1% No CGM
- A1c had been > 8.5% “for years” after Dx
  - Basal/bolus insulin (Novolog/Levemir): 150 units/day
  - In-office glucose: 413 mg/dl
- BCVA 20/20 in each eye

What Severity?

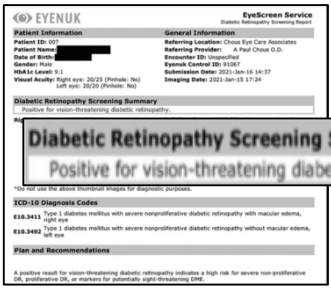


Images courtesy of A. Paul Chous, OD.

What Severity?



Images courtesy of A. Paul Chous, OD.



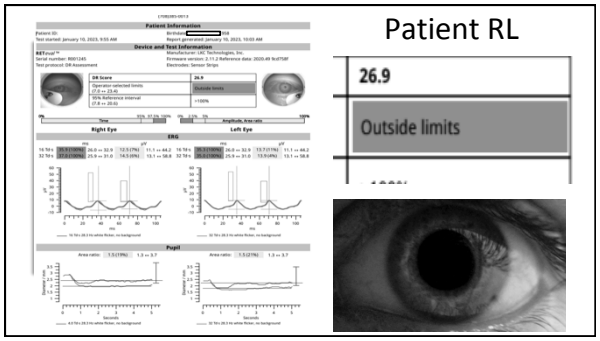
- Severe NPDR OU
- AI confirms VTDR
- Pt declines referral as he has no symptoms
- hotos and
- Reviewed ETDRS stats
- Showed example of improvement with anti-VEGF
- Pt still intransigent

PANORAMA & PROTOCOL W

Treatment with anti-VEGF Pulls Patients with Severe NPDR and PDR Back From th Edge of the Cliff

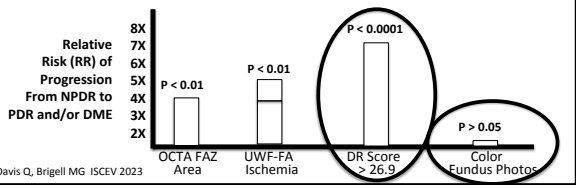
ffERG and Pupil Response
Are Significantly Diminished
With worsening Diabetic Retinopathy

2 minute test
Assesses global retinal function



Progression from Any Stage of NPDR to PDR and/or DME over 48 weeks

- RetEval DR Score ≥ 26.9 single best predictor
  - **RR = 7.2** vs a DR score < 26.9 for all NPDR stages



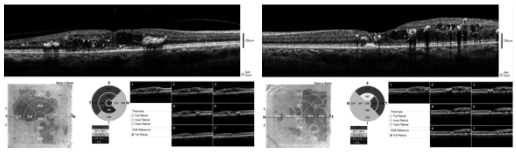
Davis Q, Brigell MG ISCEV 2023

T2DM, A1c 8.0 w lee 2yrs

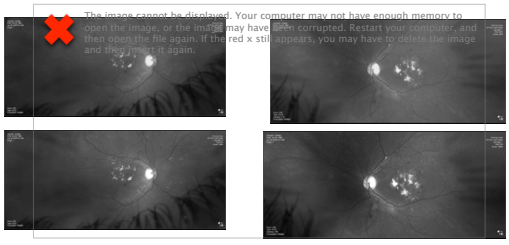
cc: blurry vision

OD: bcva 20/20

OS: bcva 20/40

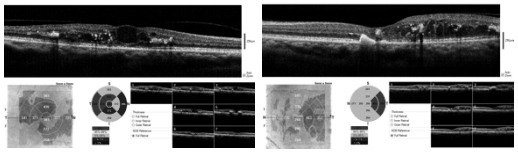


Color and red free



After 1st injections

20/30 **20/40**



After 3rd injection

20/20 **20/30**

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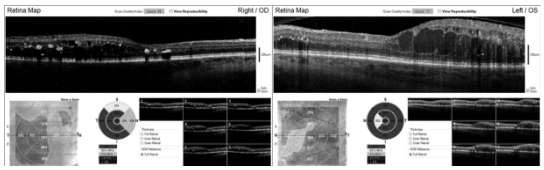
The image cannot be displayed. Your computer may not have enough memory to open the image, or the image may have been corrupted. Restart your computer, and then open the file again. If the red x still appears, you may have to delete the image and then insert it again.

Same day. 48yo, DM x 16 yrs, ?A1c

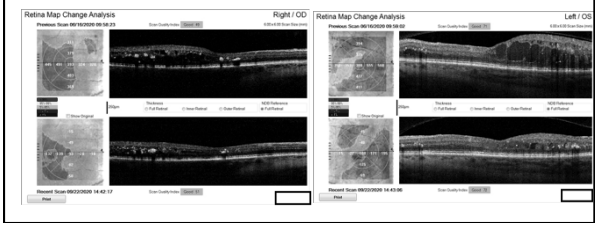
20/20- **20/30**



Color and red free

3 mos later. s/p Eylea injection x3

20/20 **20/30**



s/p 3 injections

Outcome?

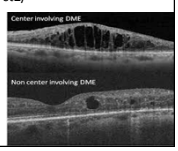
- Still TBD
- Not everybody has an ideal outcome
- Time will tell, but with time comes the risk of LTF

DRCR.net Protocol V

- Is there benefit to 'preventive' anti-VEGF or focal laser therapy in patients with center-involved DME and very good visual acuity?

Accessed at https://clinicaltrials.gov/ct2/show/NCT01909791

- 20/25 or better at enrollment
- Main outcome is % with loss of $\geq$ 5 ETDRS letters at 2 years



Results

- % of patients losing ≥ 5 ETDRS letters at 2 years
  - 16% aflibercept Q 4 wks PRN
  - 17% grid/focal laser
  - 19% observation

NO Stat Significant Difference

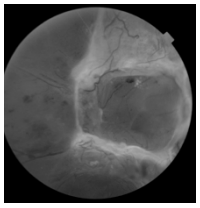
  - No significant difference in subjects losing ≥ 2 lines
  - Mean VA at baseline and 2 years wa 20/20 in all 3 groups
  - 3/4 of laser group and 2/3 of observation group **did not** require AVT @ 2 years

PRP vs Ranibizumab

- Protocol S by DRCR.net
- Ranibizumab non inferior to PRP

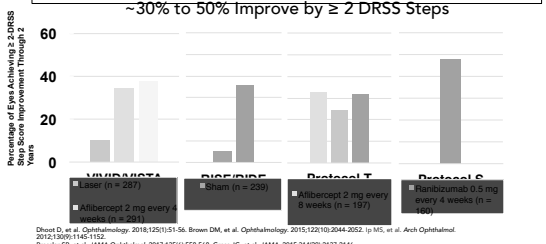
Real life implications?

- About 1/3 of patients referred to retina never make it to their first appointment
- Frequent loss to follow-up which leads to sub-optimal outcomes
  - Potential for TRD and disatsterous results



DR IMPROVES WITH ANTI-VEGF TREATMENT

~30% to 50% Improve by ≥ 2 DRSS Steps



Dhoot D, et al. *Ophthalmology*. 2018;125(1):51-56. Brown DM, et al. *Ophthalmology*. 2015;122(10):2044-2052. Ip MS, et al. *Arch Ophthalmol*. 2012;130(9):1145-1152.
Bressler SB, et al. *JAMA Ophthalmol*. 2017;135(6):558-568. Gross JG, et al. *JAMA*. 2015;314(20):2137-2146.

NNT for Level 47/53 NPDR

Only 3 patients with moderately severe or worse NPDR need to be treated to prevent 1 vision-threatening Complication (PDR/ASNV or CI-DME)

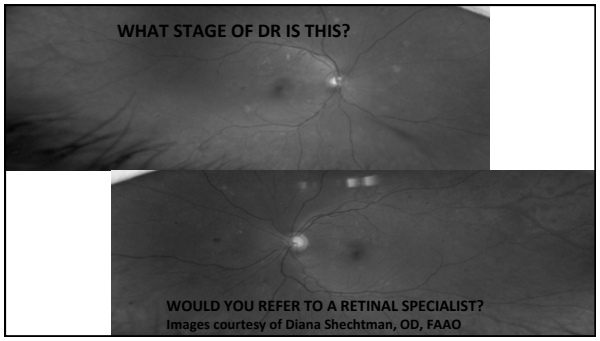
Is this a favorable NNT?

- NNT to prevent one CV death with 5 years of statin therapy in a patient with known heart disease = 83
  - NNT to prevent one non-fatal MI is 39 (NNT = 104 if no Hx of CVD)
- NNT = 333 to prevent a first, non-fatal MI with aspirin therapy
- NNT = 17 to prevent one case of PDR and/or CSME with oral fenofibrate therapy in T2DM with mild NPDR

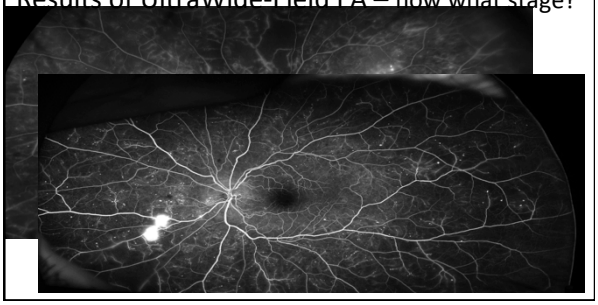
Data from thennt.com, accessed September 14, 2019
Lancet 2007;370(9600):1687-97

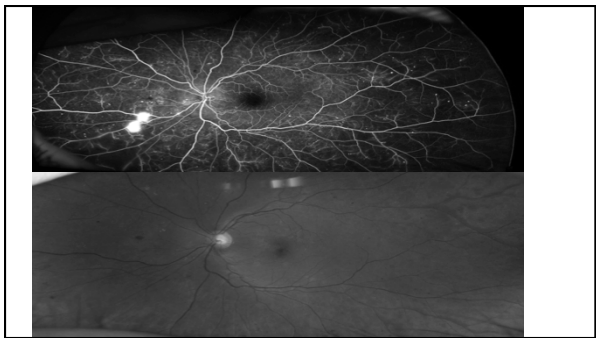
Case Example

- 58 year-old female
- Recently Dx by PCP with T2DM and referred for baseline dilated fundus examination
- Meds: metformin, Lantus, lisinopril, atorvastatin
- Recent HbA1c = 10.1% & in-office Spot Glucose = 412 mg/dl
- Ant Seg shows 2+ NS
- BCVA is 20/25 in each eye with a 2-diopter myopic shift



Results of UltraWide-Field FA – now what stage?





DO YOU COMMUNICATE WITH PCPs?

- Doesn't have to be lengthy or complicated
- Does need to happen (HEDIS)
- Did you see the patient and is there any NPDR

KISS

Communication and Support Are Essential

Eye care patients with diabetes need:

- Clear explanations about their eye conditions
- Information about the links between diabetes and eye disease
- Support—not scare tactics
- Key messages:
  - Being able to read an eye chart and see OK in daily life ≠ healthy eyes.
  - Having regular dilated eye exams is the way to protect your vision from diabetes complications.

- BONUS CASE IF NEEDED

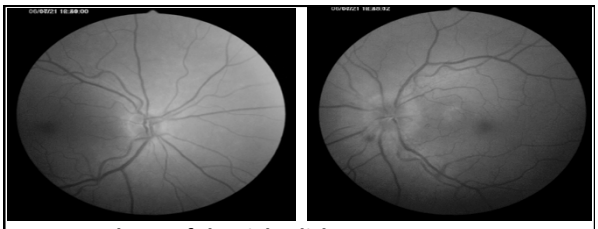
ST – the unexpected

- 63 yo female with T2DM x 18 yrs w blurred DVA
- Last HbA1c = 10.3% on metformin monotherapy
- Lisinopril, simvistatin, ASA
- 15 lb weight gain during pandemic (BMI = 34 Kg/M^2)
- BP = 162/104
- 3 diopter myopic shift → 20/20 OD/OS
- Minimal cataract, no DR or DME
- Advised to see PCP for intensified Tx & RTO when A1c < 8% and spot glucose < 180 mg/dl
- **"Can't I just have new glasses now?"**

ST

- Patient returns in 10 mos with HbA1c = 6.8%
- Has lost 11 lbs BP measures 135/88
- New Meds: semaglutide (Ozempic®), insulin degludec (Tresiba®) and atenolol
- Myopic shift now a mere diopter BUT
  - BCVA now 20/20 and 20/30-
- No DR or DME minimal cataract looks the same
- Optic disk swelling OS

What Do You Wanna Know?



- **No edema of the right disk**
- **Normal pupils & visual fields**
- **What she got?**

Diabetic Papillitis/Papillopathy

- A rare variant of AION – may progress to AION
- VA typically better than 20/40
- Associated with rapid reduction in blood glucose levels
- GLP-1 analogs (Ozempic) cause vasodilation
  - May have blocked axoplasmic flow
- Prognosis excellent (referred to RS who referred to neuro-oph)
- Patient had 20/20 BCVA 3 months later with resolution of disk edema OS

Optom Vis Sci. 2009;86(4):e395-e403.

Patient Perceptions

- **Diabetes patients are frequently unaware of:**
  - **The need for regular eye examinations**
  - **The recommended frequency of dilated eye examinations**
  - **The asymptomatic nature of DR/DME at their earliest, most treatable stages**

Int J Ophthalmol 2011; 4(5):519-524

THANK YOU!!!

Jeff & Paul
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dr_chous@diabeticeyes.com

BTW

- What medications are almost all of your patients with diabetes on and why?