# Diabetic Retinal Disasters: A Roadmap to Prevention

Roya Attar, OD, MBA, FAAO

#### SPEAKER DISCLOSURE

 Assistant Professor & Director of Optometric Services at the University of Mississippi Medical Center Dept of Ophthalmology

#### Disclosures

Advisory board member for Apellis
 Advisory board member for Visus
 Pharmaceuticals



#### **Expected Learning Objectives**

#### At the end of the session, attendees should be able to:

- 1. To review demography and pathophysiology of diabetes and diabetic retinopathy
- 2. To review classification of diabetic retinopathy
- 3. To discuss appropriate follow-up intervals and indications for medical and/or surgical intervention for diabetic retinopathy
- 4. To review the common pitfalls preventing appropriate eye care in patient populations
- 5. To provide guidelines for proper patient education and communication with patients as well as other healthcare providers to improve overall disease outcomes
- 6. To exhibit case examples of very advance cases to demonstrate the catastrophic nature of neglected diabetic retinopathy as compared to successfully followed and managed patients



# Preventable Diabetic Disasters







#### The most common causes of death in the United States

(August 2011)—CDC Data indicates that the deaths from CLRD has surpassed CVA as 3rd leading cause of the death in the US. CLRD= asthma, chronic bronchitis, emphysema, others

2000

		All causes	1,989,841		All causes	2,403,351
	1	Diseases of heart	761,085		Diseases of heart	710,760
	2	Malignant neoplasms [Cancer of All Types]	416,509		Malignant neoplasms [Cancer of All Types]	553,091
3	3	Cerebrovascul ar diseases	170,225		Cerebrovascul ar diseases	167,661
2	4	Unintentional injuries	105,718	*	Chronic lower respiratory diseases	122,009
Am Lung Assoc. 2009, 21% US	5 📩	Chronic obstructive pulmonary diseases	56,050		(CLKD) Unintentional injuries	97,900
Adults smoke	6	Pneumonia and influenza	54,619		Diabetes mellitus	69,301
	7	Diabetes mellitus	34,851		Influenza and pneumonia	65,313

1980





# Vascular anatomy

#### Vascular anatomy



Mechanism of Retinal Vascular Disorders

- Conditions that physically alter blood vessels (Retina a/o choroid)
  - Locally or systemically
  - Arteriosclerosis
  - Atherosclerosis
- Conditions that effect hemodynamics
   Systemic hypertension
- Conditions that alter blood chemistry
- Conditions that do some or all of the above

# Diabetes

- A group of metabolic diseases associated with high serum glucose level, either due to the body's inability to produce sufficient insulin, or cells do not respond to the produced insulin
- Incidence/Epidemiology (www.diabetes.org)
  - In 2015 1.5 million new cases among <u>></u>18. 1 in 4 adult have diabetes (>7 mil unaware)
- Type 2: primarily lifestyle factors
- Type 1: Multifactorial



# Diabetes

#### Morbidity and Mortality

Major cause of death

#### Complications

- Nephropathy, Neuropathy, Retinopathy
- Heart disease and stroke
- Hypertension
  - In 2003–2004, 75% of adults with also had hypertension
- Amputation
- More than 60% of non-traumatic lower limb amputations



#### Diabetes

- Diabetic
  Microangiopathy
  - Glycosylation
  - BM damage leak
  - Advance Glycation end Products "AGE" deposition
- Hyperglycemia
  - Abnormal blood viscosity
    (hemodynamic changes)

#### Diabetic Retinopathy

- Most Common Vascular Retinopathy
- Diabetes is the leading cause of new cases of adult-onset blindness
- Research
  - ClinicalTrials .gov (more than 900 studies listed)
  - DRCR.net (Diabetic Retinopathy Clinical Research Network)

Diabetic Disasters: Roadmap to Prevention

# **Diabetic Retinopathy**



How to detect



When and how to manage



Who to Refer



How to Co-Manage





# Challenges in Diagnosis

ls this a normal macula?



**Pitfall:** What may look normal or nearly normal may not be normal!





#### Patient in her late 30s diabetic, Sent for Diabetic Eye Examination



20/20 OU all testing "normal" Fundus exam as below



#### Early Detection



- Visual Acuity
- A1c, Blood Sugar
- Concomitant disease







#### Detection









# Pertinent Information for Management

- Type
- Duration
- Control (Daily and Overall)
- Smoker (Y or N)
- Any other medical Dx (HTN, Sleep Apnea, Obesity)
- Any (other) associated complications (Renal Failure)
- Pregnant or plan to be





# Hypertriglyceridemia

#### 45 Y/O WM DM +



#### PDR + lipemia retinalis

#### Based on these pictures, how would you manage?











# Does this change your plans for this patient?

#### Effect of previously mentioned pertinent info on management







# How to Manage





- Properly assess the condition
  - Classification
- Consider all the associated factors discussed
- PATIENT EDUCATION
- Follow-up under the standards of care
- Know who and when to refer

36 Y/O F 20/40 1+ NS 2-3 Cortical Symptomatic OD DM 10+yrs A1C 13

What is patient's assessment of OS? What is the doctor's Assessment? How would this be followed?









# <sup>20/100</sup> Patient Education Timely DX and Management



#### Stages

Diabetic Retinopathy: A Position Statement by the American Diabetes Association

Diabetes Care 2017;40:412-418 | DOI: 10.2337/dc16-2641

Sharon D. Solomon,<sup>1</sup> Emily Chew,<sup>2</sup> Elia J. Duh,<sup>1</sup> Lucia Sobrin,<sup>3</sup> Jennifer K. Sun,<sup>4</sup> Brian L. VanderBeek,<sup>5</sup> Charles C. Wykoff,<sup>6</sup> and Thomas W. Gardner<sup>7</sup>

www.diabetes.org

stage	Description Small areas of balloon-like swelling in the retina's tiny blood vessels, called microaneurysms, occur at this earliest stage of the disease. These microaneurysms may leak fluid into the retina.				
Mild NPDR					
Moderate NPDR	As the disease progresses, blood vessels that nourish the retina may swell and distort. They may also lose their ability to transport blood. Both conditions cause characteristic changes to the appearance of the retina and may contribute to DME.				
Severe NPDR	Many more blood vessels are blocked, depriving blood supply to areas of the retina. These areas secrete growth factors that signal the retina to grow new blood vessels.				
PDR	At this advanced stage, growth factors secreted by the retina trigger the proliferation of new blood vessels, which grow along the inside surface of the retina and into the vitreous gel, the fluid that fills the eye. The new blood vessels are fragile, which makes them more likely to leak and bleed. Accompanying scar tissue can contract and cause retinal detachment—the pulling away of the retina from underlying tissue, like wallpaper peeling away from a wall. Retinal detachment can lead to permanent vision loss.				

\*Adapted from https://nei.nih.gov/health/diabetic/retinopathy.

#### International Classification of DR (ICO)



# International Classification of DME

- OCT: most sensitive test
- No DME: No Thickening, or Exudates in the Macula
- Non-Center involving DME: Thickening outside of 1mm of fovea
- Center involving DME: Thickening within the 1 mm diameter





#### **ETDRS Diabetic Retinopathy Severity Scale**



• DR, diabetic retinopathy; ETDRS, Early Treatment Diabetic Retinopathy Study; NPDR, non-proliferative DR; PDR, proliferative DR.

• 1. ETDRS. Ophthalmology. 1991;98:823-833. 2. Ip MS, et al. Arch Ophthalmol. 2012;130:1145-1152.


# MAs































## **Typical Progression**

- Patients may present at any stage
- Some still asymptomatic or attribute their symptoms to needing spectacle Rx change
- Most will not understand the significance of the condition



• This patient is suffering chronic macular edema obviously needing referral



## Neglected-Leading to Further Progression



Now the Patient is Symptomatic and has Severe Disease









And Now, the Patient has Significant Irreversible Damage, even after Resolution of Edema with Tx

















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C) Q, B, Q, MN + I L1000 1100 Dep Viscola Pesas





-

Deep Vascular Plexue

Avascalar Leyers

























## 26 y/o - Type 1, First Dilated Exam









Subtle Hints of Advancing Disease

## **Crucial Follow-up Care** Unreliability of Symptoms







#### OS: HM .....





## Screening and Follow-up

2017 American Diabetic Association Guidelines

- Adults with type 1 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist within 5 years after the onset of diabetes. B
- Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist at the time of the diabetes diagnosis. B
- If there is no evidence of retinopathy for one or more annual eye exams, then exams every 2 years may be considered. If any level of diabetic retinopathy is present, subsequent dilated retinal examinations for patients with type 1 or type 2 diabetes should be repeated at least annually by an ophthalmologist or optometrist. If retinopathy is progressing or sight-threatening, then examinations will be required more frequently. B



## Screening and Follow-up

2017 American Diabetic Association Guidelines

- Women with preexisting type 1 or type 2 diabetes who are planning pregnancy or who have become pregnant should be counseled on the risk of development and/or progression of diabetic retinopathy. B
- Eye examinations should occur before pregnancy or in the first trimester in patients with preexisting type 1 or type 2 diabetes, and then these patients should be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy. **B**
- While retinal photography may serve as a screening tool for retinopathy, it is not a substitute for a comprehensive eye exam, which should be performed at least initially and at intervals thereafter as recommended by an eye care professional. E

Diabetes History; Medical History; Current Medication; Biochemical Parameters







Table 2. Screening and Referral Recommendations Based on International Classification of Diabetic Retinopathy\* and Diabetic Macular Edema for High-Resource Settings

Classification	Re-examination or Next Screening Schedule	Referral to Ophthalmologist
DR		
No apparent DR, mild nonproliferative DR, and no DME	Re-examination in 1–2 yrs	Referral not required
Mild nonproliferative DR	6–12 mos	Referral not required
Moderate nonproliferative DR	3-6 mos	Referral required
Severe nonproliferative DR	<3  mos	Referral required
Proliferative DR	<1 mo	Referral required
DME		-
Non-center-involving DME	3 mos	Referral required
Center-involving DME	1 mo	Referral required

DME = diabetic macular edema; DR = diabetic retinopathy.\*In cases where diabetes is controlled.

# ICO Follow-up Care Exceptions

 Antenatal Screening • If No DR then 28 Pregnancy weeks • If DR 16-20 weeks • DR and DME can progress faster with Cat SX • Cat SX when visually or Optically Significant • Severe NPDR PRP before SX Cataract • DME Focal or Anti-VEGF stabilize DME • If View not adequate for laser (if DME anti-VEGF before SX) monitor closely after cataract surgery

## When to Refer

🕅 🔍 🔍 98% 👻 🛨 1:1 pixel 1:1 µm



Reference: 1/31/2011

Examination: 8/14/2018

#### Any Macular Edema

#### Severe NPDR, Suspicious of NV

NV (PDR), VH, TRD

### **NVI urgent**

## CSME/DME

• Focal Laser: Safe, Durable, Effective







#### Large perifoveal MA identified



#### 1 month after laser



#### 3 months after laser





## Heavy Focal Examples

After 360 foveal focal by outside doctor



#### After a series of Avastin injections



## Focal-(example of poor TX)





## Heavy Focal Examples





Chorioretinal scars, foveal atrophy, CNV



## DME-IVIs



DME










### DME-Chronic Care 9/25/2012-- IVA



# DME-Neglected (24 Y/O F)



# Increased Exudates After DME TX





# Moderate and and Severe NPDR

- New Paradigm in Managing
  - Ride and Rise Studies
    Demonstrated Reversal
  - Protocol S (DRCR)
    - Compared ranibizumab (Lucentis) to PRP FDA approves it for NPDR (Jan 2017)
  - Panorama (Regeneron)
- Anti-VEGF for Severe NPDR (EDTRS 47 and 53 severity) will perhaps become standard of care
  - Many unanswered



Both patient's OD Anti-VEGF treated upper slides before treatment Bottom slides 2 months later (two monthly treatments)

# PDR

- PRP
- Anti-VEGF
- Combo
- Vitrectomy

# Reversal of w/ treatment! (Anti-VEGF and PRP)







# **Reversal with Treatment**

# PDR-NV (IVA)



# S/P IVA



Subsequent recurrence followed by additional PRP, recent VH

# PDR Treatment Anti-VEGF Only

Ischemia not fixable







Predictable changes over time (complaint patient)









# Need for Continued Follow-ups Post Treatment

## Preretinal fibrosis, Inactive NVE

#### Actively Leaking NV



Significant Nonperfusion

# IVA before PPV



#### To delay or avoid PPV

# PRP IVI vs. PPV





Pre-Post-PPV

#### Which Eye More Important to Treat?



Patient perception OD recent onset poor vison OS no problems

# PDR-(Over Tx)









Clinical Outcomes of Patients with Ant Seg NV Treated w/ IV bevacizumab: Advances in Therapy Feb 2009



Vision	Vision not indicator presence, absence or a measure for level and status of retinopathy
Know	Patients undergoing treatment must know this is a chronic condition needs chronic and continuous care
Convey	Patient education must convey understanding of the gravity of the condition and avoidable catastrophes

Establishing a relationship with the treating provider

Your comfort level to deal with high risk high complexity conditions

Having the proper diagnostic tools

Recognizing the chronicity of these conditions some requiring long-term care

Diabetic Retinopathy is a Chronic Disease Needing Continuous Care



# Pitfalls Leading to Disasters

- Beyond patient's misconceptions
  - Poor follow-up compliance
- Inadequate screening
  (Examination)
- Inadequate attention to certain findings



"I was not having any vision problems don't know how this happened to the RE and I have no problems with my LE don't want treatment!"



Interoperation and Clinical Correlation and Knowing Limitation of Each Device and Technique

# Attention signs of Advancing Disease













# **Diabetic Retinopathy Progression**





Examining the patient at one point in time, with poor attention to past and future!





# **Diabetic Retinopathy Progression**





# **Diabetic Retinopathy Progression**

# **Diabetic Retinopathy**

Focal for ME





2.5 years is it really getting better?

Callousness to what may not make sense

# **More Pitfalls**



# Exhibit 3 (NPDR to PDR) FA vs Clinical Exam







A disease that does not always have the "classic" textbook presentation



#### Spectrum of Disease and co-factors






Subtle Hints of Advancing Disease



# Case Example Challenges!

The ravages of the disease! 26 Y/O WM type 1 uncontrolled

IVI OU 1 Mo











1 Mo later IVA OS



1 Mo later No Tx Return 6 weeks







### Challenges!

### The ravages of the disease! 26 Y/O WM type 1 uncontrolled

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### 4 months later

IVA

1 Mo later IVA Patient is starting college, care transferred to local clinic





Patient returns 17 mo later Patient neglected follow-up care Still not well controlled





### Challenges!

### The ravages of the disease! 26 Y/O WM type 1 uncontrolled

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# **Case Examples**

Patient 2





What would you do as far as referring these patients?

When it doesn't add up!

# Patient 2















## Patient 2





Patient 2





#### Patient 1 OD



#### Patient 2 OD



# Case of unexpected findings and patient's disappointment! When it doesn't add up!

- 55 Y/O BF
- DM x20yrs
- Referred as emergency "macular on" RD recent onset vision loss (NPDR OS) Patient arrives end of the day!!!
- OD:HM OS:20/50
- "Wants her vision fixed today need to get back to work!"





-Future of this area
-Mechanism of sight
loss
-What can be done
about it?



# -Status of Fellow Eye -Coexisting Disease





# Macula On vs. OFF


### When patient not happy with the outcome



#### I have been blinded by treatment! (should not have had it, will tell everyone laser blinds you!!!)



When patient blames the doctor or treatment



#### Crucial Follow-up Care- Unreliability of Symptoms





OS: HM .....

#### VOD predictable changes (noncompliant patient)



### **PDR Progression**



April 2011

### **PDR** Progression



April 2012 by June 2012 Vas 20/40 OD/OS Ongoing Treatment and much improved.

Noncompliance not by choice!

### **PDR** Progression



Missed Jul 2012 appt shows Late sep HM OU (Now on kidney dialysis)





# PDR Progression (following first IVA)







### PDR Progression (following second IVA)





1 Day Post-op 20/200

# PDR Progression (OD following PPV)

### PDR Progression (OD following PPV)





New View of Fundus Sch for PPV

# PDR Progression (OS following PPV)





# Eventually got to this point and started noncompliance by choice!

20/400





#### Compliant patient PRN anti-VEGF Fellow Eye NLP

### PDR-Other Factors (Ischemic disease/Renal Failure)



40 Y/O Af/Am F

Multiple Treatment, Active Disease, Evidence arterial attenuation and occlusion!

#### Limitation of treatment outcomes

### PDR-Other Factors (Ischemic disease/Renal Failure)



In and out of hospital CHF, Renal Dz Active NV, IVA Complete arterio-venous occlusion HM/LP

#### Poor prognosis PDR-TRD (Highly Vascularized Retina Pre-OP)







#### PDR-TRD (Highly Vascularized Retina Post-OP)



#### Next time you see this



#### Remember these!

Thank you



