I'm Diabetic. When do I need to get my eyes examined? Maintaining optimal vision and eye health

Ballantrae Zoom talk 3 Dec 2020

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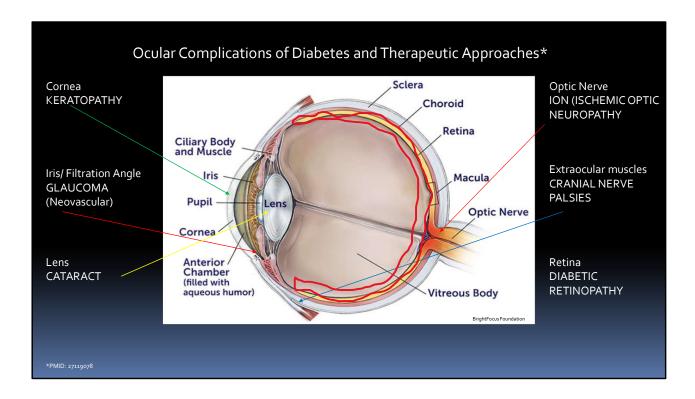


Thank you to the group for the opportunity to promote ocular health for diabetics; therefore, preserving eyesight and maintaining quality of life

My goal is to help you understand WHEN - not IF - eye examinations are essential for ALL diabetics. Let's ask 2 important questions:

First and foremost; How might diabetes affect your eyes, or those of a family member or friend

And secondly; Why you should get examined, or advise patients, to be seen in a timely fashion

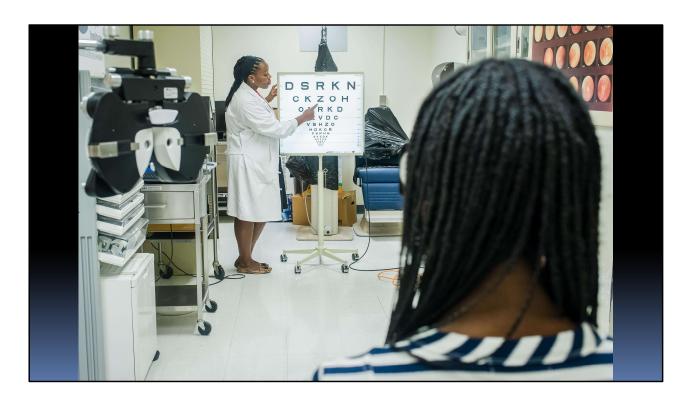


# Let's look briefly from the front to back of the eye and potential diabetic ocular complications

Diabetes can impact any of the structures outlined, For the purpose of our talk today I will emphasize the **importance of diabetic retinopathy**, **BECAUSE**, **worldwide**, it is the leading cause of visual loss in the working-age group; 20-64 years old

Now that you understand potential ocular complications in diabetes how will your physician, ophthalmologist, or optometrist examine you for treatable pathology?

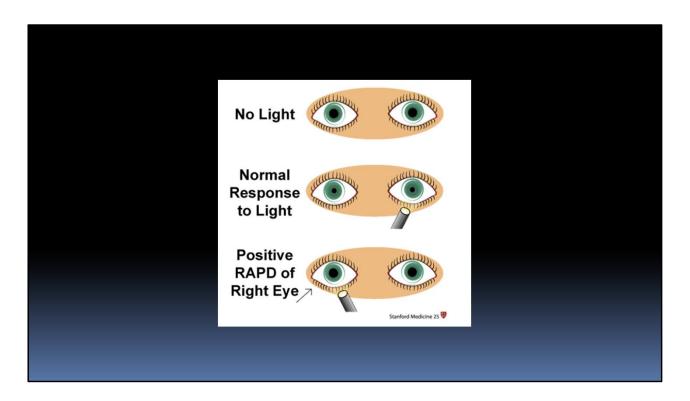
\*Ocular complications of Diabetes and Therapeutic Approaches; Vieira-Potter et al. 2016 Review (PMID: 27119078)



First and foremost, we measure your visual acuity or **VA**; this determines your ability to measure the resolvable gap between high-contrast letters

Snellen letters, commonly used in most clinical settings, are viewed at 6 metres or 20 feet. 20/40 VA means a person with "normal vision" sees the standard letter from 40 feet away, but you need to be 20 feet away to identify the same letter

"Normal vision" for most of the population is 6/6 (20/20) in adults but some, including children, achieve 6/4.5 (20/15) Visual Acuity

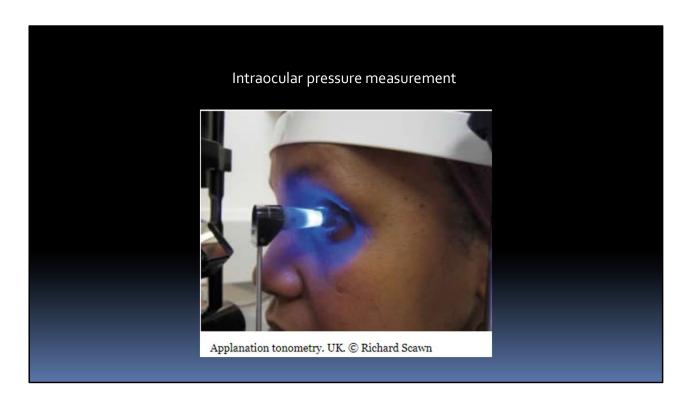


Your physician will check your pupil responses **to bright light,** BEFORE, inserting any eye drops which DILATE the pupils. Pupil dilation is an important part of a complete eye examination



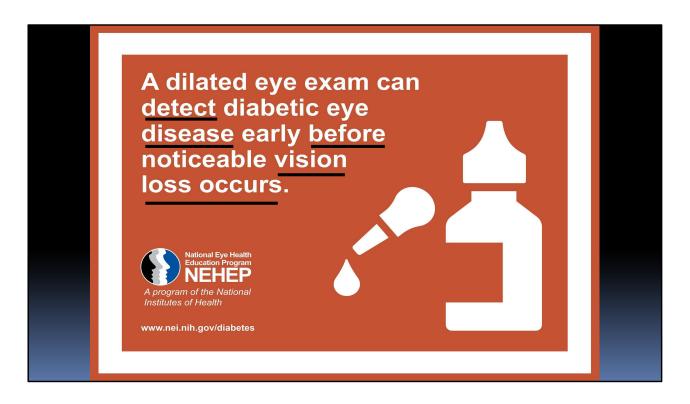
Magnification of the eye is aided using the slit lamp; the workhorse of ophthalmologists. We examine the cornea, check the intraocular, or eye pressures, look for signs of glaucoma and cataracts; then proceed to examine the back of the eye – essentially the retina and optic nerve – referred to anatomically as the FUNDUS

A variety of lenses are utilized by the ophthalmologist to better view details of the back of the eye



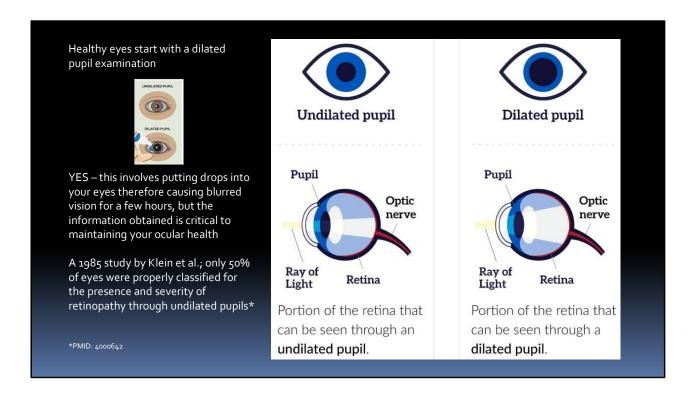
This lady is having her intraocular, or eye, pressure measured, with an applanation tonometer, after topical anaesthetic was instilled in the eye

As we discussed earlier dilating the pupils with eye drops is a critically important part of the eye examination. Why is this the case?



The dilated pupil exam, loosely referred to as the "dilated eye exam" can detect eye disease early, therefore PRIOR to any symptoms or vision loss

Imagine, for a moment, you are looking into a room through a very small keyhole. How much more of the room, you could visualize, simply by opening the door?

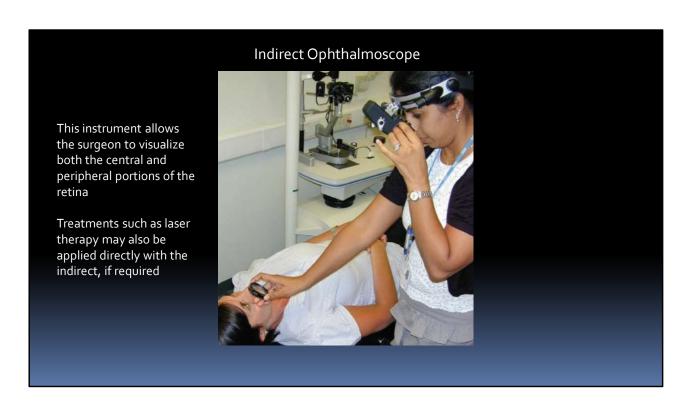


By opening the door, or pupil, we have an opportunity to gain better diagnosis and treatment. YES – this involves putting drops into your eyes therefore causing blurred vision for a few hours, but the information obtained is critical to maintaining your ocular health

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Klein et al. in 1985 published a paper in the journal **Ophthalmology** – only 50% of eyes were properly classified for the presence and severity of retinopathy through **undilated** pupils. New high tech extra-wide-field cameras are frequently used in screening programs worldwide, including remote Arctic regions of Canada, and **pupil dilation is routine protocol**.

\*Diabetic Retinopathy as detected using ophthalmoscopy, a nonmydriatic camera and a standard fundus camera. Klein R, et al. Ophthalmology.1985. April. PMID: 4000642

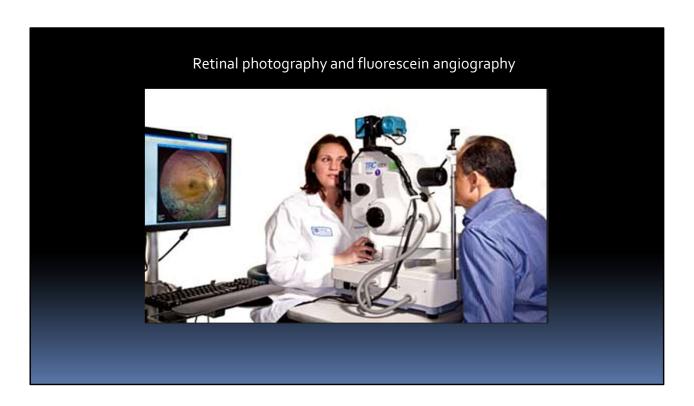


Another advantage of a dilated pupil allows use of the indirect ophthalmoscope

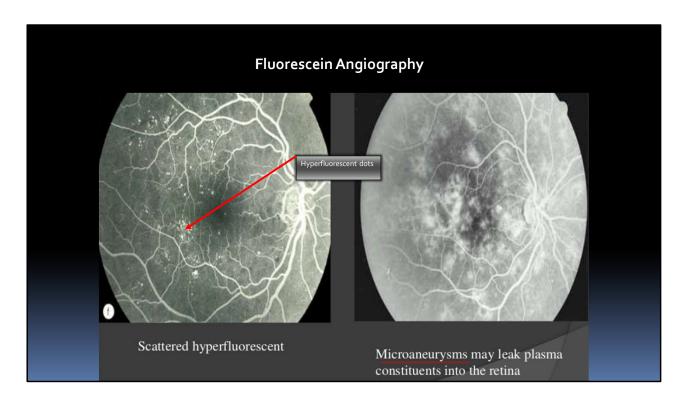
Additional specialized tests may be performed by your eye care specialist depending on your findings:

- 1. Retinal photography
- 2. Fluorescein angiography
- 3. OCT (Ocular Coherence Tomography)

Sometimes additional tests will be recommended by your health care provider

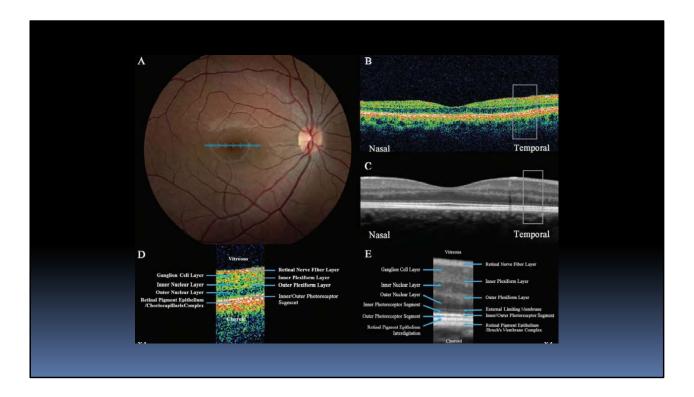


Here is a high-tech fundus camera for photography and fluorescein angiography. Pictures are normally taken **AFTER** the **pupils** have been **dilated** with eye drops



Fluorescein dye has been injected into a peripheral vein and abnormalities to retinal blood vessels are easily identified such as microaneurysms demonstrated here as hyperfluorescent dots on the left photo

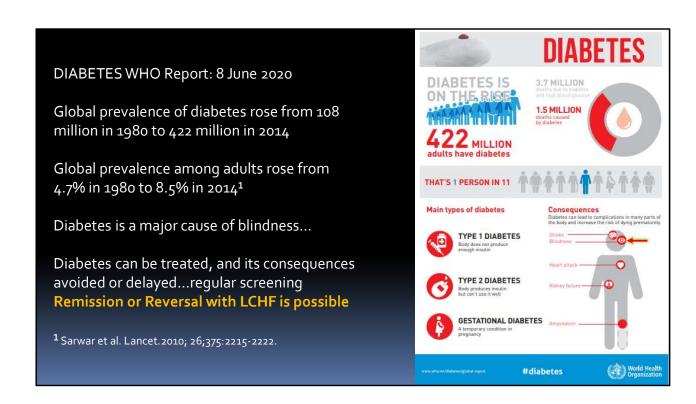
The picture on your right was taken minutes later showing leakage of dye into surrounding retina



A picture is worth a thousand words; the reason I fell in love with medicine, and especially ophthalmology.

The photograph on the upper left is taken with a fundus camera – AFTER eye drops were instilled. Physicians can literally diagnose hundreds of **systemic** and local diseases simply by viewing the retina and optic nerve i.e., "**the fundus**".

Optical Coherence Tomography, or OCT, is a non-invasive imaging test, utilizing light waves to take high resolution cross-sectional images of your retina. OCT resolution of 2 microns, approximately 1/4 the size of a red blood cell, allows "optical biopsies" in real time. Color and black and white OCT images are shown on the right and below the fundus photo



Is the trend of increasing diabetes rates and blindness continuing from 1980-2014 and beyond?

Is the prevalence of Diabetes decreasing in world since the WHO 2014 data?

463 million people have diabetes in 2019¹

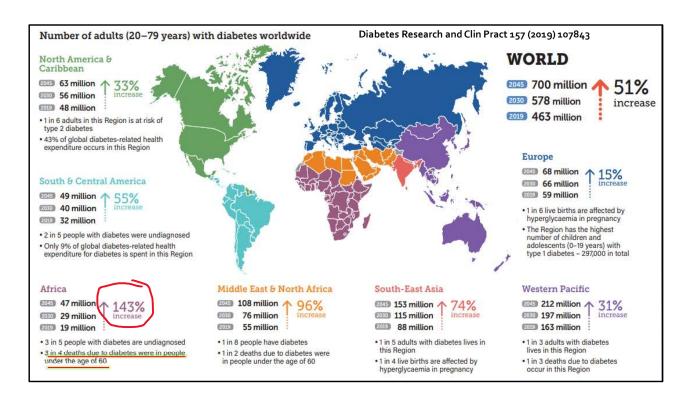
What are current projections for future?

¹Global and regional diabetes prevalence estimates for 2019 and projections for 2013 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9<sup>th</sup> edition. Saeedi P et al. Diabetes Research and Clinical Practice. 2019; 157:1-10.

463 million diabetics in 2019 worldwide

Diabetes Prevalence is clearly <u>not</u> decreasing with 41 million people added between 2014 and 2019

What are current projections for the future?



Sadly, best estimates suggest, 578 million by 2030, and **700 million** diabetics worldwide **by 2045**, an astonishing **51% increase**. No country is immune.

Developing countries are especially at risk – **Africa**, for example, **will increase 143%** -- between today and 2045

>50% of blindness globally from DR exists in the Asia-Pacific Region alone

Is the prevalence of Diabetes decreasing in world since the WHO 2014 data?

463 million people have diabetes in 20191

What are current projections for future?

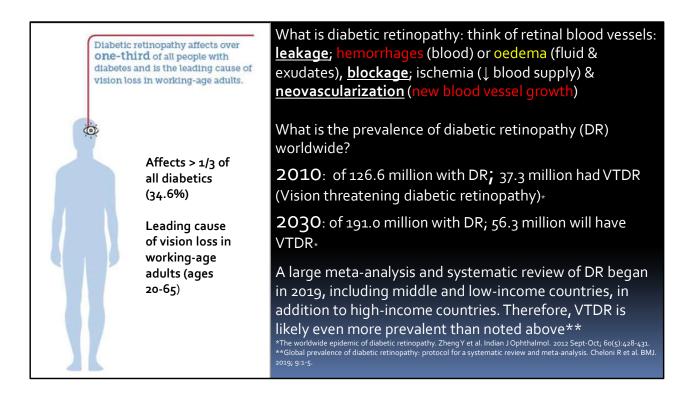
578 million predicted to have diabetes in 2030 and 700 million by 2045 (a staggering 51% increase over today; this is equivalent to 1 in 9 adults)

What is the relevance of increasing diabetes prevalence as related to eye disease?

<sup>1</sup> Global and regional diabetes prevalence estimates for 2019 and projections for 2013 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9<sup>th</sup> edition. Saeedi P et al. Diabetes Research and Clinical Practice. 2019; 157:1-10.

Concentrate on the yellow highlighted portion of the slide. All estimates suggest 1 in 9 adults, or 11.1%, will be diabetic worldwide in 2045.

This brings us to the significance of increasing diabetes prevalence as related to eye disease.

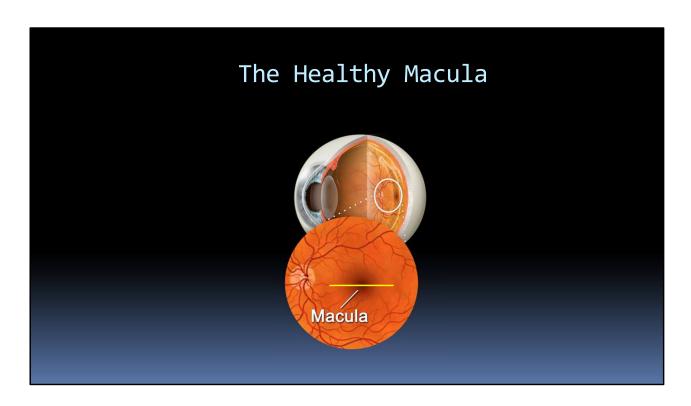


The longer the diabetes duration—the greater the % of retinopathy

Let's now quickly explain what diabetic retinopathy looks like, and we will subsequently return to the meaning of, Vision Threatening Diabetic Retinopathy (VTDR)

1.34 million Americans, out of 6 million with DR, have Vision Threatening Diabetic Retinopathy (VTDR) in 2020 AAO-PPP 2019

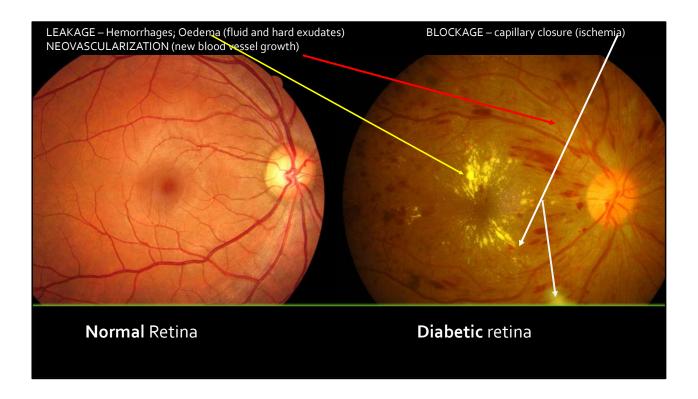
The worldwide epidemic of diabetic retinopathy. Zheng Y et al. Indian J Ophthalmol. 2012 Sept-Oct; 60(5):428-431. This systematic review and meta-analysis included data up until 2008 did not include data from Low-and-Middle-Income countries (LMIC). The following study, still in progress in 2020, addressed this issue: Global Prevalence of Diabetic Retinopathy: Protocol for a systemic review and meta-analysis. Cheloni R et al. BMJ. 2019:9;1-5.



So, here's the anatomical macula -- the central retina.

It is 5-6 mm across -- and accounts for the central 21 degrees of vision.

This is a healthy macula -- consistent with good vision – think 6/6 or 20/20 or better visual acuity



If you have visited an ophthalmologist and he or she tells you that "diabetic retinopathy" is present it normally means that blood vessels in the back of the eye are leaking, have become blocked or new abnormal blood vessels are growing. Some of these changes require urgent treatment to prevent vision loss.

It's important to know that severe diabetic changes may occur in the eye with NO symptoms.

No abnormalities  Microaneurysms only  Moderate NPDR (see Glossary)  More than just microaneurysms but less than severe NPDR  Evere NPDR  U.S. definition  Any of the following (4-2-1 rule) and no signs of proliferative retine quadrants  Definite venous beading in 2 or more quadrants  Moderate IRMA in 1 or more quadrants  Any of the following and no signs of proliferative retinopathy:  More than 20 intraretinal hemorrhages in each of 4 quadrants  Definite venous beading in 2 or more quadrants  One or both of the following:  NeovascularIzation  Vitreous/preretinal hemorrhage
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Neovascularization
Vitreous/preretinal hemorrhage
MA = intraretinal microvascular abnormalities; NPDR = nonproliferative diabetic retinopathy; PDR = coliferative diabetic retinopathy
OTES:

Disregard the details of the severity of diabetic retinopathy shown only for completeness. The greater the leakage and/or blockage, the greater the severity of **non-proliferative** disease. The greater the extent of new blood vessel growth and hemorrhage, the greater the severity of **proliferative** retinopathy.

# Clinically Significant Macular Edema (CSME)

Retinal thickening and/or hard exudates that involve the center of the macula or threaten to involve it: normally requires prompt treatment\*

## **CSME**

- ci-CSME (center-involved)
- nci-CSME (non-center-involved)



\*Retinal thickening at or within 500 µm of the center of the macula; and/or hard exudates at or within 500 µm of the center of the macula if associated with thickening of the adjacent retina; and/or a zone or zones or retinal thickening 1 disc area in size, any part which is within 1 disc diameter of the center of the macula

When fluid leaks into the central part of our retina (the center) it becomes thicker and functions poorly and may lead to vision loss. This normally requires treatment by your ophthalmologist to preserve your vision.

What is the meaning of VISION-THREATENING diabetic retinopathy (VTDR)?

It is defined as severe non-proliferative DR;

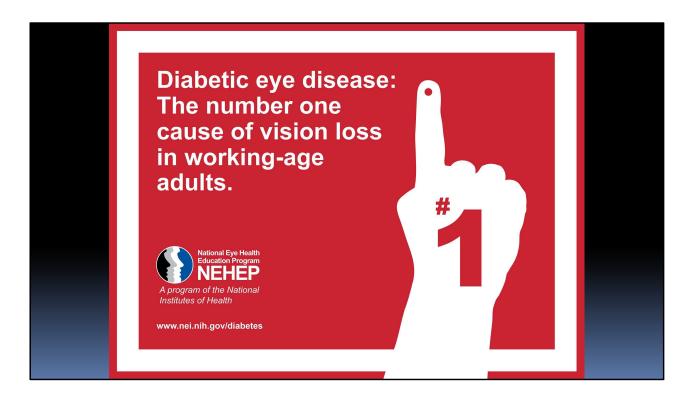
or proliferative DR;

Severe diabetic eye disease often has NO SYMPTOMS

Why does this matter?

- Severe VTDR often presents with NO SYMPTOMS
- VTDR is the leading cause of visual loss in the working-age group; 20-64 years old

The main point is you can be in serious danger of losing permanent vision in the absence of symptoms when you have vision-threatening diabetic retinopathy



Ophthalmologists have much better chance and results, preventing VA loss, if we can examine and treat patients at an early stage

The NEHEP (National Eye Health Education Program) defines working-age as 20-74 years



Quality of life matters! This is how you might view the world: a person with normal vision on the left, in contrast to diabetic retinopathy on the right.

# RISK FACTORS for DIABETIC RETINOPATHY Major Risk Factors\* Duration of Diabetes Glycemic control T1D > T2D Moderate Risk Factors Systolic blood pressure (intensive bp control no better than standard treatment)\*\* Minor Risk Factors Lipid-lowering agents (i.e., Control your blood glucose ase in CSME and progression of retinopathy, CSME is NOT clinically relevant and blood pressure BECAUSE LIFESTYLE INTERVENIONS (LCHF), including the VIRTA Health Study, improve all the risk factors above, large RCTs would be the obvious next step \*PMID: 22927798; 22212499; 25637717; 24526393 \*\*PMID: 9732337; 12667031 \*\*\*PMID: 29487821

Not surprising to most readers is the fact that the poorer your blood glucose control, the longer you have diabetes and how well you control your blood pressure all affect the degree to which you get retinopathy.

## How do we treat diabetic retinopathy?

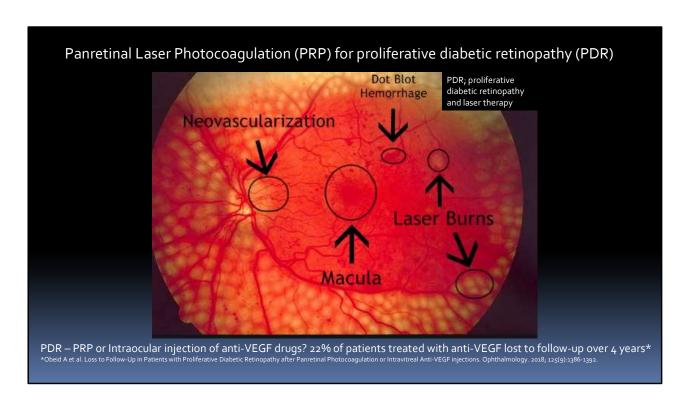
- Observation: VTDR is always treated early, because treatment can reduce vision loss 90-95%. Observation of some higher-risk patients may be acceptable, however close follow-up is critical
- Laser therapy
- Intravitreal injections of anti-VEGF and occasionally steroids
- Vitrectomy

Before briefly considering the treatments for diabetic retinopathy a very important point needs to be emphasized: A multitude of recent studies have demonstrated reversal or remission of Type 2 diabetes (T2D) with low carbohydrate lifestyle changes – meaning restrict your intake of sugars and refined carbohydrates

## How do we treat diabetic retinopathy?

- Medical management: glycaemic control, systolic blood pressure and lipids(?)
   Lower carbohydrate diets have been shown in studies to reverse many of the associated diseases seen with diabetes
- Observation: VTDR is always treated early, because treatment can reduce vision loss 90-95%. Observation of some higher-risk patients may be acceptable, however close follow-up is critical
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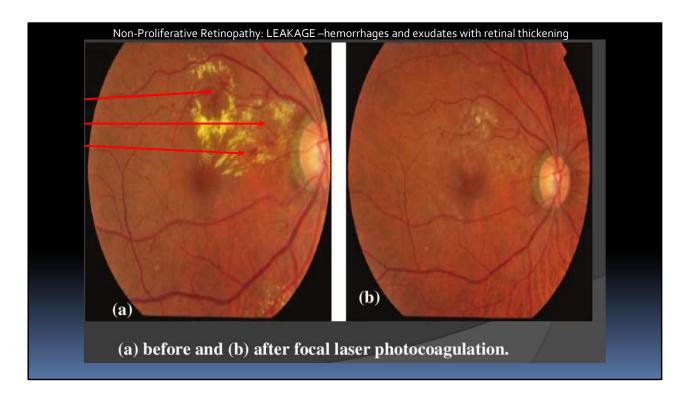
Now what is laser therapy used for?



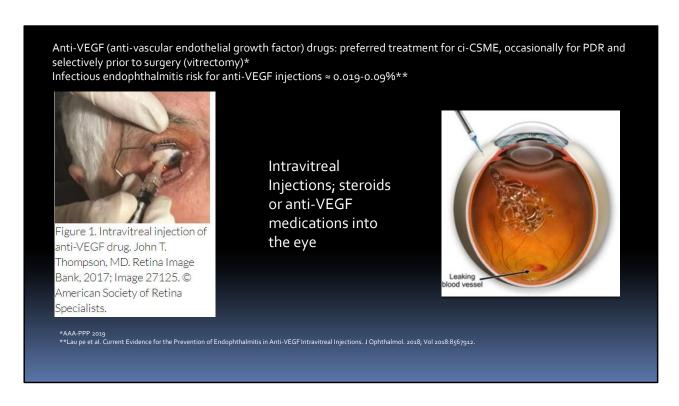
PDR; Proliferative Diabetic Retinopathy - new blood vessels are abnormal, hemorrhage, and lead to blindness if left untreated. Laser therapy is generally the most common Rx, supported by multiple clinical trials

Panretinal photocoagulation places 1200-1600 laser burns, avoiding the central vision region of the anatomical macula. Anti-VEGF drugs can also be an acceptable treatment , via an injection into the eye, however a 2018 study revealed 22% of PDR patients with anti-VEGF Rx were lost to follow-up over 4 years – natural history suggests those patients will quickly become legally blind without appropriate intervention

Obeid A et al. Loss to Follow-Up in Patients with Proliferative Diabetic Retinopathy after Panretinal Photocoagulation or Intravitreal Anti-VEGF injections. Ophthalmology. 2018; 125(9):1386-1392.



We can also treat clinically significant macular edema with focal laser. Multiple RCTs suggest center-involved CSME responds best to anti-VEGF injection, however your ophthalmologist may use focal laser if the edema does not respond after 3 injections. Outside the anatomical macula, or central vision, we still treat CSME with focal laser Focal laser was applied to leaking blood vessels seen on the left picture with a repeat photo taken 3-4 months later. The fluid and hard exudates, and therefore abnormal retinal thickening, has resolved



Intravitreal injections: Apart from the psychological trauma of getting a needle inserted into your eye the risk of serious intraocular infection, or endophthalmitis is  $\approx 0.019-0.09\%$  (1.9 to 9/10,000 injections) for anti-Vascular Endothelial Growth Factor drugs

Common anti-VEGF drugs include:

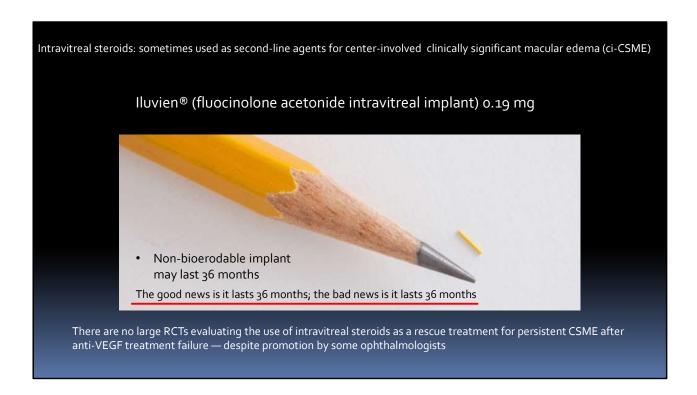
Avastin (bevacizumab)

Lucentis (ranibizumab)

Eylea (aflibercept)

Beovu (Brolucizumab) 2019

Most people who get anti-VEGF injections will need injections once a month for at least the first 3 months

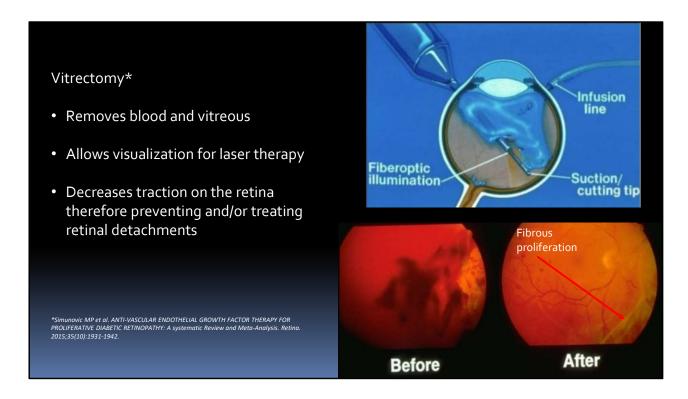


What about intravitreal steroids: Multiple studies demonstrate high rates of cataract formation and secondary glaucoma (i.e., high eye pressure) requiring additional surgical intervention. Therefore, intravitreal steroids are generally used as second line agents for center-involved CSME (ci-CSME).

There are no large RCTs evaluating the use of intravitreal steroids as a rescue treatment for persistent CSME after anti-VEGF treatment failure — despite promotion by some ophthalmologists.

This picture depicts the relative size of the implant injected into the vitreous cavity Iluvien (fluocinolone acetonide intravitreal implant) – slow release: <u>Good news</u> if no complications implants last 36 months; <u>bad news</u> is they last 36 months if associated with complications and may require surgical removal

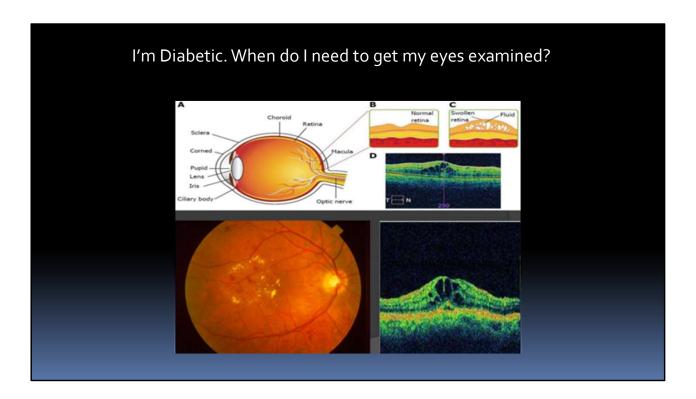
The largest retinal group in the world, backed by NIH funding, **D**iabetic **R**etinopathy **C**linical **R**esearch **Net**work (DRCR.Net) — >115 sites and > 400 ophthalmologists throughout the US. Several RCTs have increased our understanding of Diabetic Retinopathy as a result.



<u>Surgical vitrectomy</u>: After intravitreal blood was removed the fibroproliferative, abnormal tissue, leading to traction retinal detachment and intraocular bleeding is revealed.

A 2015 meta-analysis reports **strong evidence** that anti-VEGF therapy at the time of vitrectomy decreases intra and post-operative hemorrhage, operating time and retinal tears\*

\*Simunovic MP et al. ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY FOR PROLIFERATIVE DIABETIC RETINOPATHY: A systematic Review and Meta-Analysis. Retina. 2015;35(10):1931-1942.



We have now come full circle to answer our initial inquiry. When do I need to get my eyes examined?

I often asked my medical students, interns or residents the following question: If you have a newly diagnosed T1D, 4 years of age, and a 62-year-old newly diagnosed T2D which patient should be seen 1<sup>st</sup> by an ophthalmologist? **You only have one appointment available**. Perhaps surprising to some --the correct answer is the T2D! Why? Because the insulin resistance, and ongoing inflammatory damage, has likely been brewing in some cases for 20+ years.

The Hyperglycaemic hyperinsulinaemic inflammatory dyslipidaemia (HHiD), that Prof Noakes describes, has likely been brewing, in some cases for 20+ years.

Diabetes Type	Recommended Initial Evaluation	Recommended Follow-up*
Type 1'	5 years after diagnosis <sup>34</sup>	Yearly <sup>34</sup>
Type 2'	At time of diagnosis <sup>40,122</sup>	Yearly <sup>40,122</sup>
Pregnancy‡ (type 1 or type 2)	Soon after conception and early in the first trimester 123-125	<ul> <li>No retinopathy to mild or moderate NPDR: every 3-12 months<sup>123-125</sup></li> </ul>
		<ul> <li>Severe NPDR or worse: every 1–3 months<sup>123-125</sup></li> </ul>
NPDR = nonprolife	erative diabetic retinopathy	
* Abnormal finding	gs may dictate frequent follow-up examinations.	
'Pubertal patients	require increased vigilance due to increased risk	of progression
	elop gestational diabetes do not require an eye	
appear to be at ir	icreased risk for diabetic retinopathy during pre	gnancy. PPP; AAO 2019

International Guidelines: T1Ds <u>do not</u> need an ophthalmological examination for 5 years after diagnosis, unless they reach puberty

I cannot emphasize enough, the importance of eye examinations AT THE TIME OF DIAGNOSIS for T2D

Pregnant pre-existing diabetic patients require close follow-up early in the first trimester

Gestational diabetes DOES NOT increase the risk of retinopathy therefore NO ophthalmological exam is required.

Red flags, both in T1D & T2D, involve <u>large swings in hormones</u> — **puberty** or **pregnancy** 

### Take home messages:

- 40% of diabetics do not receive comprehensive dilated pupil examinations by ophthalmologists
- In people with type 2 diabetes, retinopathy may be present in 21% to 39% soon after clinical diagnosis\*; therefore T2D require prompt screening at time of diagnosis and, at least yearly, after that time
- · Glycaemic and blood pressure control lowers retinopathy risk and/or progression: emphasize HgA1c and BP control
- People with T1D should have annual screening for DR beginning 5 years after diagnosis
- Aspirin therapy does not prevent DR progression it is NOT contraindicated in management of diabetics regardless of high-risk retinopathy or vitreous hemorrhage
- Diabetic women who become pregnant must be followed closely soon after conception; in contrast Gestational diabetes does NOT pose a risk factor for retinopathy and ophthalmological exams are not required
- Carefully observe any T<sub>1</sub>D or T<sub>2</sub>D patients who reach puberty
- Intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents are effective in center-involved clinically significant macular edema (ci-CSME). Focal laser photocoagulation is the treatment of choice for non-center-involved CSME and pan-retinal photocoagulation (PRP) laser treatment remains the mainstay of therapy for proliferative diabetic retinopathy (PDR).

\*PMID: 2357354, 2689119, 25502808

A summary of the most important points in this presentation are noted on the slide



Thank you so much for the opportunity to discuss the importance of eye care in the diabetic population. We will overcome this COVID challenge and are so fortunate to live in this community. My beautiful wife, despite losing her lung function to chemotherapy, fulfilled her bucket list with SHEER DETERMINATION in Nepal - Mount Everest is in the background in this picture with our daughter. Luckily, she may not recall me waking her at 0400 hours and climbing from Ghorepani with headlamps at -5C, with windchills of -15-20C, in order to reach Poon Hill lookout for sunrise; elevation 3193m, or 10475 feet.

