

# LATER STAGE DIABETIC RETINOPATHY – A PRIMARY CARE PERSPECTIVE

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## Introduction - Objectives

- ❑ My primary goal is to empower you to be confident and competent to care for a patient with active diabetic retinopathy.
- ❑ I define the later stage diabetic as NPDR moderate or two risk factors in 4 of 4 quadrants with no risk factors within 1 disc diameter from the FAZ.
- ❑ In addition, I will be focusing on physical examination skills; e.g. direct fundus view.

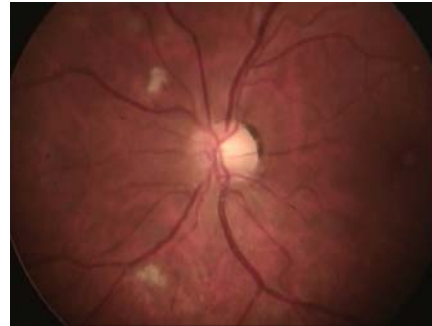
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## Risks? Body Type? Co Morbidities?



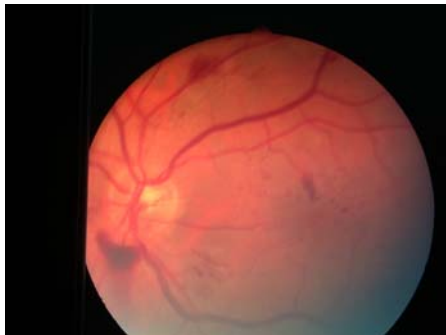
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## When to Hold



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## When to refer



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## Primary Care Medicine?



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## My Background

7

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## Who is Dr Hom

8

- Coordinator, Primary Care Optometry, San Mateo Medical Center. (0.4 Ophthalmologists, 2.5 Optometrists), 40,000 medically indigent
- Grantee, CHCF Project ,Tele ophthalmology project for the County of San Mateo
- Master of Public Administration Candidate, San Francisco State University, est. 2011
- Contributing Editor, Optometric Management (1989)
- 5 year sabbatical from optometry to work for various large computer companies in product management

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## A Common Definition of Diabetes

9

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## Definition of Diabetes

10

- "Diabetes" is borrowed from the Greek word meaning "a siphon."
- The 2nd-century A.D. Greek physician, Aretus the Cappadocian, named the condition "diabetes." He explained that patients with it had polyuria and "passed water like a siphon."
- Diabetes is a metabolic condition whereby the body's tissues cannot use or adequately use the glucose in the blood stream.

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## What is Type 1 Diabetes?

11

- Marked inability of the pancreas to secrete insulin because of autoimmune destruction of the beta cells.
- It commonly occurs in children, with a fairly abrupt onset; however, newer antibody tests have allowed for the identification of more people with the new-onset adult form of type 1 diabetes mellitus called latent autoimmune diabetes of the adult (LADA).
- In T1DM, ketoacidosis can develop, a life threatening emergency. Ketones are in such high concentration in the blood, it will develop. Therefore, exogenous insulin is necessary.

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## What is Type 2 Diabetes

12

- Type 2 DM is a heterogeneous disorder developing insulin resistance and abnormal insulin secretion.
- "...studies support the view that insulin resistance precedes insulin secretory defects..."<sup>2</sup>
- Glutamic acid decarboxylase (GAD) antibodies vs. Islet cell Antibody tests?
- Ketosis-prone T2DM (T1.5DM, atypical diabetes) in Umpierrez et. al. (2006)

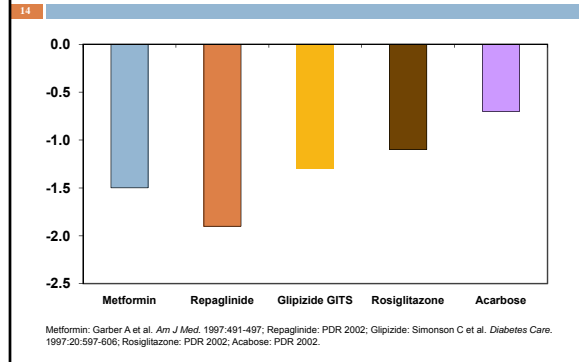
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## OADs: Subclasses

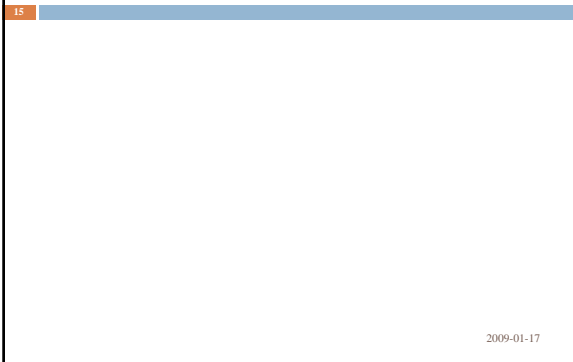
Secretagogues		Sensitizers		Inhibitors
<b>Sulfonylureas</b>	<b>Meglitinides</b>	<b>Biguanides</b>	<b>Thiazolidinediones</b>	<b>α-glucosidase inhibitors</b>
Glimepiride (Amaryl) Glipizide (Glucotrol) Glipizide-GITS (Glucotrol XL) Glyburide (Micronase, Diabeta) Glyburide micronized (Glynase)	Repaglinide (Prandin) Nateglinide* (Starlix)	Metformin (Glucophage)	Pioglitazone (Actos) Rosiglitazone (Avandia)	Acarbose (Precose) Miglitol (Glyset)

\*Nateglinide is not technically a meglitinide.

## A1C: Effects of Various Medications



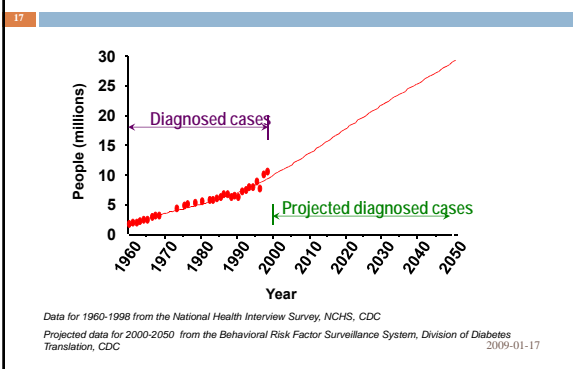
## Why is Diabetes a Problem?



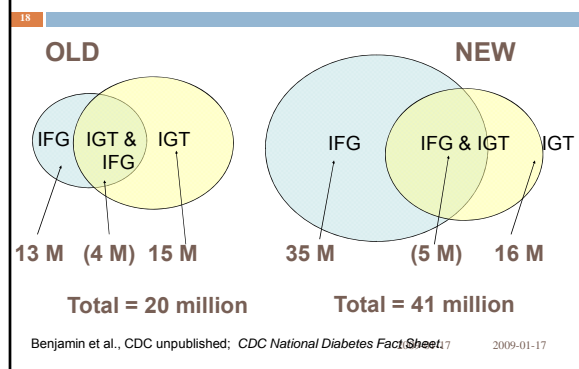
## The Problem

- There is a veritable epidemic of diabetes.
  - Diabetes affects approximately 18 million U.S. adults, of whom an estimated 30% have undiagnosed diabetes, and imposes an increased risk for eye disease. The number of people with DM increases with the age of the population, ranging from an incidence of ~1.5% in individuals from 20 to 39 years to ~20% of individuals >75 years.
  - Visual impairment and blindness affect an estimated 3.4 million U.S. adults aged ≥40 years.
- Source: MMWR Morb Mortal Wkly Rep. 2004 Nov 19;53(45):1069-71.

## U.S. Prevalence of Diagnosed Diabetes



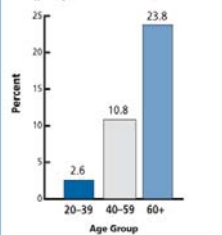
## Pre-Diabetes in the US population, age 40-74 by Old and New Criteria, 2000



## U.S. Prevalence of Diagnosed Diabetes

19

Estimated prevalence of diagnosed and undiagnosed diabetes in people aged 20 years or older, by age group, United States, 2007



**Total:** 23.6 million people—7.8% of pop

**Diagnosed:** 17.9 million people  
**Undiagnosed:** 5.7 million people  
**Age 20 years or older:** 23.5 million, or 10.7%

**Age 60 years or older:** 12.2 million, or 23.1%

**Men:** 12.0 million, or 11.2 percent,  
**Women:** 11.5 million, or 10.2 percent,

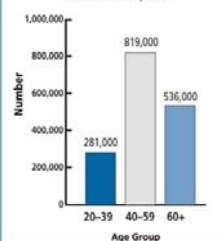
**Non-Hispanic whites:** 14.9 million, or 9.8 percent, of all non-Hispanic whites aged 20 years or older have diabetes.

**Non-Hispanic blacks:** 3.7 million, or 14.7 percent, of all non-Hispanic blacks aged 20 years or older have diabetes.

## U.S. Prevalence of Diagnosed Diabetes

20

Estimated number of new cases of diagnosed diabetes in people aged 20 years or older, by age group, United States, 2007



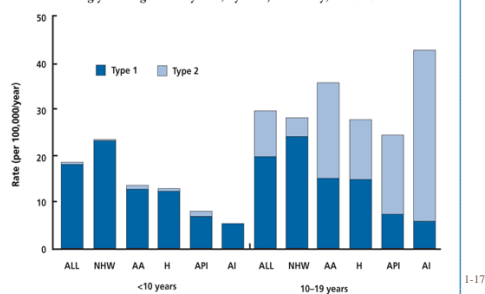
A total of 1.6 million new cases of diabetes were diagnosed in people aged 20 years or older in 2007.

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## U.S. Prevalence of Diagnosed Diabetes

21

Rate of new cases of type 1 and type 2 diabetes among youth aged < 20 years, by race/ethnicity, 2002-2003



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## The Problem <sup>3</sup>

22

- The geographic variation of Type 1 DM
  - ✓ Scandinavia has the highest rate of type 1 DM (in Finland, incidence is 35/100,000 per year).
  - ✓ The Pacific Rim has a much lower rate (in Japan and China, incidence is 1 to 3/100,000 per year) of type 1 DM
  - ✓ Northern Europe and the United States share an intermediate rate (8 to 17/100,000 per year).
  - ✓ Much of the increased risk of type 1 DM is believed to reflect the frequency of high-risk HLA alleles among ethnic groups in different geographic locations..."

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## The Problem <sup>4</sup>

23

- The geographic variation of Type 2 DM
  - "...highest in certain Pacific islands,
  - "...intermediate in countries such as India and the United States,
  - "...relatively low in Russia and China.
- This variability is likely due to both genetic and environmental factors.
- There is also considerable variation in DM prevalence among different ethnic populations within a given country..."

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## The Problem

24

- The Baltimore Eye Study
  - ✓ The prevalence of visual impairment was 2.7% in whites and 3.3% in blacks
  - ✓ The age-adjusted relative prevalence (B/W) was 1.75 (P = 0.01).
  - ✓ The leading causes of visual impaired eyes were cataract (35.8%), age-related macular degeneration (14.2%), diabetic retinopathy (6.6%), glaucoma (4.7%), and other retinal disorders (7.3%).

Source: Rahmani B, Teisich JM, Katz J, Gottsch J, Quigley H, Javitt J, Sommer A. The cause-specific prevalence of visual impairment in an urban population: The Baltimore Eye Survey. *Ophthalmology*. 1996 Nov;103(11):22-6

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#### 4The Problem

25

- The incidence of DM is similar in men and women throughout most age ranges but is slightly greater in men >60 years.
- The prevalence of DM is approximately twofold greater in African Americans, Hispanic Americans, and Native Americans than in non-Hispanic whites, and the onset of type 2 DM occurs, on average, at an earlier age in the former groups than in the non-Hispanic white population..."

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#### The Problem

26

- Los Angeles Latino Eye Study (LALES) 2004, projected that nearly half of all adult Hispanic/Latino individuals in the United States with diabetes have some type of diabetic retinopathy.
- The average age of diagnosis of diabetes are significantly lower among Latinos/Hispanics compared with other population groups.

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#### The Problem – Lim (2008)

27

- UCSF study of nearly 1,073 patients had retinal photographs taken in an "underserved population from a mobile ophthalmology van.
- There were relative equal proportions for each ethnicity studied with any kind of retinopathy
  - ✓ White, 14.0%
  - ✓ African-American, 13.9%
  - ✓ Hispanic, 16.6%
  - ✓ Asian, 16.5%

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#### The Problem (in Latin America <sup>7)</sup>)

28

- "...The incidence of type 1 diabetes in Latin America ranges from 0.4 to 8.3 cases per 100,000 children under 15 years of age...."
- "...and the prevalence of type 2 diabetes ranges from 1.2% to 8%, with higher prevalence rates in urban areas..."
- "...The frequency of diabetes in Latin America is expected to increase by 38% over the next 10 years, compared with an estimated 14% increase in the total population..."

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#### Prevalence of DM 2 (in Asian Indians <sup>8)</sup>)

29

- "...Asian Indians (people from India, Pakistan, and Bangladesh) have remarkably high prevalence of type 2 diabetes compared to Caucasians. However, the incidence of obesity, an important risk factor in the development of type 2 diabetes, is significantly lower in Asian Indians compared to Caucasians...."

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#### Diabetic Retinopathy is Inevitable

30

- Retinopathy of some kind is inevitable, occurring as much as 95% of the patients who have had diabetes for more than 25 years.
- In 40% of the long term diabetics, it leads to significant vision loss.
- It knows no boundaries of ethnicity, social class or geographic limitation.
- Its effects are system wide. The whole body is involved.

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## Diabetes – Laboratory Tests

31

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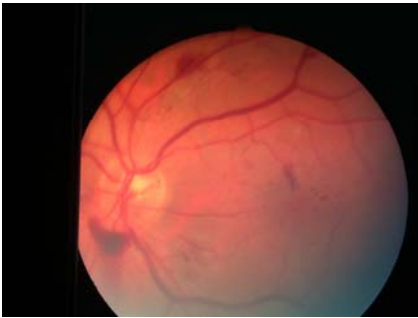
## A Pause – Clinical Tips

32

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## Pre-retinal hemorrhage, What else?

33



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## Measuring Blood Sugar Levels

35

- Fasting Blood Glucose Level – also known as the Fasting Plasma Glucose (FPG)
- Random (non-fasting) Blood Sugar – also known as the casual blood glucose test
- Oral Glucose Tolerance Test– also known as the 2 Hour Post Prandial Test
- Hemoglobin A1c Test – also known as any of the following: Glycosylated hemoglobin test, Hemoglobin A1c, HbA1c, Glycohemoglobin, Glycated hemoglobin

Source: <http://www.nlm.nih.gov/medlineplus/ency/article/000313.htm>

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## Criteria for the Diagnosis of DM

36

Random / Fasting Blood Glucose	
From 70 to 99 mg/dL (3.9 to 5.5 mmol/L)	Normal glucose tolerance
From 100 to 125 mg/dL (5.6 to 6.9 mmol/L)	Impaired fasting glucose (pre-diabetes)
126 mg/dL (7.0 mmol/L) and above on more than one testing occasion	Diabetes

## The HgbA1c Test

37

- Glycosylated hemoglobin or hemoglobin A1c (HgbA1c) is valuable in monitoring diabetics and possibly screening for diabetics
- Glycation is the nonenzymatic addition glucose to hemoglobin called glycation. Formation of glycated hemoglobin is essentially irreversible. Blood levels depends on both the lifespan of the red blood cell (approximately 120 days) and the blood glucose concentration.
- The rate of formation of glycated hemoglobin is directly proportional to the blood glucose concentration of the past 6-8 weeks.

<http://www.compunetlab.com/0601a.pdf>

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## The HgbA1c Test

38

Glycated hemoglobin by the HgbA1c Measurement Method(%)  
Average Blood Glucose Level (mg/dl)

4	60
5	90
6	120
7	150
8	180
9	210
10	240
11	270
12	300
13	330

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## What is wrong with the HgbA1c Test?

39

- First is that the test is only a measure of average blood sugars. Second, elevated blood sugars may take 24 hours to have any long-term effect on HgbA1C, and if blood sugar is elevated for only part of each day and is normalized or too low the rest of the time, your HgbA1C results may appear deceptively low.
- Thus, if your blood sugars are only elevated for a few hours after meals, your HgbA1C may not be affected, but many tissues and organs throughout your body will be injured.

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## What is wrong with the HgbA1c Test?

40

- The other drawback is that the upper and lower ranges of "normal" values reported by most labs are usually erroneously high and low, respectively.
- In other words, the ranges are usually much too wide. Thus, it's up to your physician to decide, based upon his experience, what the proper normal range for his lab should be.

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## What is wrong with the HgbA1c Test?

41

- Many doctors have their own formulas for estimating average four-month blood sugar levels from HgbA1C. A normal value should correspond to blood sugars of about 85–95 mg/dl.
- HbA1c values can vary by 0.4% from laboratory to laboratory
- An individual's rate of glycosylation may be associated with likelihood of developing the microvascular complications associated with diabetes independent of the overall level of glycemic control

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## Some Drugs that cause Antibody Hemolysis = ?A1c

42

Antibody to RH Antigens	Stable Hapten	Unstable Hapten or unknown Mechanism
Cephalosporins	Cephalosporins	Amphotericin B etc.
Diclofenac	Fluorescein	Antazoline
Ibuprofen	Penicillin	Cephalosporins
Interferon $\alpha$	Tetracycline	Chlorpropamide
Levodopa	Tolbutamide	DIABINESE
Methyldopa		Doxepine
Procainamide		Hydrochlorothiazide
Teniposide		INH
Thioridazine		Probenecid
Tolmetin		Rifampin 2009-01-17

## Home measurement of A1c?

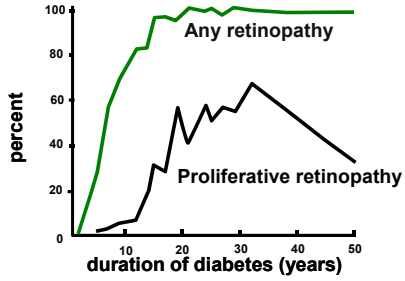
43

- Fox et. Al. reported that A1c values at home may differ as much as a third of the time and off as much as a third of the clinical setting values.
- Repeat measurements done back-to-back are inconsistent.

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## Natural history of Diabetic Retinopathy

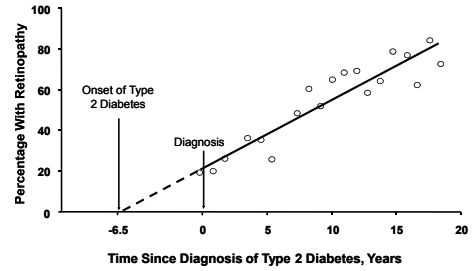
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Klein et al. Diabetes in America  
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## Late Diagnosis of Type 2 Diabetes Prevalence of Retinopathy

46



Klein R et al. Diabetes Care. 1992;15:1875-1891.

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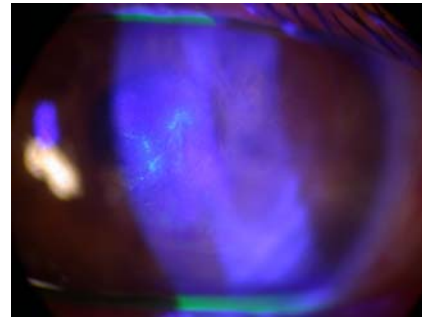
## A Pause – Clinical Tips 2

47

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## Asymptomatic Red eye x 2 weeks.

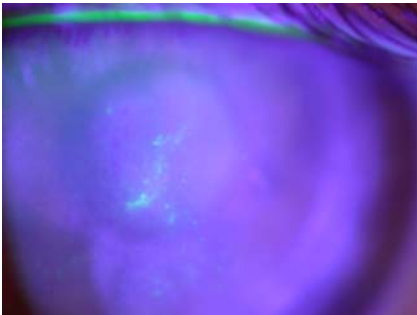
48



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## Why hasn't this gotten better in 3 days?

49



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## Diabetes – Clinical Studies

50

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## Co Morbidities Matter!

51

- Renal Insufficiency/ Chronic Kidney Disease/ Diabetic nephropathy
- Hypertension
- Serum Lipids
- Smoking
- Pregnancy

Studies such as DCCT, WEDS and the UKPDS report that there are significant association between co morbidities and worsening diabetes and retinopathy

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## DCCT: T1DM Findings

52

- Continuous relationship between A1C and microvascular complication rate:
- 10% reduction in A1C → ~35% risk reduction for retinopathy
- 10% reduction in A1C → ~25%-44% risk reduction for nephropathy
- 10% reduction in A1C → ~30% risk reduction for neuropathy
- No adverse QoL or cognitive changes with intensive treatment

\*Diabetes Control and Complications Trial (DCCT) The DCCT is a clinical study conducted from 1983 to 1993 by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The study showed that keeping blood glucose levels as close to normal as possible slows the onset and progression of eye, kidney, and nerve diseases caused by diabetes. In fact, it demonstrated that any sustained lowering of blood glucose helps, even if the person has a history of poor control.

http://diabetes.niddk.nih.gov/dm/pubs/control/what%20is

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## UKPDS: Clinically Significant Findings

53

- Continuous relationship between A1C and microvascular complication rate
- No A1C "threshold" (applies to all A1C levels)
- Lowering BP to 144/82 mm Hg → reduced diabetes-related death, stroke, heart failure, visual loss, microvascular complications
- Continuous relationship with systolic BP (no "threshold")

UK Prospective Diabetes Study was a 20-year trial which recruited 5,102 patients with type 2 diabetes in 23 clinical centres based in England, Northern Ireland and Scotland.

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## Wisconsin Epidemiologic Study

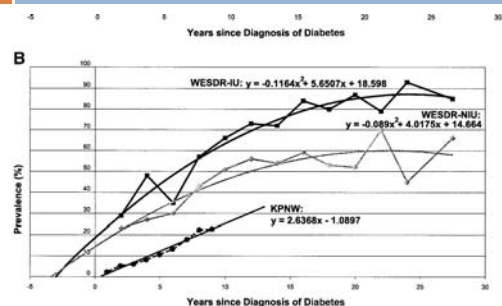
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- Klein et al (1992) suggested that serum lipid levels tend to be higher with diabetics who are non insulin users and who were diagnosed with diabetes later in life
- KPNW (2003)

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## KPNW

56



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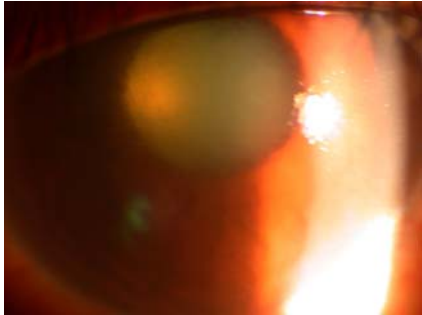
## A Pause – Clinical Tips 3

57

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## Why is this cornea hazy?

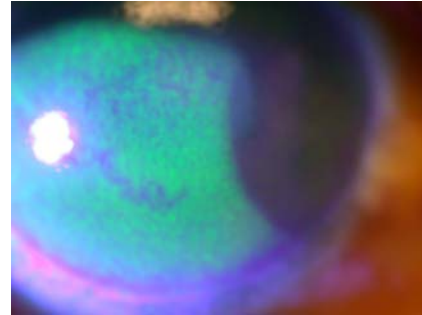
58



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## Why is this cornea hazy?

59



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## CoMorbidity

60

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## Lim, et. al. (2008)

61

### Positive Predictors for Diabetes.

- Weight
- BMI
- Waist Girth
- Hip Girth
- Abdominal and visceral fat.

### Poor Predictors for Diabetes.

1. Skin Folds.
2. Metformin has little effect on Body Fat.

Lim, et. al. Prevalence and Risk Factors of Diabetic Retinopathy in a Multi-Racial Population. Ophthalmic Epidemiology, Nov 2008, 15(6) p.402-409

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## Wong, et. al. (2008)

62

### Independent Risk Factors for Diabetic Retinopathy – A study of 3,261 patients.

- Longer duration of diabetes (1.07)
- Higher A1c (1.21)
- Hypertension (1.85)
- Increased pulse pressure (1.34)
- Older age (1.34)
- Total Cholesterol (0.75, protective? If lowered)

Wong, et. al. Prevalence and Risk Factors for Diabetic Retinopathy: The Singapore Malay Eye Study. Ophthalmology, Nov 2008, 115 (11) p.1869-1875.

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## Hypertension and CVA

63

### Multivariate Analysis of historical demographic factors and CVA

	Odds ratio	95% confidence interval
Age (per year)	1.036	1.023–1.049
Hypertension	2.6	1.9–3.5
Heart disease	4.8	3.3–7.0
Diabetic retinopathy	2.1	1.2–3.5

Sarossian, et. al. Prevalence and Risk Factors for Cerebrovascular Disease in Community-Dwelling Latinos. Clinical Neurology and Neurosurgery, Dec 2008, 11(12) 955-967

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## Body Fat Distribution

64

### Positive Predictors for Diabetes.

- Weight
- BMI
- Waist Girth
- Hip Girth
- Abdominal and visceral fat.

### Poor Predictors for Diabetes.

1. Skin Folds.
2. Metformin has little effect on Body Fat.

Fujimoto, W.Y. and et. Al. Body Size and Shape Changes and the Risk of Diabetes in The Diabetes Prevention Program. Diabetes. Vol. 56 June 2007

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## Kidney Function and Diabetes

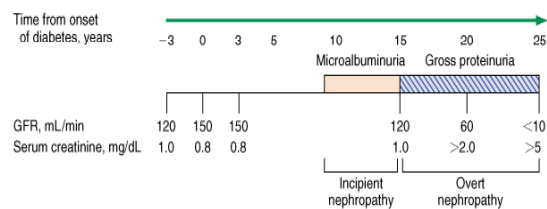
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## Renal Function

66

The relationship of time from onset of diabetes, the glomerular filtration rate (GFR), and the serum creatinine are shown.



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## Chronic Renal Disease

69

### Stages of Chronic Renal Disease CRD

Stage	Description	GFR, mL/min per 1.73 m <sup>2</sup>
At increased risk		90 (with CRD risk)
1	Kidney damage with normal or increased GFR	90
2	Kidney damage with mildly decreased	60–89
3	Moderately decreased GFR	30–59
4	Severely decreased GFR	15–29
5	Renal failure	<15 (or dialysis)

Source: [http://www.merckmedicus.com/pp/us/hcp/frame\\_textbooks.jsp?pg=http://www.accessmedicine.com/resourceTOC.aspx?resourceID=4](http://www.merckmedicus.com/pp/us/hcp/frame_textbooks.jsp?pg=http://www.accessmedicine.com/resourceTOC.aspx?resourceID=4) 2009-01-17

## Laboratory Study – Blood Urea Nitrogen

70

- A blood urea nitrogen (BUN) test measures the amount of nitrogen in your blood that comes from the waste product urea.
- Urea is a waste product formed when protein is broken down in your body. Urea is produced in the liver and eliminated from your body in urine.
- A blood urea nitrogen (BUN) test measures the amount of urea in your blood.

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## Laboratory Study of Renal Function

71

- An assessment of the BUN is used as a gross index of glomerular function.
- Because the BUN is affected by the patient's hydration status, it is a less sensitive indicator of declining renal function than a creatinine clearance test.
- A BUN of over 100 mg/dl is a panic value.

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## Laboratory Study of Renal Function

72

- Creatinine is a protein produced by muscle and released into the blood.
- The amount produced is relatively stable in a given person.
- The creatinine level in the serum is therefore determined by the rate it is being removed, which is roughly a measure of kidney function.
- If kidney function falls (say a kidney is removed to donate to a relative), the creatinine level will rise.
- Normal is about 1 for an average adult. Infants that have little muscle will have lower normal levels (0.2). Muscle bound weight lifters may have a higher normal creatinine.

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## Laboratory Study of Renal Function

73

- Serum creatinine only reflects renal function in a steady state.
- After removing a kidney, if the donor's blood is checked right away the serum creatinine will still be 1. In the next day the creatinine will rise to a new steady state (usually about 1.8). If both kidneys were removed (say for cancer) the creatinine would continue to rise daily until dialysis is begun.
- How fast it rises depends on creatinine production, which is again related to how much muscle one has. A baby may need dialysis when the creatinine reaches 2, whereas a normal adult may be able to hold off until 10, or higher

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## Blood Glucose Control and Diabetic Nephropathy

74

- "...the risk of a rapid decline of glomerular function abruptly increases when glycated hemoglobin is steadily higher than 7.5% and postprandial blood glucose is >200 mg/dl...."
- "...One word of caveat, however, needs to be raised concerning one of the results of the ALLHAT study: the higher risk of developing new-onset diabetes among hypertensive patients who are not treated with lisinopril..."

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## Retinopathy and nephropathy - Agardh (1997) –

75

- Association between diabetic retinopathy and nephropathy has been established. The relationship between nephropathy and diabetic macular edema or proliferative diabetic retinopathy isn't so clear.

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## Nephropathy and Retinopathy

76

- In conclusion, the incidence and progression of diabetic retinopathy and the progression of nephropathy at early stages are clearly associated with long-term glycaemic control.
- However, the incidence and progression of retinopathy and the progression of nephropathy at later stages are also associated with the long-term blood pressure levels, indicating that tight blood glucose control is not enough to prevent the development of these late diabetic complications, but has to be complemented with other therapeutic strategies, such as antihypertensive treatment.

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## CKD and Retinopathy (Bain, 2008)

77

- Relative incidence of retinopathy in patients with CKD per 1000 person - years
  - ✓ A1c ≤ 6.0, 15.11
  - ✓ A1c 6-7, 17.87
  - ✓ A1c 7-8, 29.78
  - ✓ A1c > 8, 35.51

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## Proteinuria and Retinopathy

78

- Strong association between the two complications
- Proteinuria or microalbuminuria predict proliferative retinopathy
- Possible mechanism include hypertension and increased plasma fibrinogen

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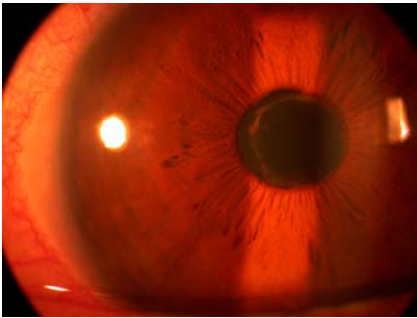
## A Pause – Clinical Tips 4

79

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## Why do we need Atropine sometimes

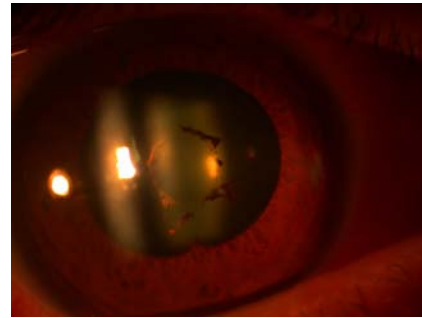
80



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## Why atropine is so good

81



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## ACE Inhibitors and Angiotensin Antagonists

82

- By the mid-1980's, ACE inhibitors were found to be superior to other antihypertensive medications in protecting the kidney from damage.
- "...Patients with type 1 or type 2 diabetes and microalbuminuria should be treated early with ACE inhibitors because these drugs can prevent, or at least delay, the occurrence of overt nephropathy..."

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## ACE Inhibitors and Angiotensin Antagonists

83

- The main common action of ACE inhibitors and AT1 antagonists is the reduction of the stimulation of the AT1 receptor by its ligand angiotensin II (AngII) (Figure 1).
- ACE inhibitors achieve this effect by blocking ACE, thus limiting the amount of AngII available for binding to the AT1 receptor, whereas AT1 antagonists directly inhibit the binding of AngII to AT1

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## Pregnancy and Retinopathy

84

- Of those without retinopathy, 12% develop during pregnancy
- Of those with retinopathy, 47% develop increased NPDR and 5% PDR during pregnancy.
- PDR can progress in pregnancy and require laser treatment.

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## Rema, et. al. (2006)

85

Lipid Parameter	T2DM w/o DR	Mild NPDR	Moderate NPDR	Severe NPDR	PDR
Serum Cholesterol	201	201	201	212	216
Serum Triglycerides	150	185	177	141	132

Source: M. Rema et. Al. (2006)- Association of Serum Lipids with Diabetic Retinopathy in urban Southern Indians – the Chennai Urban Eye Epidemiology Study (CURES) Eye Study – 2, Diabetic Medicine, Sep2006, Vol. 23 Issue 9, p1029-1036, 8p

## Serum Lipids and the Risk of Macular Edema

86

- "There was a twofold increased risk of CSME in the highest versus lowest quintile of LDL cholesterol
- "...a fourfold increased risk of CSME in the highest versus lowest quintile of total-to-HDL cholesterol ratio.
- "...the risk of hard exudate increased more than twofold for subjects in the highest quintile of total cholesterol, LDL cholesterol, or total-to-HDL cholesterol ratio and more than threefold for subjects in the highest quintile of triglycerides. other risk factors.

Source: B. Miljanovic et. Al. "A Prospective Study of Serum Lipids and Risk of Diabetic Macular Edema in Type 1 Diabetes" Diabetes 53:2883-2892, 2004

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## Laboratory Study of Serum Lipids – Total Chol/HDL

87

- The total cholesterol to HDL cholesterol ratio is a number that is helpful in predicting atherosclerosis.
- The number is obtained by dividing total cholesterol by HDL cholesterol. (High ratios indicate higher risks of heart attacks, low ratios indicate lower risk).
- The LDL cholesterol to HDL is actually a better measure but the total cholesterol to HDL ratio is much cheaper and easier to obtain.

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## Laboratory Study of Serum Lipids – HDL, LDL, Triglycerides

88

- The HDL cholesterol is a test that measures the amount of high-density lipoprotein (HDL) cholesterol in serum. It is mainly used to assess coronary risk factors
- LDL cholesterol is a lipoprotein that has a much higher proportion of fat to protein than HDL.

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## Serum Lipids and the Risk of Macular Edema

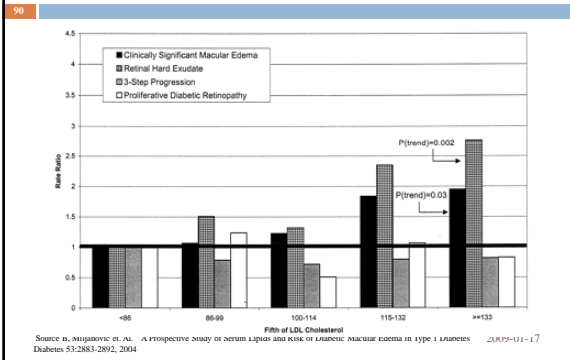
89

- Miljanovic et. Al. (2004) studied 1,441 Diabetes Control and Complications Trial (DCCT) participants to examine the relationship of the cumulative average of lipid levels (total, LDL, and HDL cholesterol, total-to-HDL cholesterol ratio, and triglycerides) with development of CSME, hard exudate, DR progression, and development of proliferative DR (PDR).
- "Both total-to-HDL cholesterol ratio and LDL predicted development of CSME"
- "Higher serum lipids are associated with increased risk of CSME and retinal hard exudate."

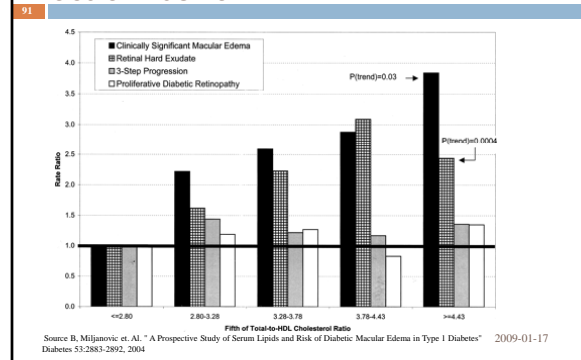
Source: B. Miljanovic et. Al. "A Prospective Study of Serum Lipids and Risk of Diabetic Macular Edema in Type 1 Diabetes" Diabetes 53:2883-2892, 2004

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## Serum Lipids and the Risk of Macular Edema



## Serum Lipids and the Risk of Macular Edema



## Effect of Smoking on Retinopathy

- 92
- Variable effect on retinopathy in clinical studies
  - A critical risk factor for macrovascular disease
  - All people with diabetes should be strongly advised not to smoke
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## Case Studies

- 93
- 2009-01-17

## Necessary elements for Effective Evaluation.

- 94
- Essential Skills; familiarity with....
    - ✓ ...Slit Lamp and at least one fundus lens
    - ✓ ...when does your referral eye surgeon first treat
  - Essential patient environment
    - ✓ A 7 mm pupil from Tropicamide, 1%, and Phenylephrine, 2.5%, 1 drop each eye, repeat after 10 minutes as needed
    - ✓ Light tolerant
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## Necessary elements for Effective Evaluation (con't)

- 95
- Essential Equipment
    - ✓ Slit lamp and binocular indirect ophthalmoscope
    - ✓ Fundus lenses (my favorite, 78D/60D), 14/15D, 20D/2.2x, 90/Superfield/SuperVitreous/Fundus
  - Essential documentation
    - ✓ Divide up the fundus into four quadrants with the center being the fovea.
    - ✓ Standardized notation or terminology.
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## Case Studies – Quick Guide to Risk Assessment

96

- A1c and number of years since first diagnosis
- Presence of hypertension, renal insufficiency and elevated serum lipids
- The number and kind of diabetic medications. Maximum medical therapy is Metformin 1000mg, #1, BID to TID; Avandia ('glitazones) 4mg, once or twice a day; and Glyburide 10mg twice a day.
- 2 risk factors in 4/4 quadrants
- Visual acuity less than 20/40 not explained by other causes.

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## Case Study #1

97

**M.H.** 48 y/o male. DM 2 x 8yr. +high cholesterol, absent left kidney, borderline hypertension

**Meds:** Glyburide, 5mg, 2#, BID; Metformin, 1gm, 1#, BID; Avandia, 4mg, 1#, BID

**PE:** 177#, BP 148/80; Resp 18; pulse 67, T98.6; RBS 254

Total Cholesterol	209 <b>H</b>
Triglycerides	248 <b>H</b>
HgbA1c	9.2 <b>H</b>
Creatinine	1.0
BUN	17
FPG	164

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## Case #1

98

OD

04/04



2009-01-17

## Case #1

99

OS

04/04



2009-01-17

## Case #1

100

OD

07/04



2009-01-17

## Case #1

101

OD

07/04



2009-01-17



## Case #1

OD

102

10/04



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## Case Study #1

103

**WHAT IS YOUR ASSESSMENT?**  
**WHAT IS YOUR MANAGEMENT ?**

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## Case Study #1

104

❑ **WHAT IS YOUR ASSESSMENT?** NPD in the presence of poorly controlled diabetes. Normal renal function

❑ **WHAT IS YOUR MANAGEMENT ?** Return in 3-6 months not for proliferative changes but for the possibility of clinically significant macular edema

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## Case Study #2

105

**I.T.** 64 y/o female. DM 2 x 10yr. +high cholesterol, absent left kidney, borderline hypertension

**Meds:** Glipizide, 10mg, 2#, BID; Metformin, 850mg, 1#, TID; Avandia, 8mg, 1#, QD; Insulin 70/30 5 units, BID

**PE:** 238#, BP 130/80; pulse 88

<b>Total Cholesterol</b>	<b>174</b>
<b>Triglycerides</b>	<b>101</b>
<b>HgbA1c</b>	<b>10.5 H</b>
<b>Creatinine</b>	<b>1.0</b>
<b>BUN</b>	<b>20</b>
<b>FPG</b>	<b>118</b>

2009-01-17

## Case #2

OD

106

04/04



01-17

## Case #2

OS

107

04/04



1-17

## Case #2

OD

108

10/04



09-01-17

## Case #2

OS

109

10/04



09-01-17

## Case Study #2

110

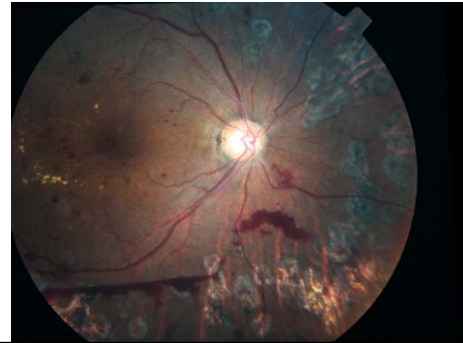
❑ **WHAT IS YOUR ASSESSMENT?** NPDR , moderate (2 risk factors) in the presence of poorly controlled diabetes. Normal renal function, normotensive and normal lipids

❑ **WHAT IS YOUR MANAGEMENT ?** Return in 3-6 months not for proliferative changes but for the possibility of clinically significant macular edema

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## Case 3 - 1000961

111



09-01-17

## Case #3 -1000961

112

❑ 65 y/o F h/o DM, (1 yr) HTN, Allergies, arthralgias

### ❑ Medications

- ✓ Metformin, 500mg, TID
- ✓ Glyburide, 5mg, QD
- ✓ Enalapril, 5mg, QD
- ✓ Neurontin, 100mg, TID
- ✓ Claritin, 10mg, QD
- ✓ Ibuprofen, PRN
- ✓ Amitriptyline, 25-50mg, QHS

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## Case #3 -1000961

113

### ❑ Laboratories

- ✓ BUN 26 Creatinine 0.7
- ✓ TC 205; TG 196; HDL 40, LDL 126;
- ✓ A1c 6.8

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## Case Study #3

114

- ❑ **WHAT IS YOUR ASSESSMENT?** PDR, (1 pre-retinal hemorrhage) in the presence of adequately controlled diabetes, normal renal function, normotensive and normal lipids
- ❑ **WHAT IS YOUR MANAGEMENT ?** Return in 2 months for further proliferative changes that may require additional focal laser.

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## Who are the the PCP's

117

- ❑ The Primary Care Provider/Physician (PCP) – BC Family Practice, Internal Medicine; PA; FNP/NP – The mantra is to maintain the morbidity of the patient.
- ❑ The Specialist – BC Internal Medicine and frequently fellowship trained sub specialist in endocrinology – aggressively manages diabetes when conventional paradigms are no longer effective. Usually intervenes when insulin and oral agents are contemplated.

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## What does an optometrist do in a hospital setting?

118

- ❑ Limited scope practice that is rigidly defined and constrained by ophthalmology.
- ❑ Wider scope practice with responsibilities port of entry for eye problems.
- ❑ Optometric participation are cost effective
- ❑ Success depends not only upon clinical skill but team work with PCP (whether physicians or nurses), understanding the medical model and paradigm of hospital services.

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## The OD and the Treating Physician

119

- ❑ The consultation vs referral.
- ❑ Private vs institutional (hospital practice)
- ❑ The direct or explicit vs indirect or implicit consultation.
- ❑ Medical Panels
- ❑ Medicare

2009-01-17

## The Referral Letter

120

I had the pleasure of seeing Mr/Ms \*\* for a diabetic eye examination today upon your advice/referral. The patient is under your active medical management and denies any problems with his vision His last diabetic eye disease evaluation was about \*yrs/months ago.

The retinal exam was unremarkable with no visible or obvious vascular abnormalities. The retina should be stable for another year and would recommend another evaluation then.

Kind Regards

2009-01-17

## The Referral Letter #2

121

I had the pleasure of seeing Mr/Ms \*\* for a diabetic eye examination today upon your advice/referral. The patient is under your active medical management and reports some recent vision problems.

The retinal exam was noteworthy for mild nonproliferative diabetic retinopathy in either eye but is insufficient for specific surgical intervention at this time. The retinopathy is likely to progress within a year especially if there is chronic hyperglycemia (A1c over 8.0); elevated serum lipids and continuously elevated blood pressures. I would like to see Mr/Ms \* again in one year/3months and will keep you appraised of his/her retinopathy

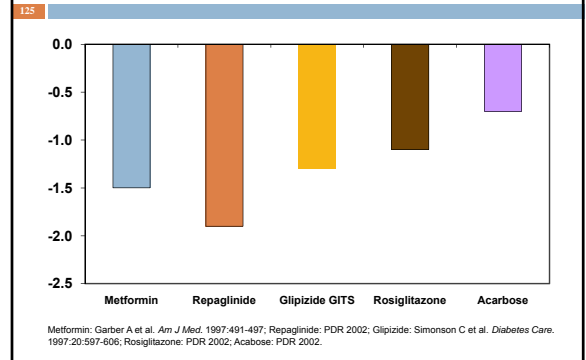
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## OADs: Subclasses

124				
Secretagogues		Sensitizers		Inhibitors
<b>Sulfonyl-ureas</b>	<b>Meglitinides</b>	<b>Biguanides</b>	<b>Thiazolidine-diones</b>	<b>α-glucosidase inhibitors</b>
Glimepiride (Amaryl) Glipizide (Glucotrol) Glipizide-GITS (Glucotrol XL) Glyburide (Micronase, Diabeta) Glyburide micronized (Glynase)	Repaglinide (Prandin) Nateglinide* (Starlix)	Metformin (GlucoPhage)	Pioglitazone (Actos) Rosiglitazone (Avandia)	Acarbose (Precose) Miglitol (Glyset)

\*Nateglinide is not technically a meglitinide.

## A1C: Effects of Various Medications



## Insulin Analogs

- 126
- Produced by recombinant technology
  - Rapid-acting: reduced hexamer formation speeds absorption
    - Aspart (NovoLog®) substitutes AA b28 proline with aspartic acid
    - Lispro (Humalog®) reverses b29 lysine with AA b28 proline
  - Long-acting: crystallization delays subcutaneous absorption
    - Glargine: a21 asparagine replaced with glycine and 2 arginines added at positions b31 and 32

## Insulin Formulations

- 127
- Prandial/supplemental insulin
    - Rapid-acting analogs
      - Insulin Aspart (NovoLog®)
      - Insulin Lispro (Humalog®)
    - Short-acting
      - Regular (soluble)
        - Novolin® R, Humulin® R
  - Basal
    - Intermediate-acting
      - NPH (Neutral Protamine Hagedorn, Isophane)
        - Novolin® N, Humulin® N
      - Lente (Insulin Zinc Suspension)
        - Novolin® L, Humulin® L
    - Long-acting
      - Ultralente (Extended Insulin Zinc Suspension)
      - Insulin Glargine (Analog)