Medications for the Metabolic Syndrome

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Medications for the Metabolic Syndrome

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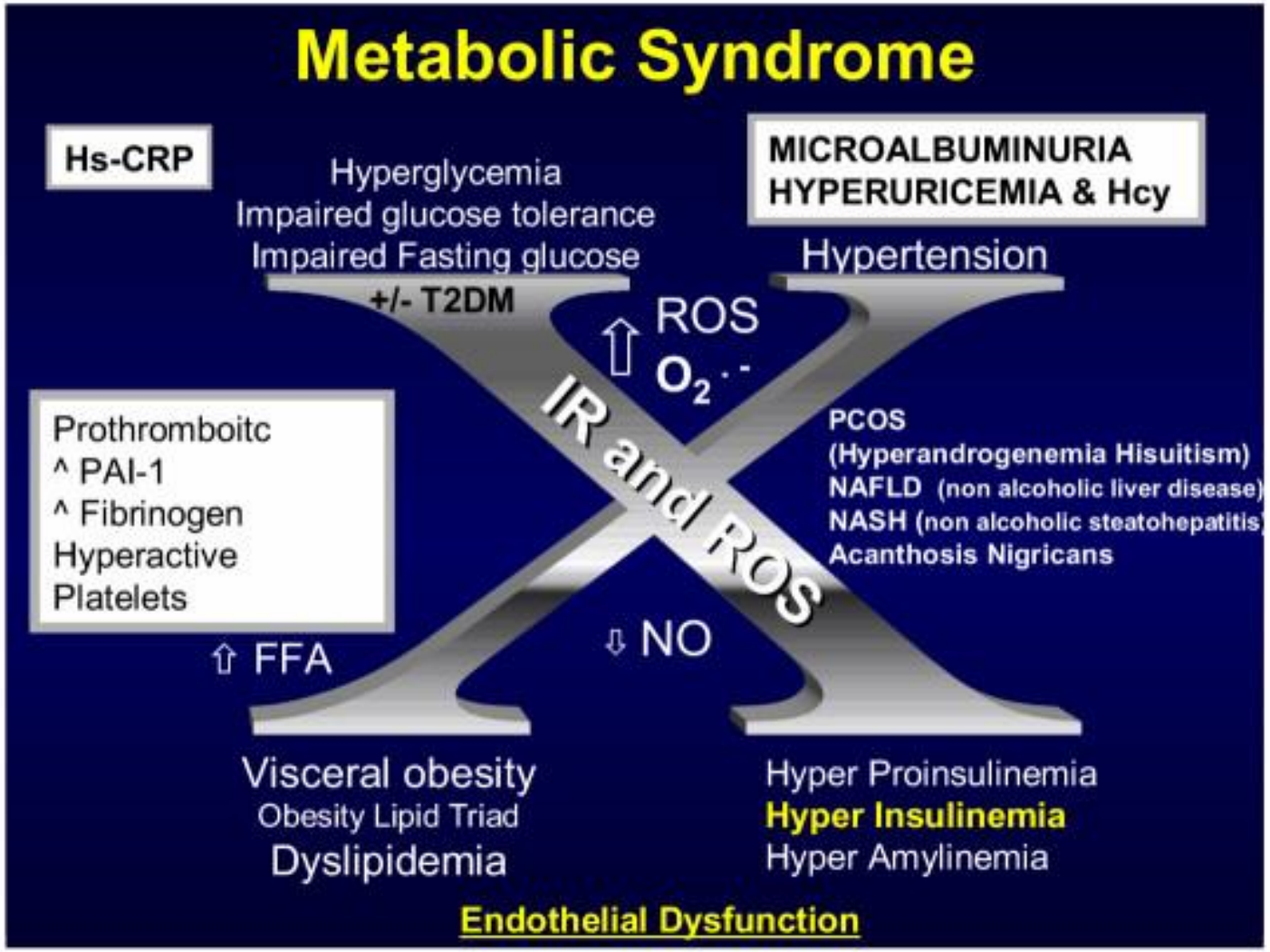
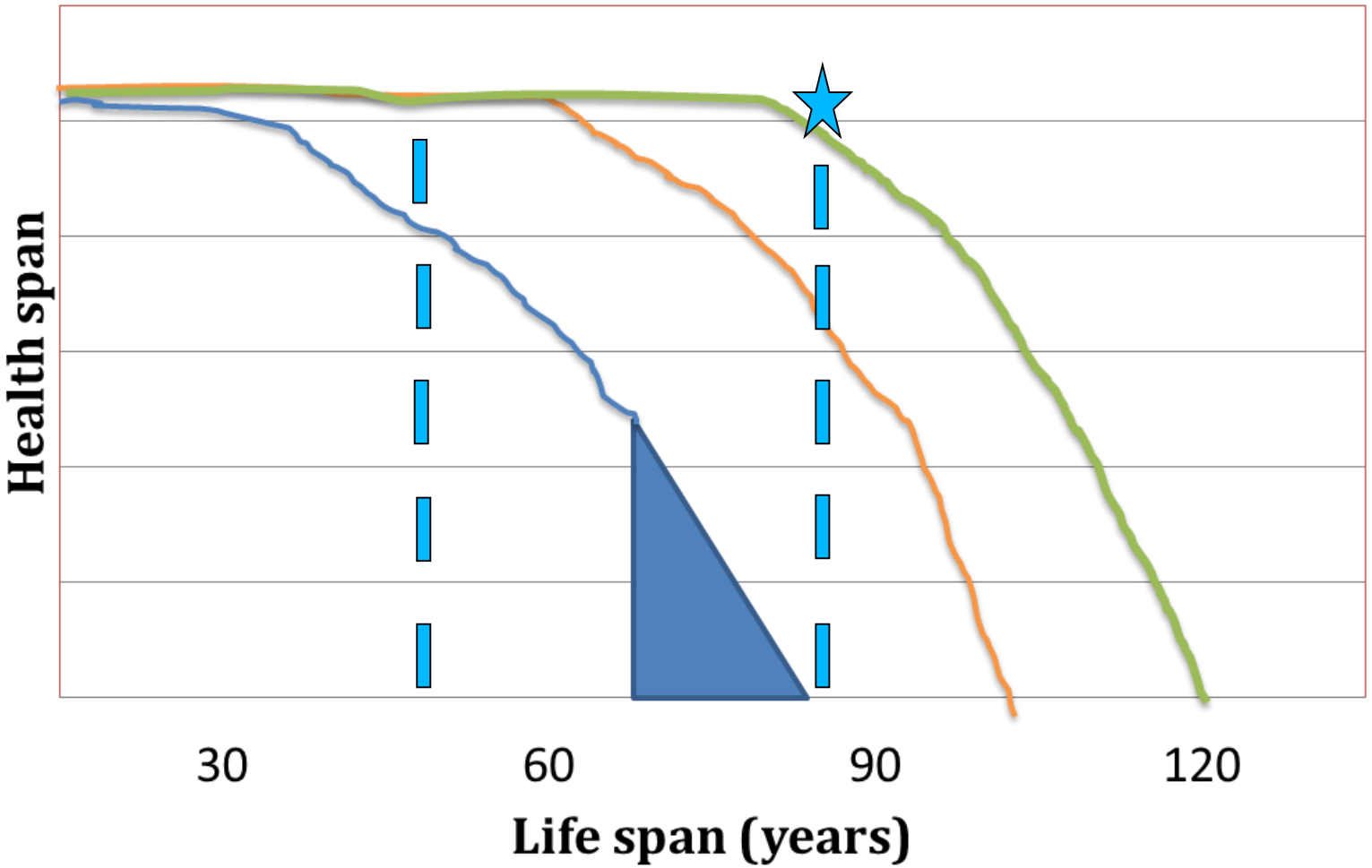


The metabolic syndrome and not obesity is the problem

Longevity – Geriatric Medicine



↑ Heart disease, ↓ Cancer, = NDD, Falls, Pneumonia - Centenarians die from the following

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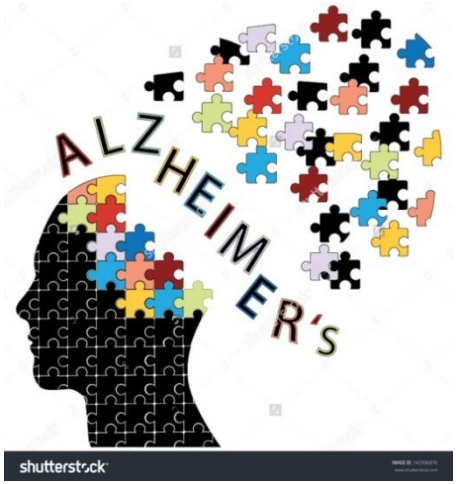
So with this information can we now reverse engineer longevity ?

The systemic manifestations of obesity
Why the eye care professional should be concerned

Heart disease / Cerebrovascular disease

Cancer

Neurodegenerative disease



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Diabetic Types

Type 1 Diabetes is caused by an abnormal auto-immune reaction against the pancreatic cells that produce insulin

This auto-immune reaction leads to destruction of the pancreatic cells therefore, decreased insulin production

Type 2 diabetes accounts for 90% of patients with Diabetes in the US

Part of the "Metabolic Syndrome" or "Syndrome X" -> DM-2, dyslipidemia, obesity, hypertension

Gestational diabetes – 5% of pregnancies in the United States

Can lead to 10 to 12 pound births

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Diabetes in the United States: ADA 2018

Treatable and preventable disease

Diabetes = 34 million individuals (10.5% of US population)

1.5 million = Type 1

32.5 million = Type 2

27 million diagnosed
7 million undiagnosed

Pre-diabetes (HbA1C 5.7%-6.4% or FBS 100-125 mg/dl) **=** 88 million people
(37% of individuals > 20 years old)
(85% of patients with prediabetes don't know that they have it)!

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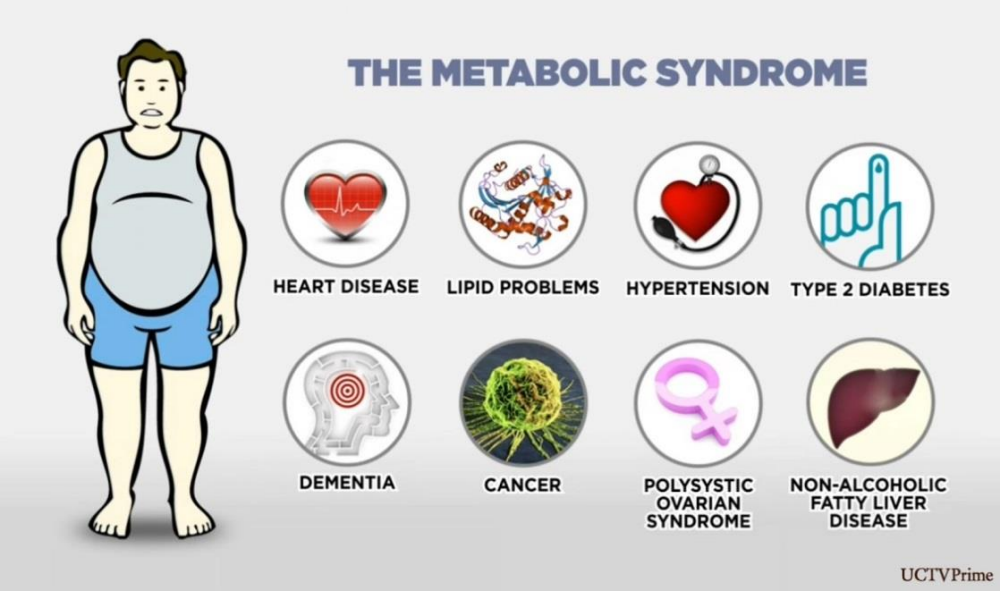
So what is the metabolic Syndrome (syndrome X) ?

- Increased Hb A1C
- Increased blood pressure
- Increased BMI >30

- Low HDL

- Increased triglycerides

Must have 3 of the 5 above



The metabolic syndrome is responsible for 75% of all healthcare dollars in the United States

HDL / Triglyceride ratio should be 2 , example 100 TG/ 50 HDL = 2
150 TG/ 30 HDL = 5 (16% increase of heart heart attack)

Think diabetes in the future !!!!

Total cholesterol, LDL, HDL, Triglyceride, Apo A1, Apo B, Apo B to Apo A ratio, small density LDL and Lp(a)

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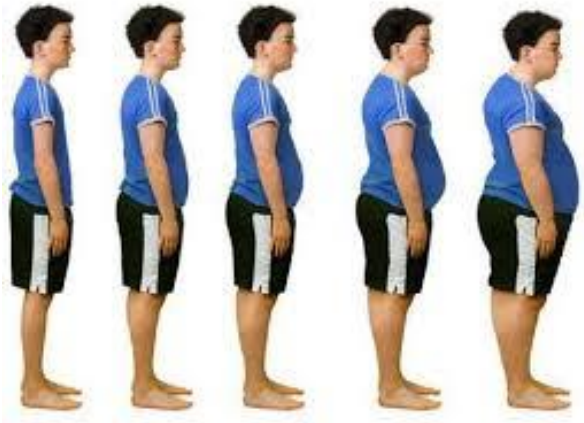
Obesity = BMI (body mass index) > than 30

Visceral vs. Subcutaneous fat

BMI 30 - 35 Type I Obesity

BMI 35 – 40 Type II Obesity

BMI > 40 Extreme Obesity



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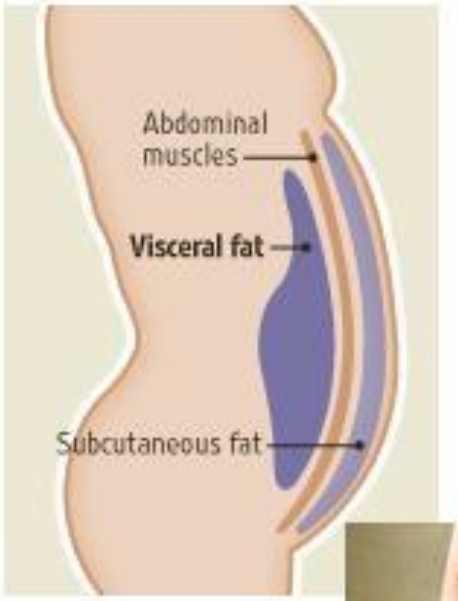
Visceral vs. Subcutaneous Fat = TOFI



Visceral fat increases risk of diabetes, heart disease, dementia and cancer

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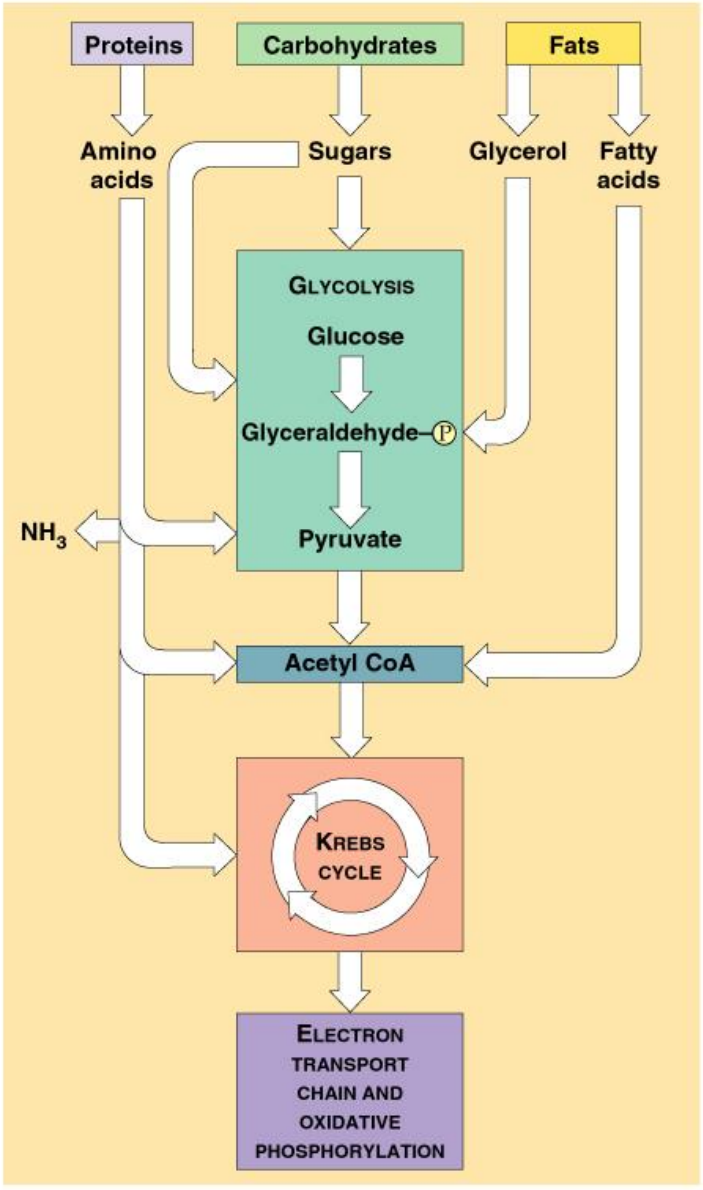
Macronutrients

Glycemic index (GI) assigns a numeric score to a food based on how quickly it makes your blood sugar rise. Foods are ranked on a scale of 0 to 100, with pure glucose (sugar) given a value of 100. The lower a food's glycemic index, the slower blood sugar rises after eating that food. In general, the more cooked or processed a food is, the higher its GI, and the more fiber or fat in a food, the lower its GI.



Glycemic load how much glucose will be delivered. It gives a more accurate picture of a food's real-life impact on blood sugar.

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20 oz bottle a day / year = 25 lb of fat per year

Beer belly = Soda belly

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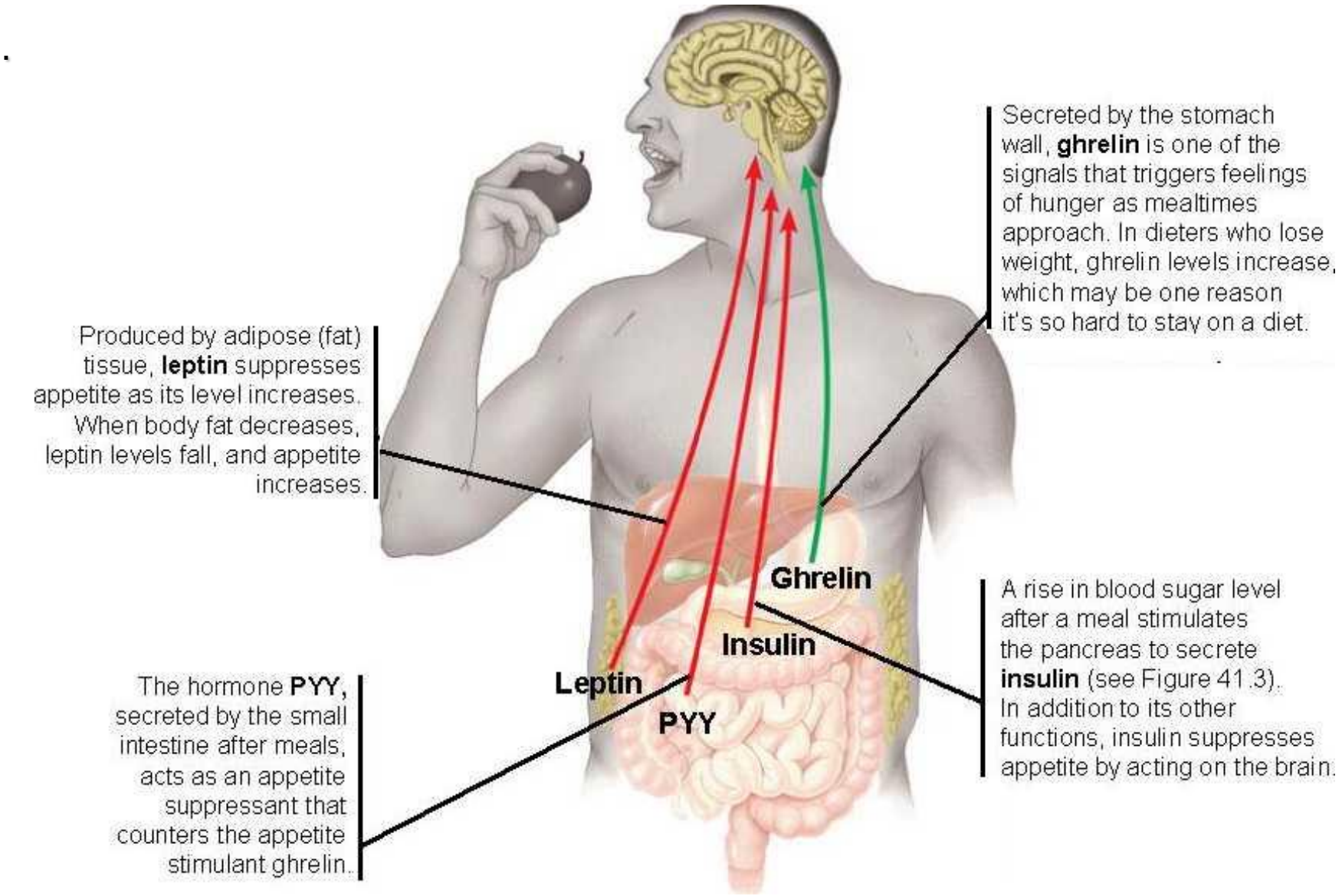

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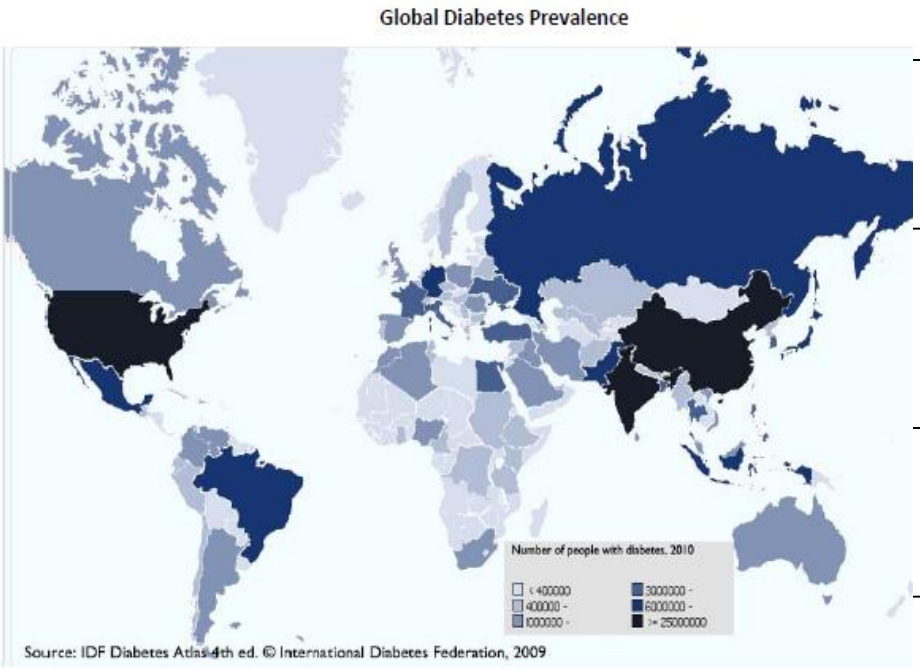
A Global Epidemic……



1 in 3 children born today will develop diabetes in their life

50% of the global diabetes population is undiagnosed

Up to 50% of diabetes is detected because of a clinical complication (e.g. retinopathy, nephropathy)

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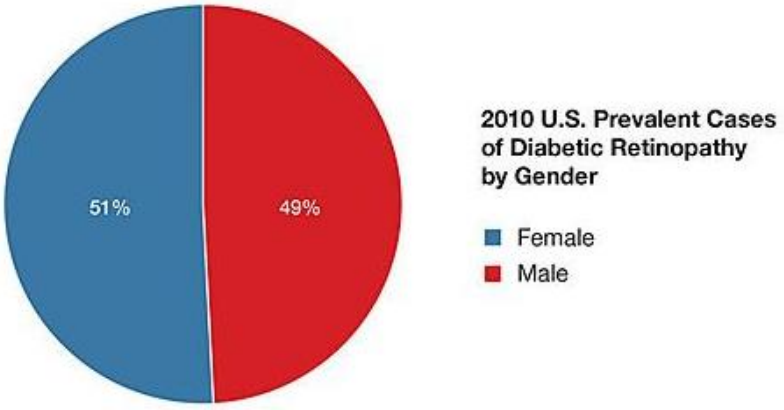
The Prevalence of Diabetic Retinopathy

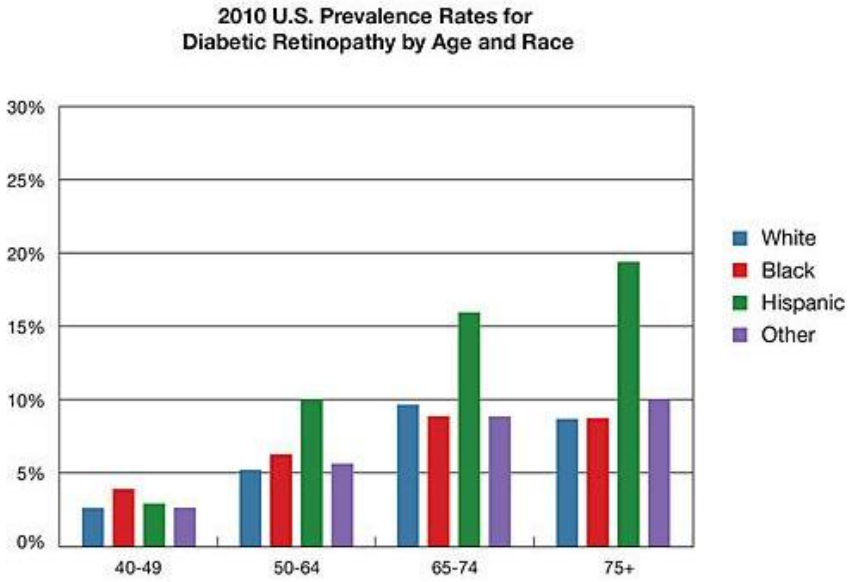
Hispanic population = the highest prevalence rates of DR

African Americans = highest rates of vision threatening DR

No difference between genders were seen in the prevalence of DR

The prevalence of diabetic retinopathy is in older age groups





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Nei.nih.gov

Diabetes and Ocular Manifestations

Early Cataract

Blurred vision

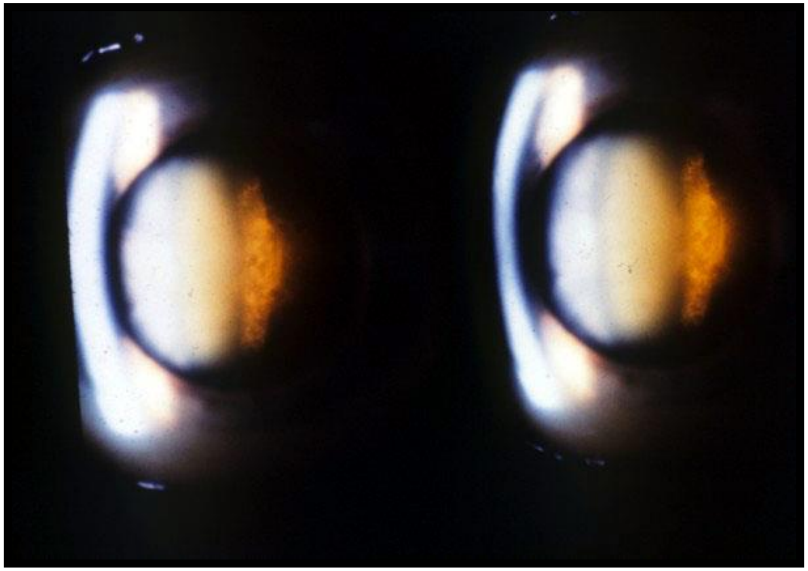
Glaucoma

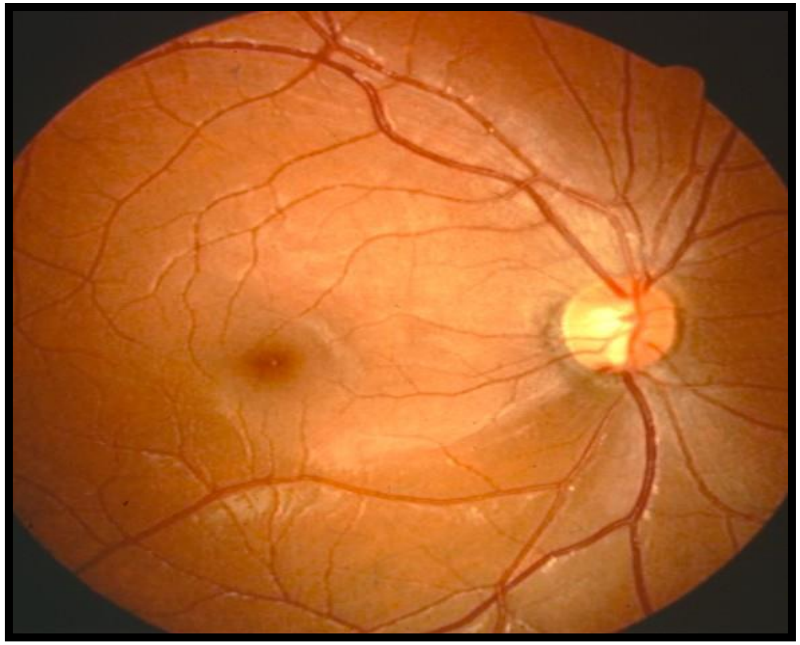
Optic Neuropathies

Retinopathy

Ocular Ischemic Syndrome

CRVO / BRVO





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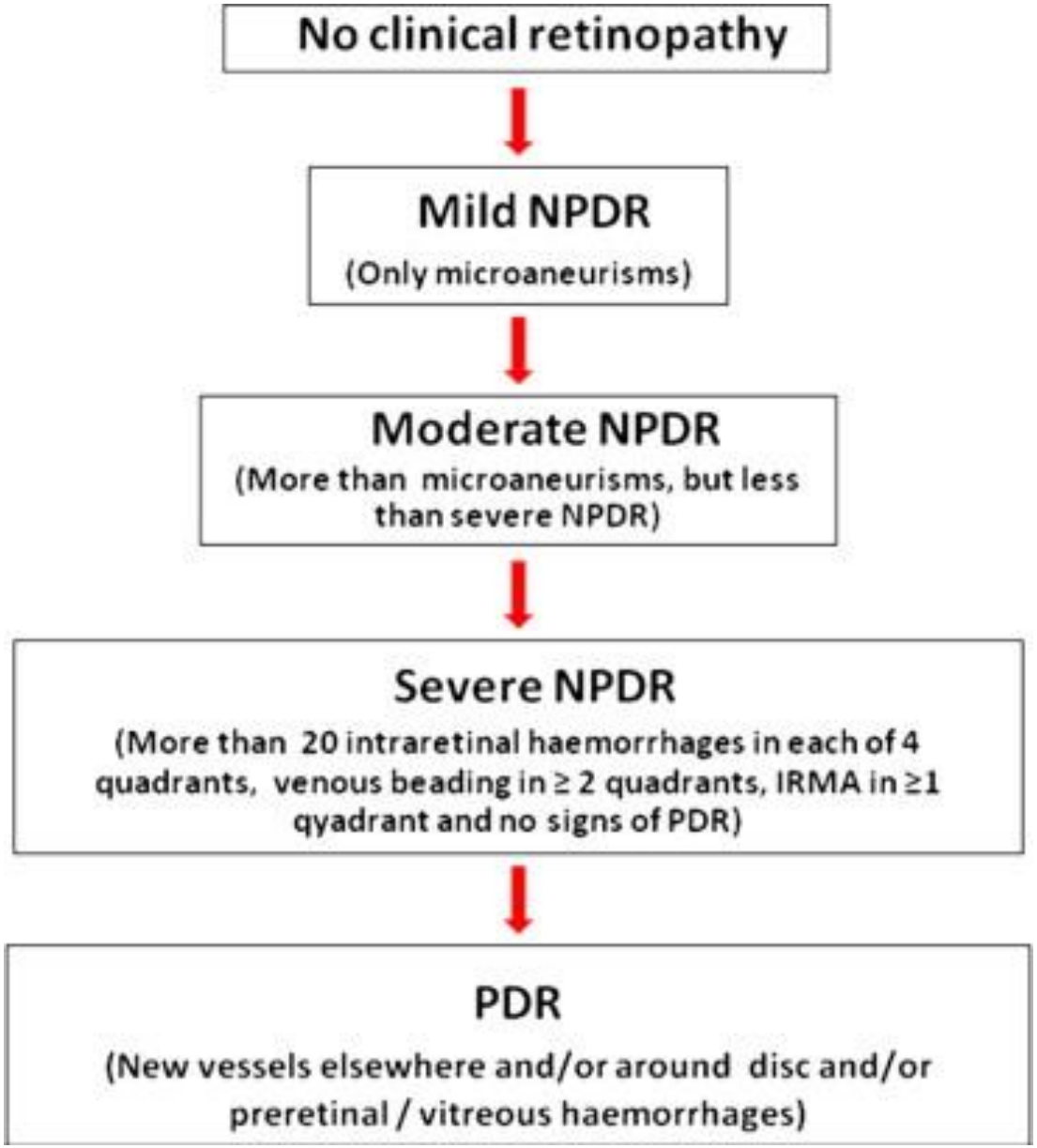

Researchgate.net

Non- Proliferative
Diabetic Retinopathy

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Cotton wool spot, dot and blot hemorrhages and IRMA

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Diabetic Macular Edema

Diabetic Papillopathy

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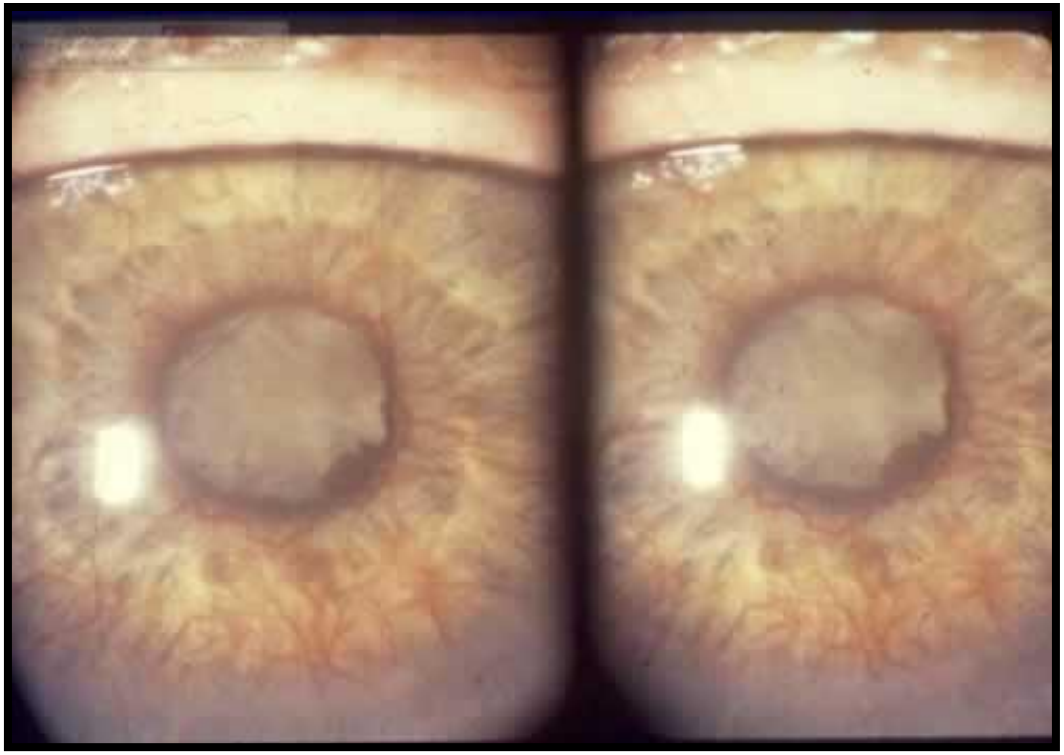

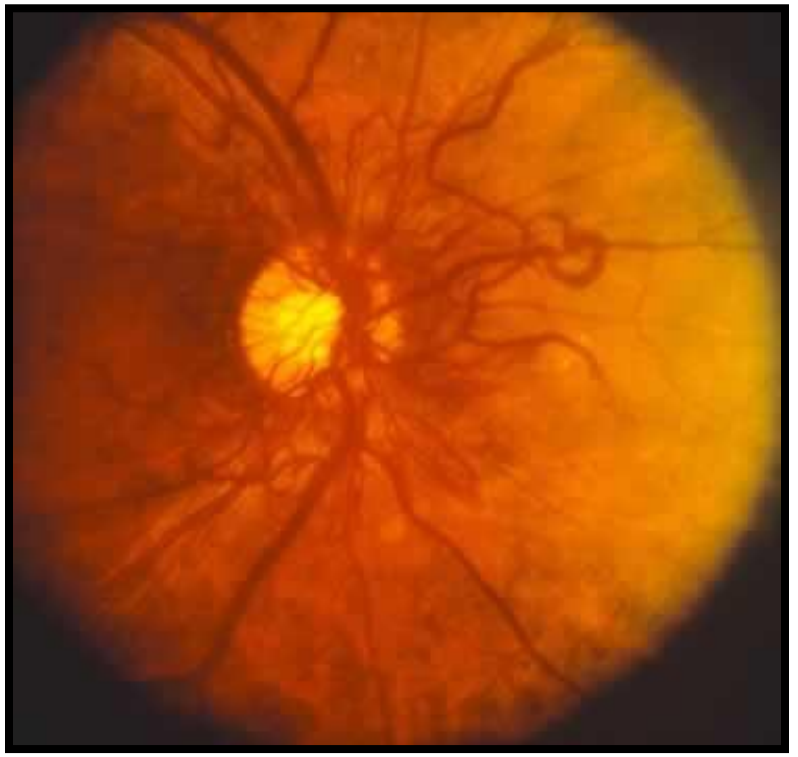

"Proliferative" Diabetic Retinopathy

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"Proliferative" Diabetic Retinopathy

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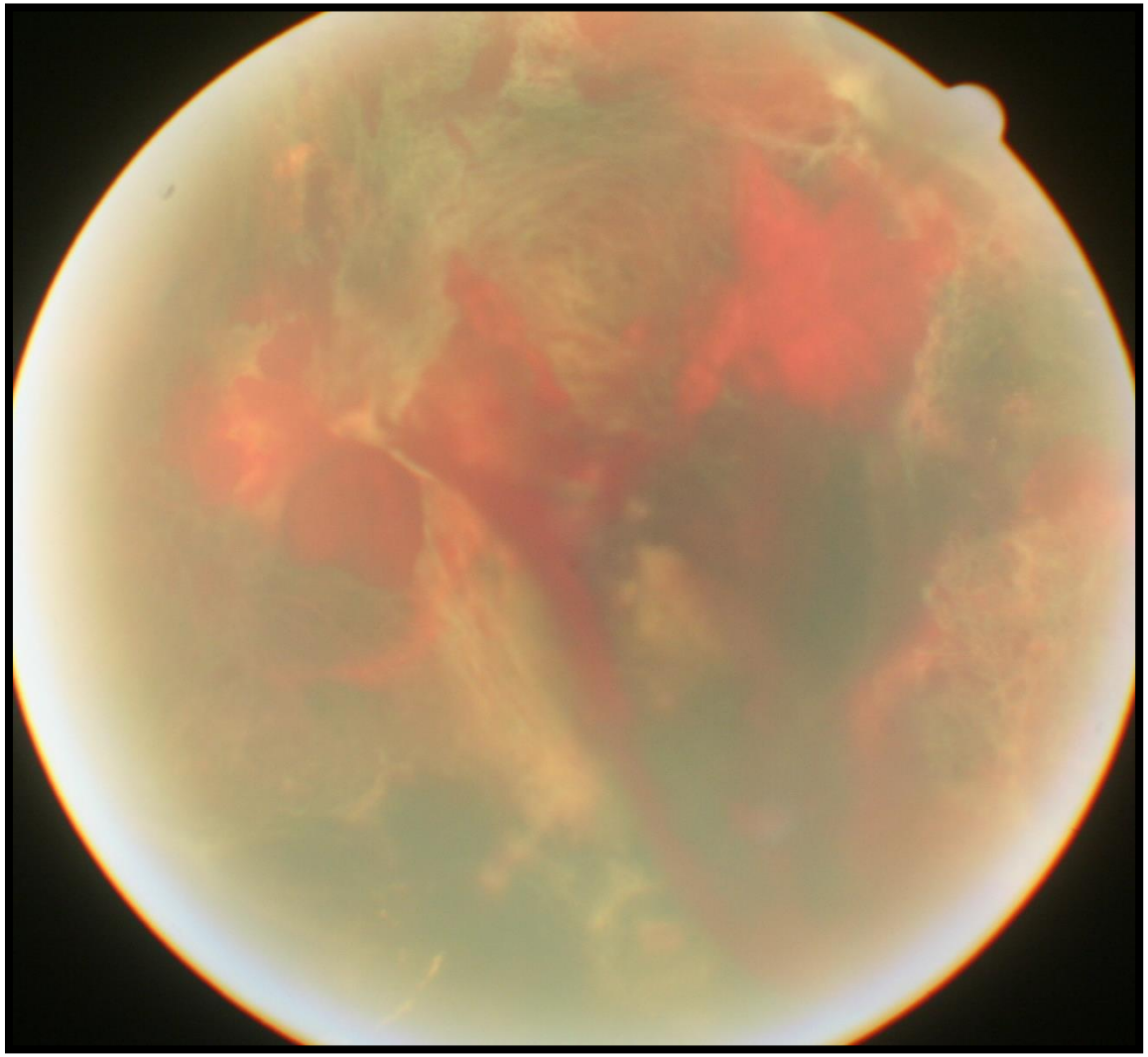

"Proliferative" Diabetic Retinopathy

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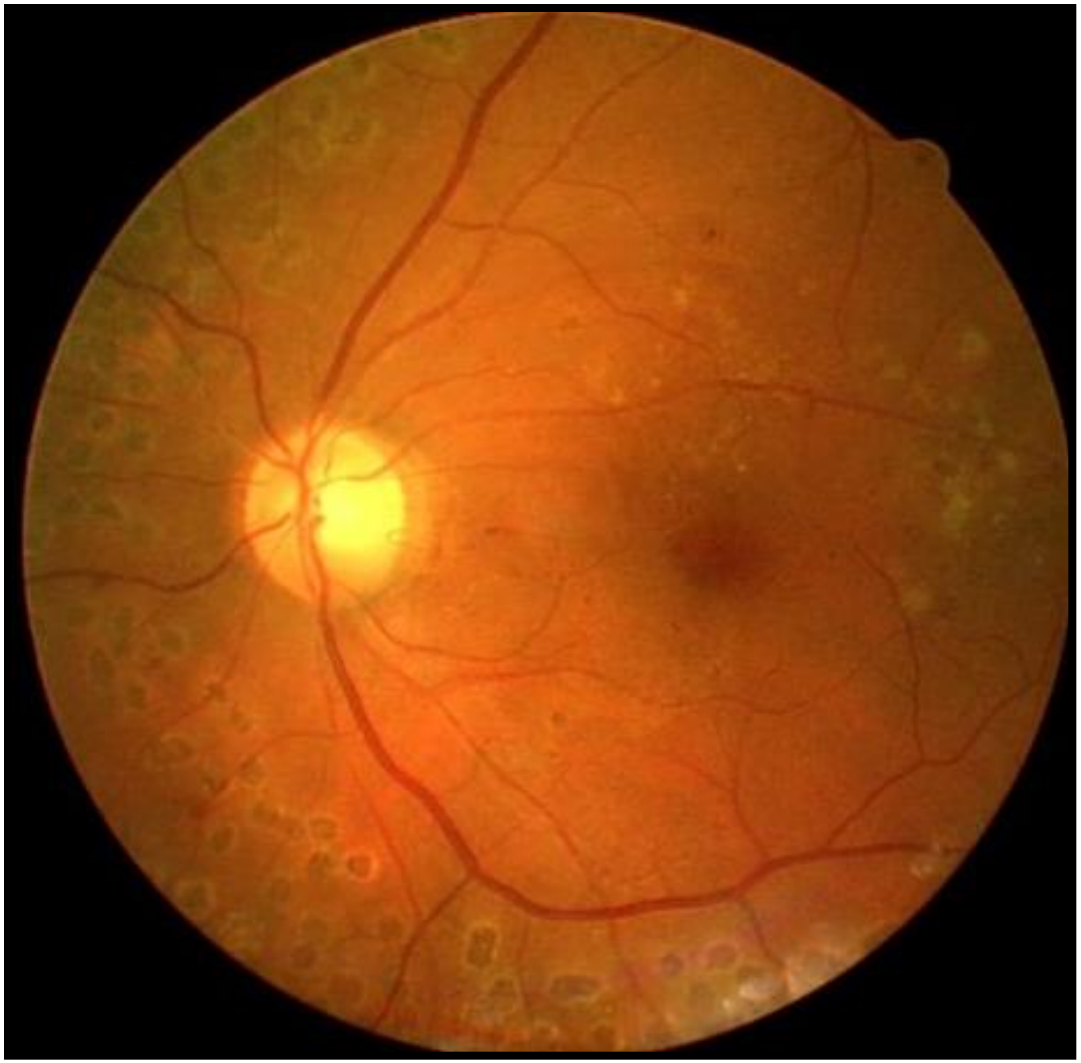

Pan retinal photocoagulation for PDR

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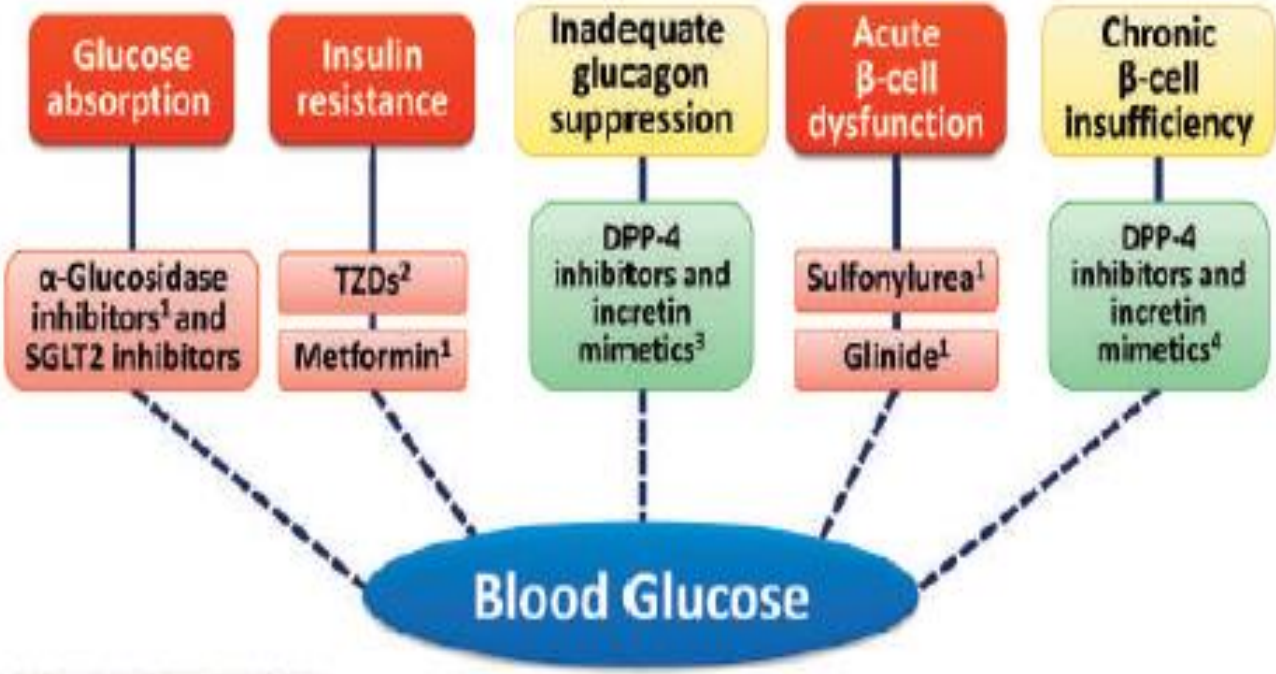
Multiple Treatments Are Needed to Address All Core Defects in T2DM



T2DM = type 2 diabetes mellitus.

1. Inzucchi SE. *JAMA*. 2002;287:360-372. 2. DeFronzo RA. *Br J Diabetes Vasc Dis*. 2003;3(suppl 1):S24-S40.
3. Nauck MA. *Am J Med*. 2011;124(suppl 1):S3-18. 4. Garber AJ. *Diabetes Care*. 2011;34(suppl 2):S258-S263.

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Diabetic medications

Biguanides – these drugs slow glucose production in the liver to lower glucose (metformin)

Sulphonylureas – cause the pancreas to increase production of insulin to lower glucose (glyburide, glipizide, gliclazide, Glimepiride)

Glucosidase inhibitors – block the alpha - glucodidase enzyme in the intestine to control blood – glucose levels (Acarbose, Miglitol)

Thiazolidinediones – activate insulin to lower glucose in the blood(Rosiglitazone, Pioglitazone)

GLP- 1 Receptor Agonist – act on the glucagon-like peptide1 in the small intestine to reduce glucose in the blood (Exenatide, Liraglutide)

DPP-4 Inhibitors – inhibit the dipeptidyl peptidase-4 to block the breakdown of GLP-1 - reduce glucose in the blood (Sitagliptin, Vildagliptin)

SGLT2 Inhibitors – inhibit the subtype 2 sodium-glucose transporter protein from producing glucose (Canaglifozin). Cause the kidneys to remove sugar

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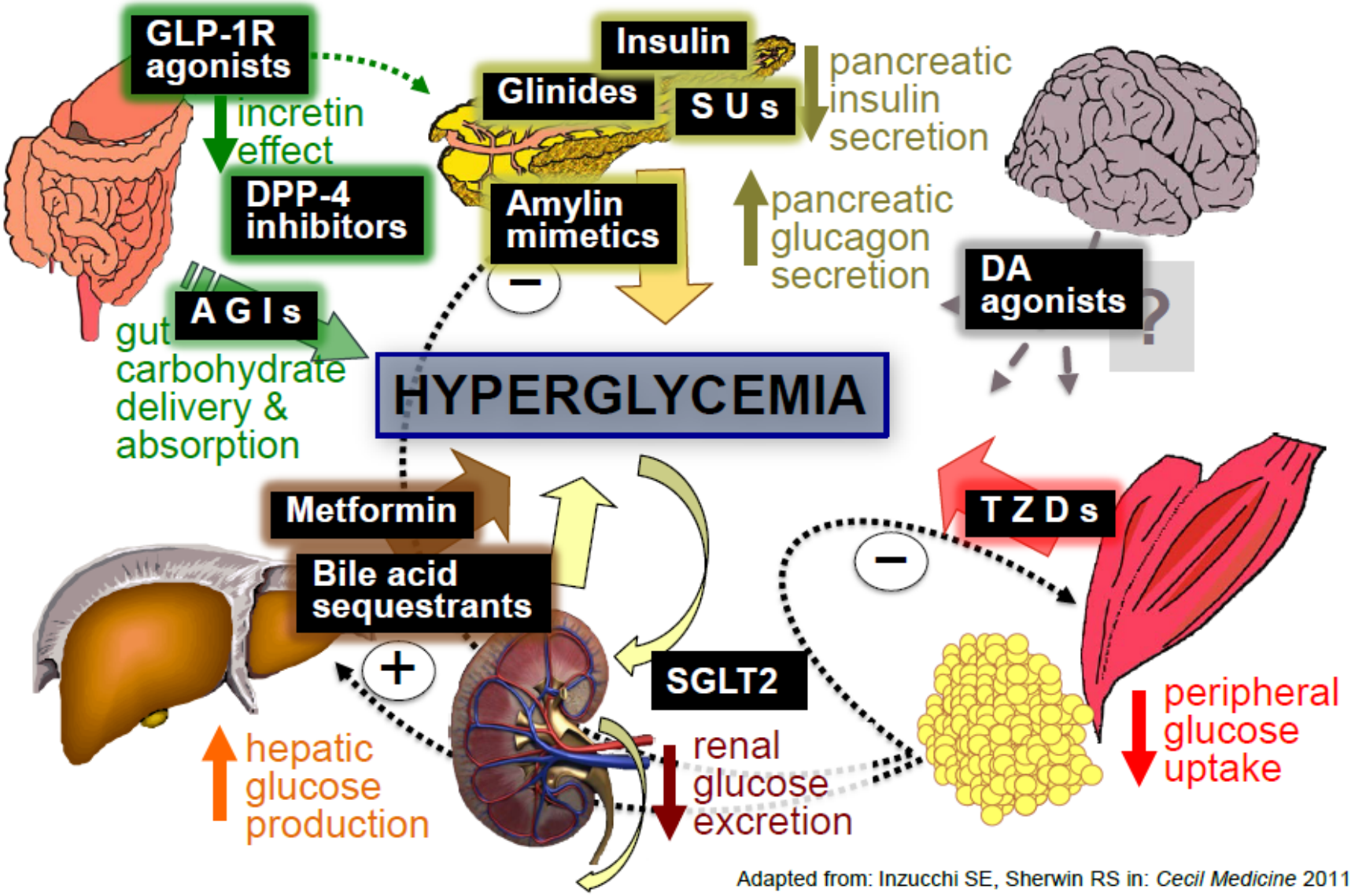

Adapted from: Inzucchi SE, Sherwin RS in: *Cecil Medicine* 2011

Biguanide

Metformin (Glucophage)

- Initial Drug of Choice / Cornerstone of Therapy

- Mechanism of Action (MOA)
  - Inhibits hepatic and renal gluconeogenesis
  - Stimulation of glucose uptake in peripheral tissues
  - Inhibits absorption of glucose from the GI tract
  - Lowers HbA1C about 2% at maximum

Benefits:

Does NOT cause weight gain; weight loss?

Does NOT cause hypoglycemia (kidney/dehydration)

Decreases TC, LDL, and TG; Increases HDL

Decreases risk of macrovascular complications

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Metformin

- Effective in preventing new onset of T2DM
- Side Effects
  - GI disturbances (diarrhea)
  - Lowers vitamin B_{12} levels
  - Lactic acidosis
  - If eGFR is less than 60 then dosage is reduced
  - If eGFR is below 30 then dosage is stopped

Medications for longevity present and future:

- Bannister Study on metformin use
- Metformin in Longevity Study (MILES)
- Taming Aging with Metformin (TAME)

Discovered as a bacteria in the soil on Rapa Nui (Easter Island), the drug **rapamycin** is a leading candidate for the first lifespan-extension drug.

Since 1999, rapamycin has been approved by the U.S. Food and Drug Administration (FDA) as an anti-rejection drug for transplant patients.

Physicians prescribe rapamycin in some cancer chemotherapy treatments. Lifespan-extension researchers, geroscientists are working to realize the drug's potential to increase the number of healthy years in humans.

Sulfonylureas

Agents:

2nd generation agents (preferred)

- glyburide (DiaBeta, Micronase)
- glyburide, micronized (Glynase PresTab)
- **glipizide (Glucotrol, Glucotrol XL)**
- **glimepiride (Amaryl)**

Sulfonylureas

MOA: stimulate release of insulin from functioning pancreatic beta cells

Side effects:

hypoglycemia - higher incidence with glyburide

All can cause hypoglycemia ~ occurs in (40%) of patients

Weight gain

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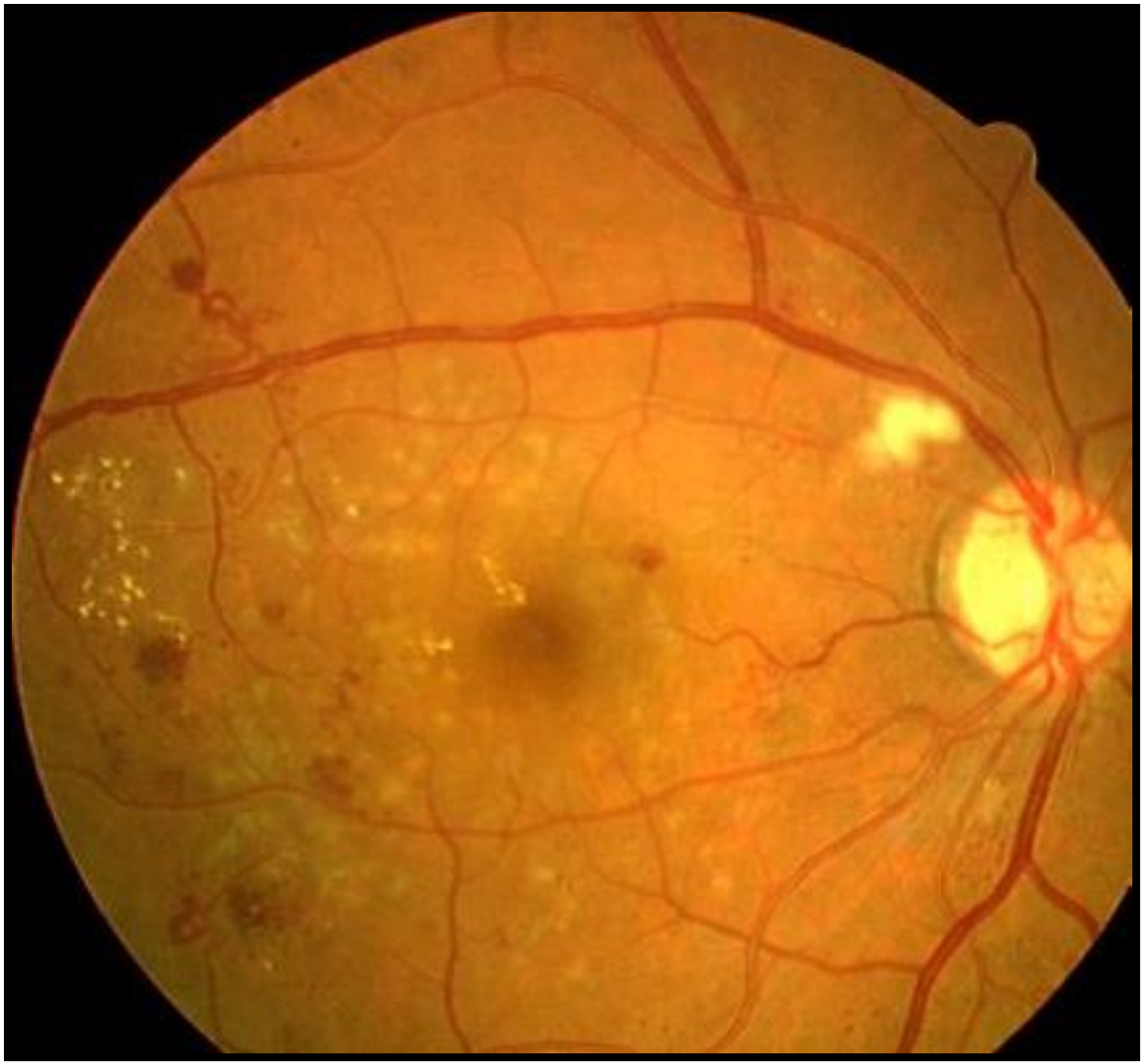

Venous beading, cotton wool spot, lipid hard exudate and IRMA

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Clinically Significant Macular Edema

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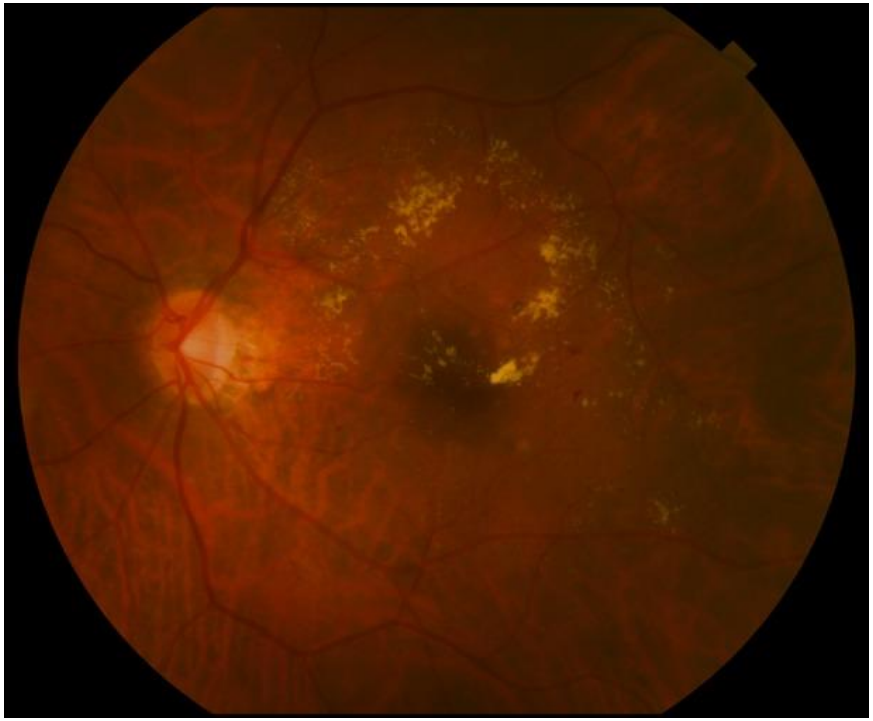
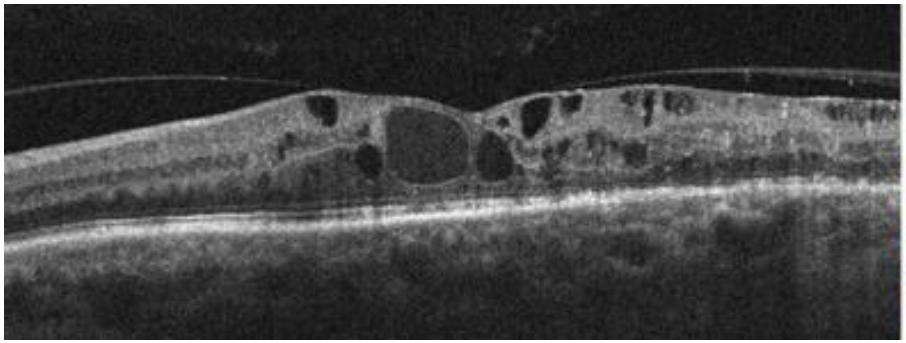
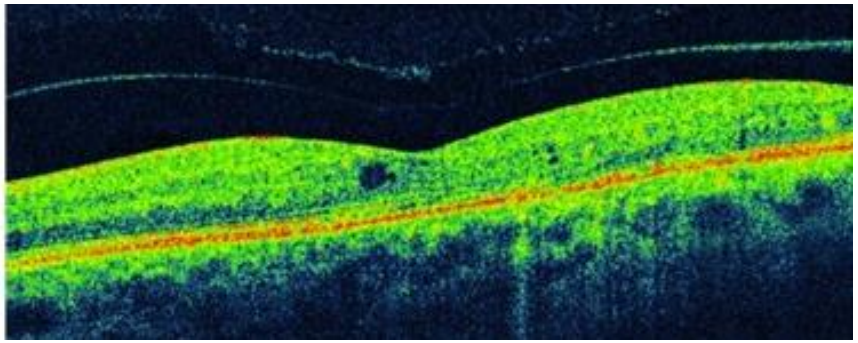


Clinically Significant Macular Edema





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Clinically Significant Macular Edema (ETDRS)

Retinal thickening within 500 µm of the center of the macula

Hard exudates at or within 500 µm of the center of the macula (if associate with retinal thickening of the adjacent retina

Retinal thickening one disc area (1500 µm) or larger, any part which is within one disc diameter of the center of the macula.

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GLP-1 Effects in Humans: Understanding the Glucoregulatory Role of Incretins

PPG control

Promotes satiety and reduces appetite

GLP-1 secreted upon ingestion of food

Pancreatic alpha cells:
↓ Postprandial glucagon secretion

Pancreatic beta cells:
Enhanced glucose dependent insulin secretion

Liver: Reduced hepatic glucose output

Stomach: Helps regulates gastric emptying

Adapted from Flint A, et al. J Clin Invest. 1998;101:515-520.; Adapted from Larsson H, et al. Acta Physiol Scand. 1997;160:413-422.; Adapted from Nauck MA, et al. Diabetologia. 1996;39:1546-1553.; Adapted from Drucker DJ. Diabetes. 1998;47:159-169.

Benefit: weight loss and heart protection

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(GLP-1) Agonists

Exenatide injection (Byetta) –SQ injection right before meal; Long-acting version (once/week) = **Bydureon**

Liraglutide injection (Victoza) – qd SQ injection at any time of the day

Abiglutide (Tanzeum) – once/week

Dulaglutide (Trulicity) – once/week

Ozempic (oral medication)

Mechanism of Action

Stimulate the GLP-1 receptor – this receptor enhances glucose-dependent insulin secretion by the pancreatic beta-cell (in response to high blood glucose levels), suppresses secretion of glucagon after meals, and slows gastric emptying; some appetite suppression and weight loss

Indications And Usage

adjunctive therapy to improve glycemic control in adult patients with type 2 diabetes mellitus who are taking other oral antidiabetic agents

(GLP-1) Agonists

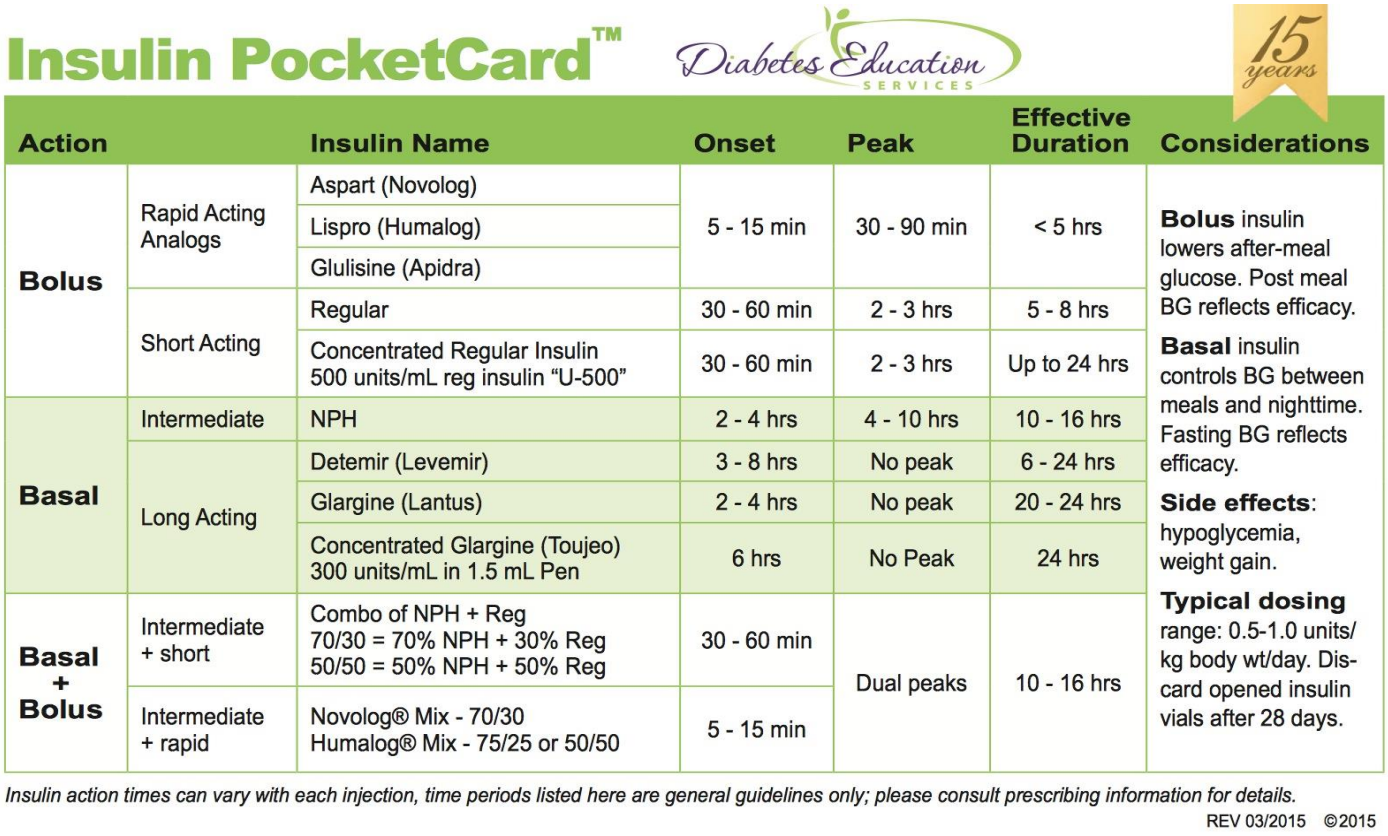
Side Effects:

In animal studies, liraglutide has been shown to cause dose-dependent and treatment duration dependent **thyroid C-cell tumors** (adenomas and/or carcinomas) at clinically relevant exposures.

Pancreatitis

GI upset

Insulin Preparations
http://www.diabetesed.net/page/_files/Insulin-PC-3-2015.pdf



Insulin PocketCard™

Diabetes Education SERVICES

15 years

Action		Insulin Name	Onset	Peak	Effective Duration	Considerations
Bolus	Rapid Acting Analogs	Aspart (Novolog)	5 - 15 min	30 - 90 min	< 5 hrs	**Bolus** insulin lowers after-meal glucose. Post meal BG reflects efficacy. **Basal** insulin controls BG between meals and nighttime. Fasting BG reflects efficacy. **Side effects**: hypoglycemia, weight gain. **Typical dosing** range: 0.5-1.0 units/kg body wt/day. Discard opened insulin vials after 28 days.
		Lispro (Humalog)				
		Glulisine (Apidra)				
	Short Acting	Regular	30 - 60 min	2 - 3 hrs	5 - 8 hrs	
		Concentrated Regular Insulin 500 units/mL reg insulin "U-500"	30 - 60 min	2 - 3 hrs	Up to 24 hrs	
Basal	Intermediate	NPH	2 - 4 hrs	4 - 10 hrs	10 - 16 hrs	
	Long Acting	Detemir (Levemir)	3 - 8 hrs	No peak	6 - 24 hrs	
		Glargine (Lantus)	2 - 4 hrs	No peak	20 - 24 hrs	
		Concentrated Glargine (Toujeo) 300 units/mL in 1.5 mL Pen	6 hrs	No Peak	24 hrs	
Basal + Bolus	Intermediate + short	Combo of NPH + Reg 70/30 = 70% NPH + 30% Reg 50/50 = 50% NPH + 50% Reg	30 - 60 min	Dual peaks	10 - 16 hrs	
	Intermediate + rapid	Novolog® Mix - 70/30 Humalog® Mix - 75/25 or 50/50	5 - 15 min			

Insulin action times can vary with each injection, time periods listed here are general guidelines only; please consult prescribing information for details.

REV 03/2015 ©2015

3 x day

1 day at HS

2.5% reduction in the HbA1C

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Insulin Preparations

Drug therapy of choice for all patients with type 1 DM and those with type 2 DM who cannot control their condition with diet, exercise.

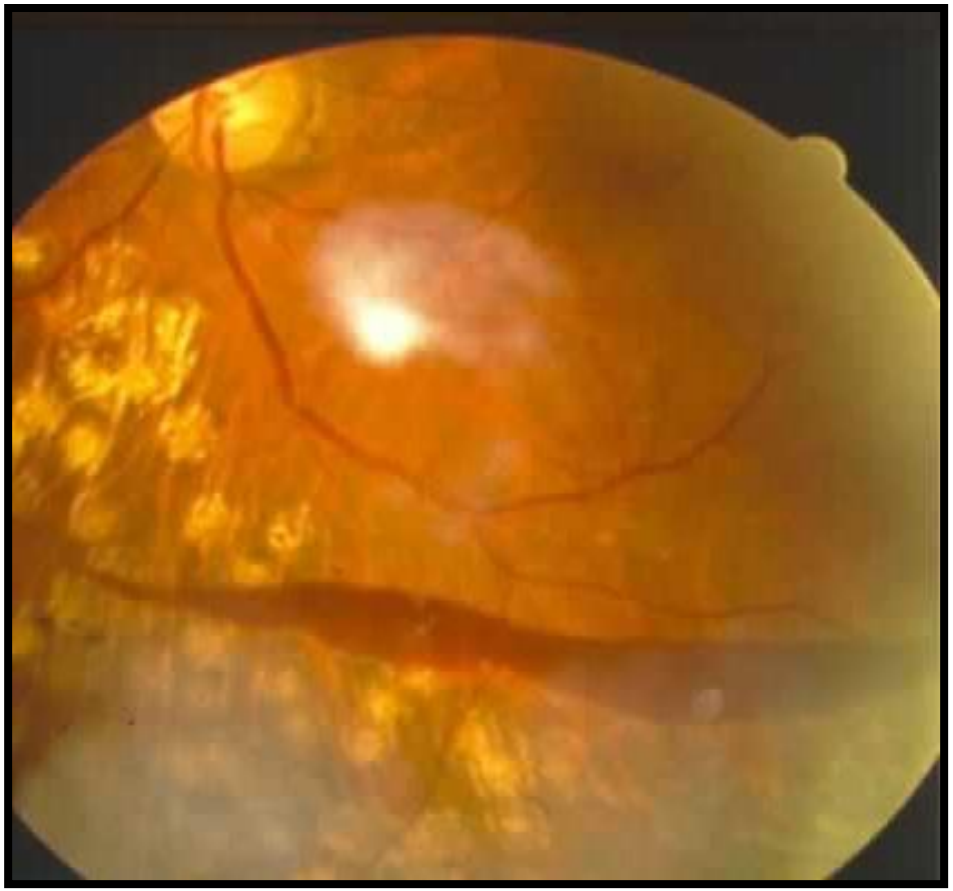
MOA: regulates glucose metabolism in the muscle and other tissues

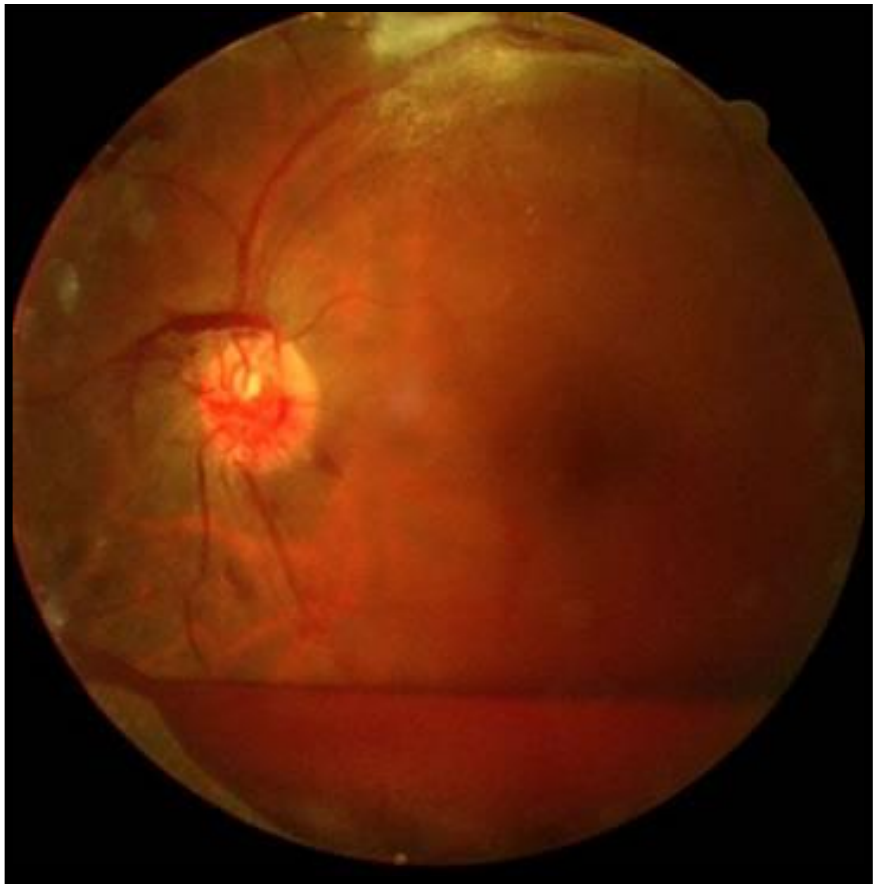
Semisynthetic (“human”) – identical amino acid composition to endogenous human insulin

Side effects: weight gain and hypoglycemia

“Proliferative” Diabetic Retinopathy

Preretinal hemorrhages





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Proliferative Diabetic Retinopathy

Hb A1C = 13 %

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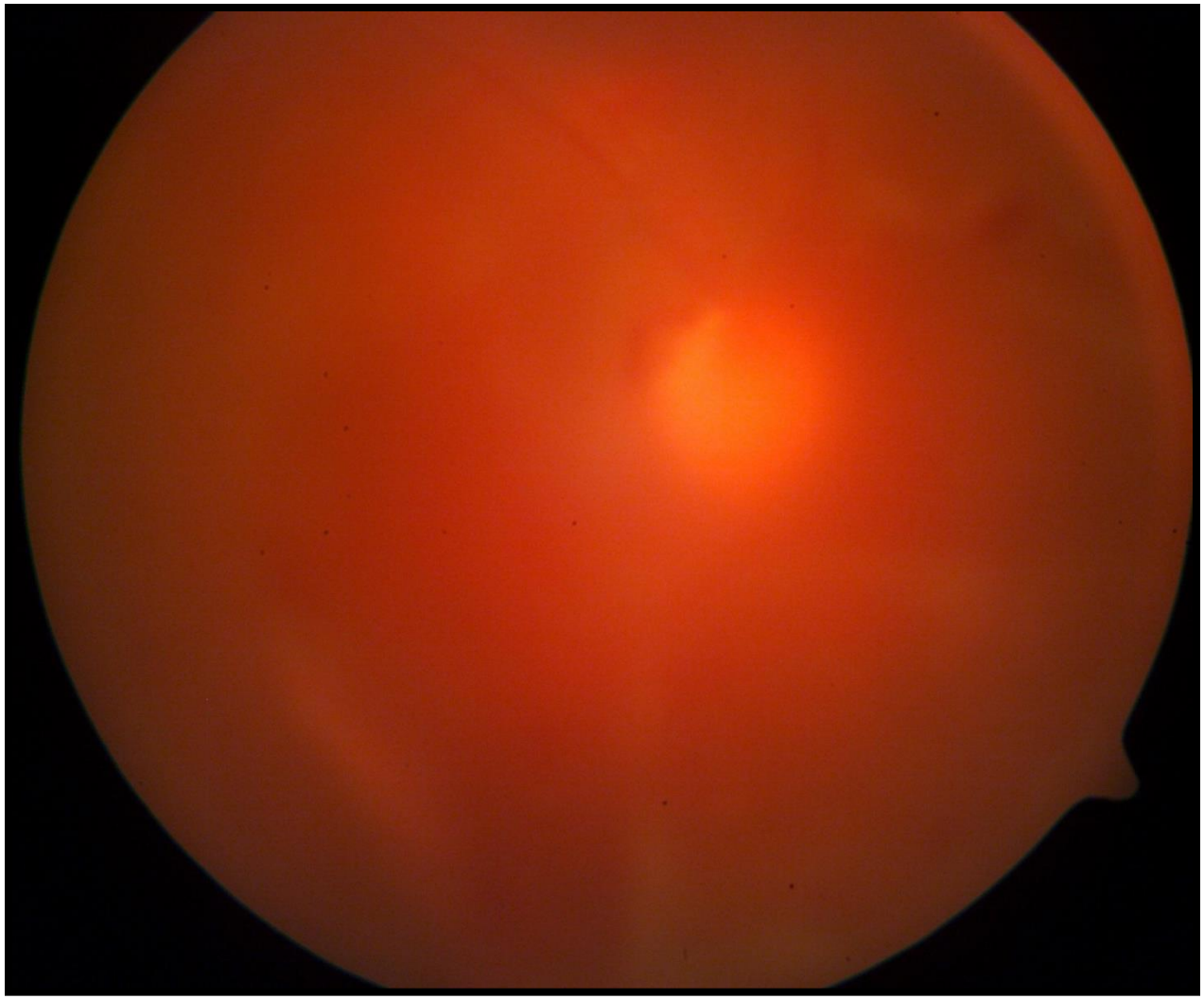

Vitreous hemorrhage in “advanced” proliferative diabetic retinopathy

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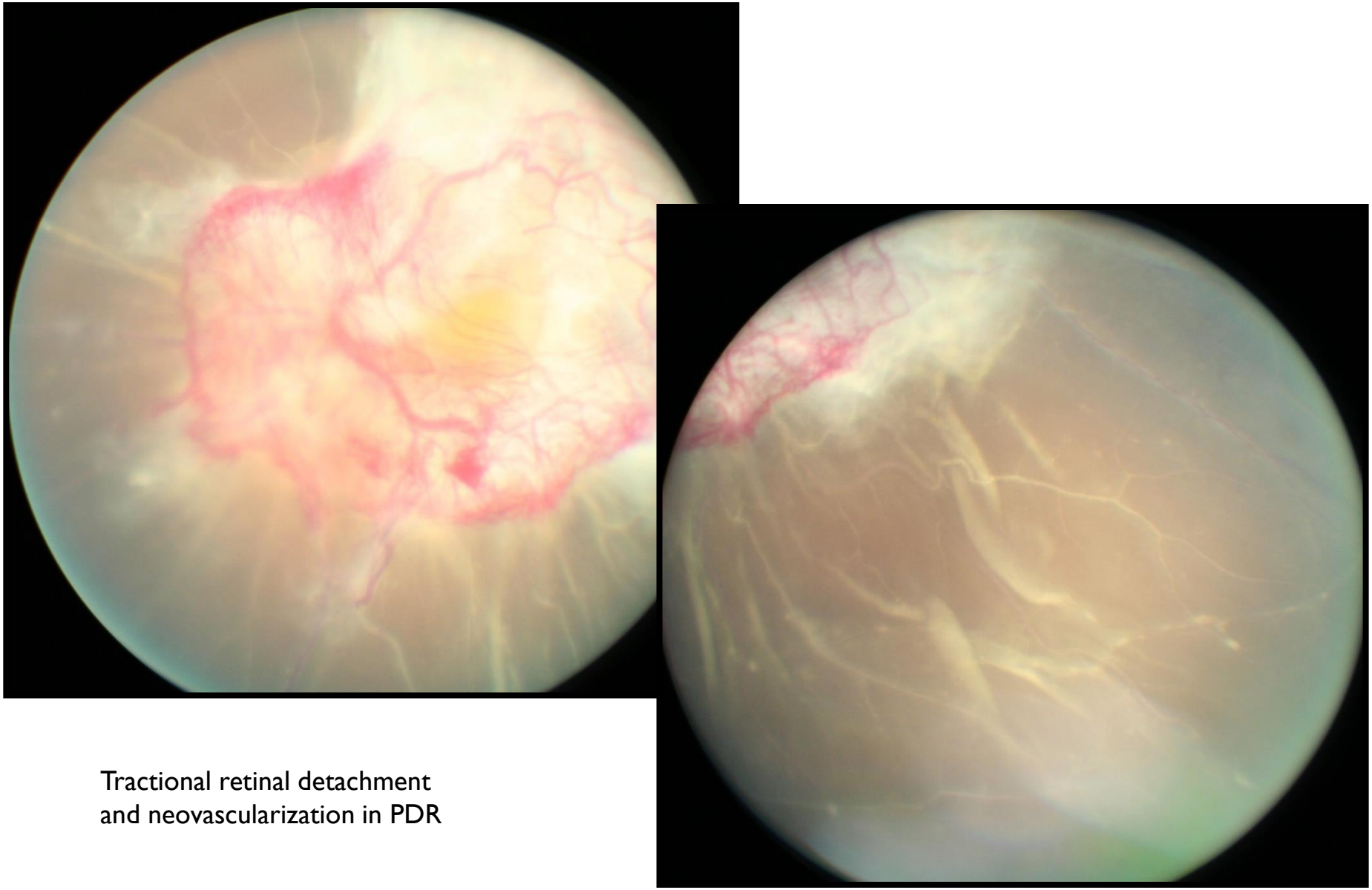

Tractional retinal detachment
and neovascularization in PDR

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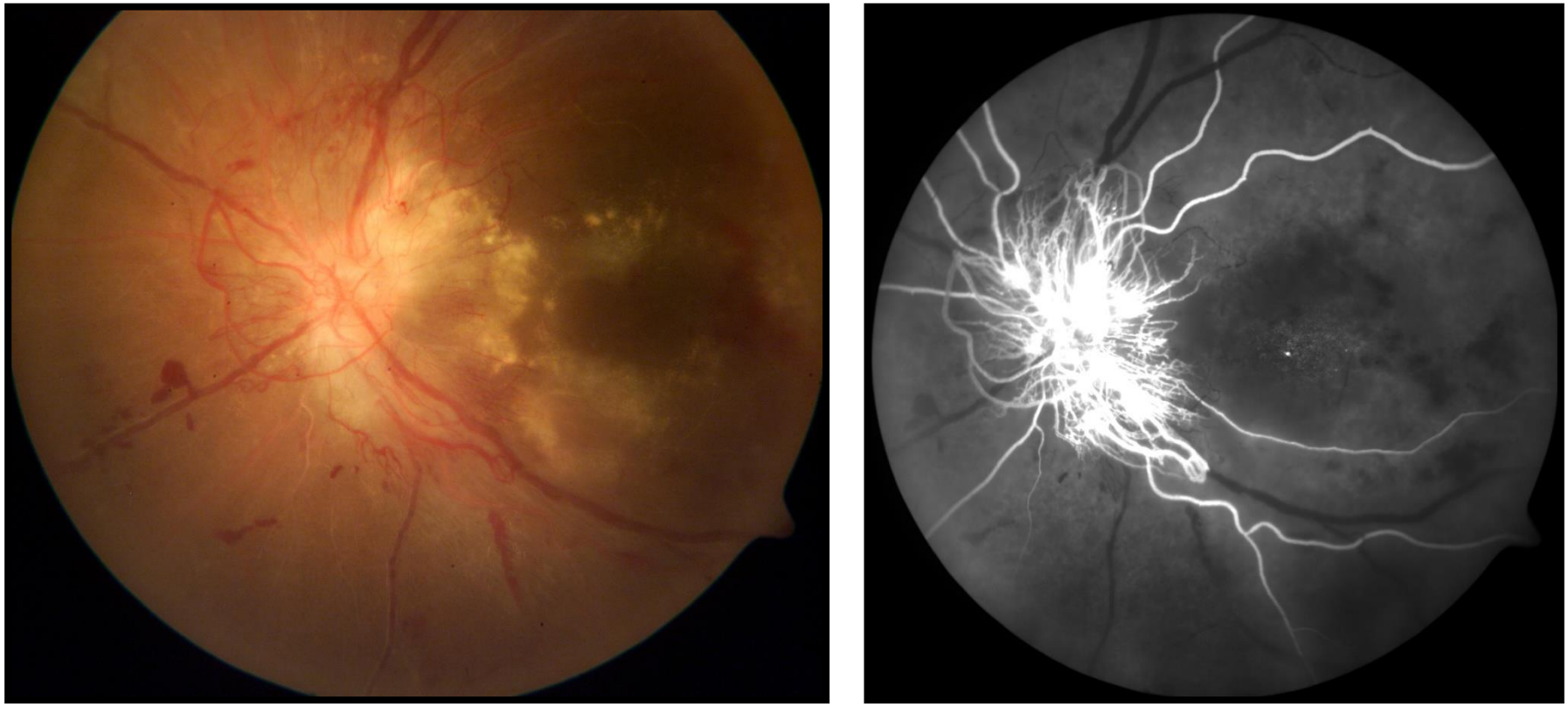

Retinal capillary non-perfusion in proliferative diabetic retinopathy

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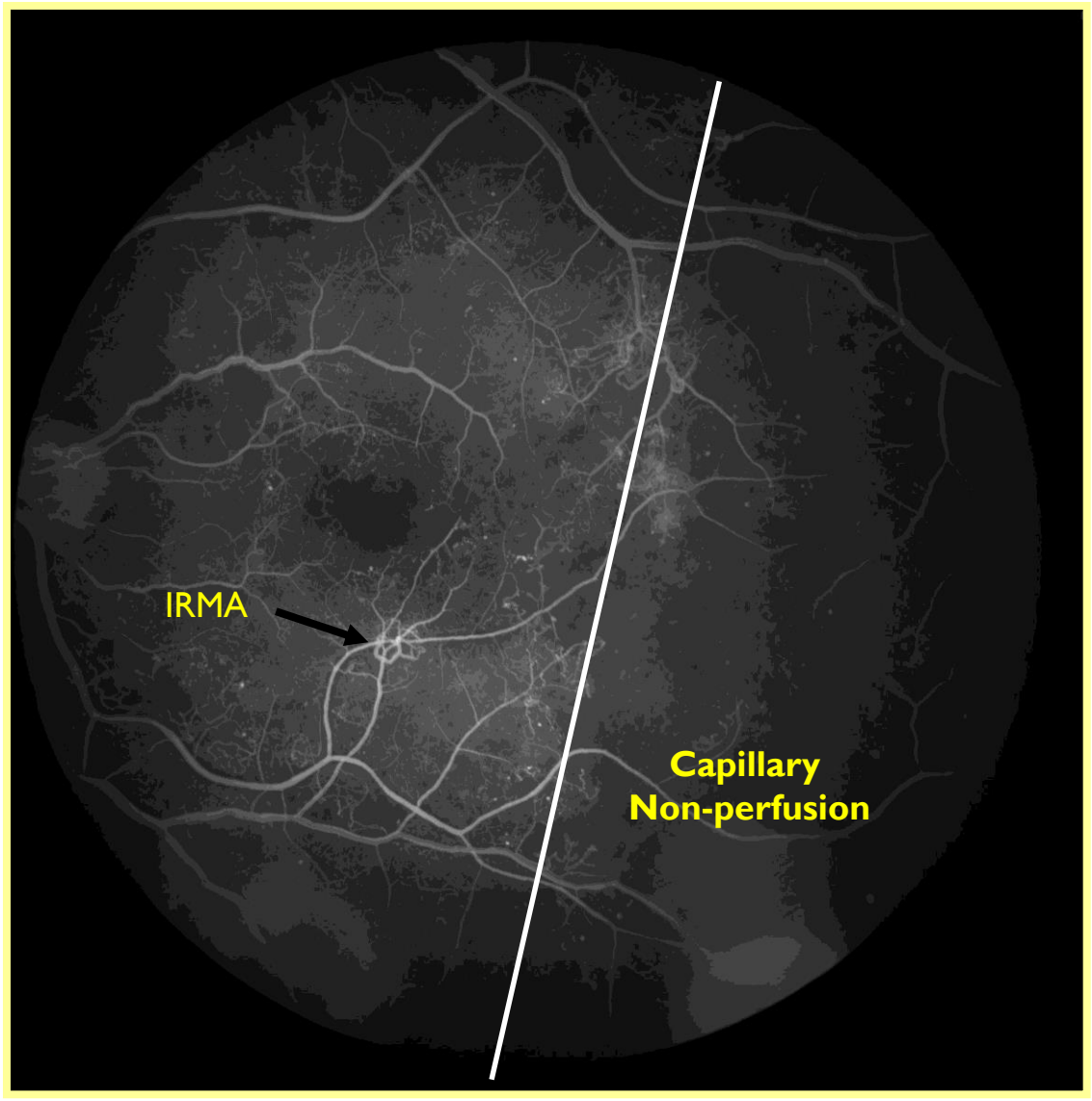
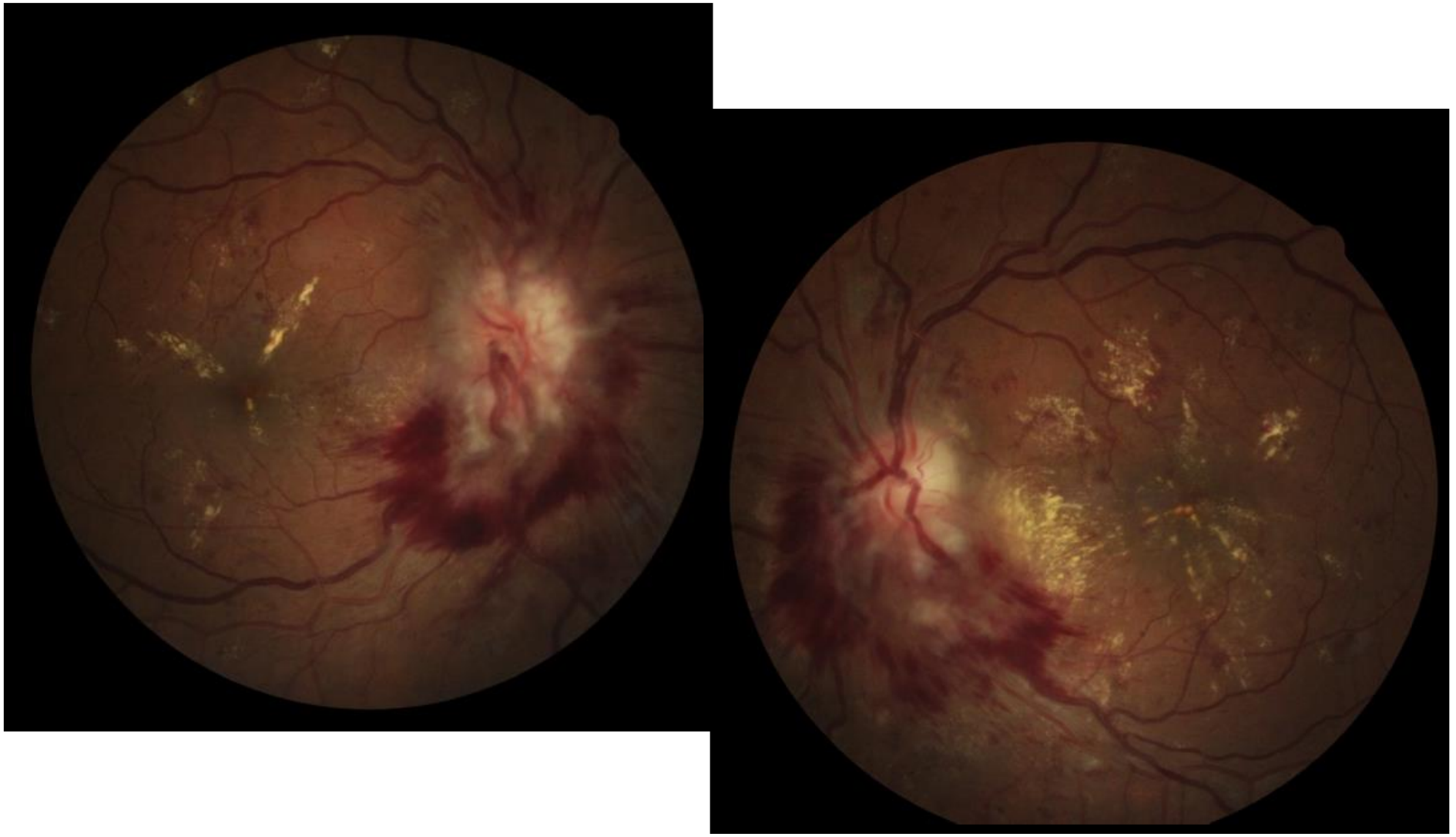


Microaneurysms and IRMA



Pseudotumor cerebri and diabetic retinopathy

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DPP4 Inhibitors (dipeptidyl-peptidase-4)

Sitagliptin Phosphate (Januvia) tablets - qd

Saxagliptin (Onglyza) tablets - qd

Linagliptin (Tradjenta) tablets – qd

Mechanism of Action

Inhibits the breakdown of glucagon-like peptide-1 (incretin); incretin stimulates insulin release from the beta cells in the pancreas (in response to food) and inhibits the liver's production of glucose = **promotes insulin activity and inhibits gluconeogenesis by preventing incretin inactivation**

INDICATIONS AND USAGE

Indicated as adjunctive therapy to improve glycemic control in adult patients with type 2 diabetes mellitus who are taking other oral antidiabetic agents.

SEs:

–very low incidence of hypoglycemia
–Acute pancreatitis with sitagliptin
–Hypersensitivity reactions

–Weight loss?

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Sodium-Glucose Co-Transporter 2 (SGLT2 Inhibitor)

Canagliflozin (Invokana)
Dapagliflozin (Farxiga)
Empagliflozin (Jardiance)

- **MOA**: Inhibition of the SGLT2 = reduced absorption of filtered glucose, lowering of renal threshold for glucose, and increasing of urinary excretion of glucose

Approved as an adjunctive to metformin, after trying typical 2nd-line treatments

Side effects: genital fungal infections
UTIs
increased urination,
thirst,
diabetic ketoacidosis

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SGLT2-I Advantages

- Low risk of hypoglycemia
- Weight loss
- Oral medication
- Lowers BP
- Able to use at any stage of T2DM

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Table 2. **Monitoring Recommendations for Patients with Diabetes and NPDR**

Severity of NPDR	Follow-up Interval, months	
	AAO	AOA
None	12	12
Mild	6-12	12
Moderate	6-12	6-8
Severe	2-4	3-4
Very Severe	2-4	2-3

Key: AAO – American Academy of Ophthalmology; AOA – American Optometric Association; NPDR – nonproliferative diabetic retinopathy

Source: AAO. Preferred Practice Pattern. Diabetic Retinopathy. 2013; AOA. Evidence-Based Clinical Practice Guideline. Eye Care of the Patient with Diabetes Mellitus. 2014.

Laser studies: DRS, ETDRS
VEGF: Lucentis (READ 2 and 3, RISE and RIDE, RESTORE),
Eylea (DA VINCI, VIVID and VISTA
Avastin (BOLT – “off label” usage

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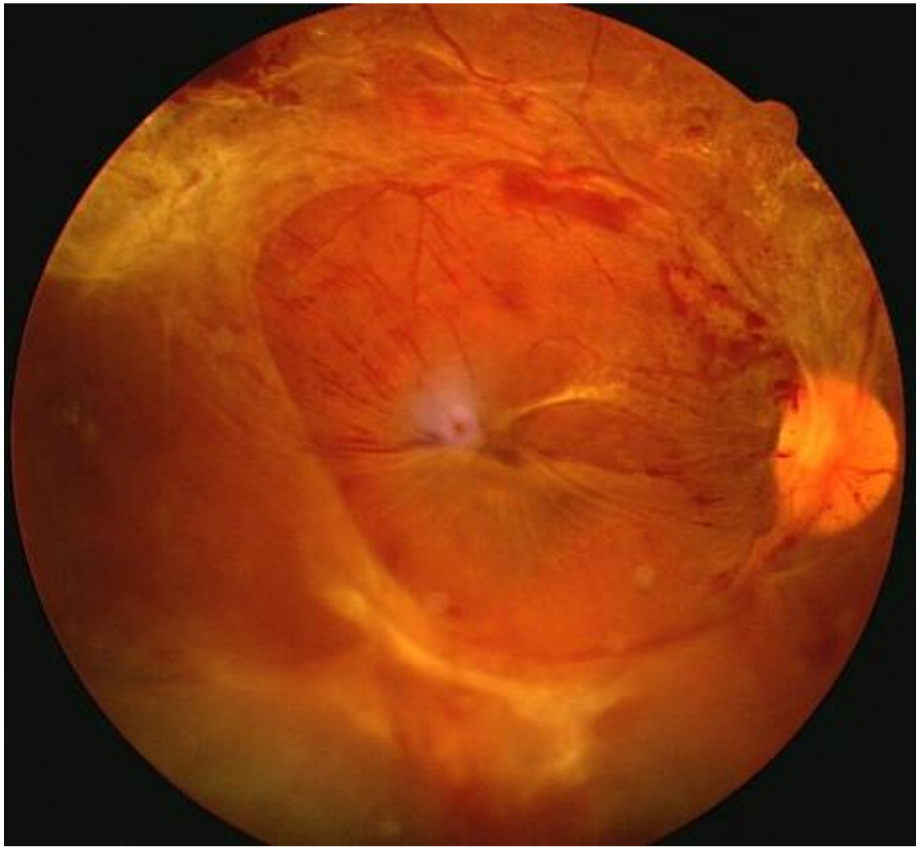
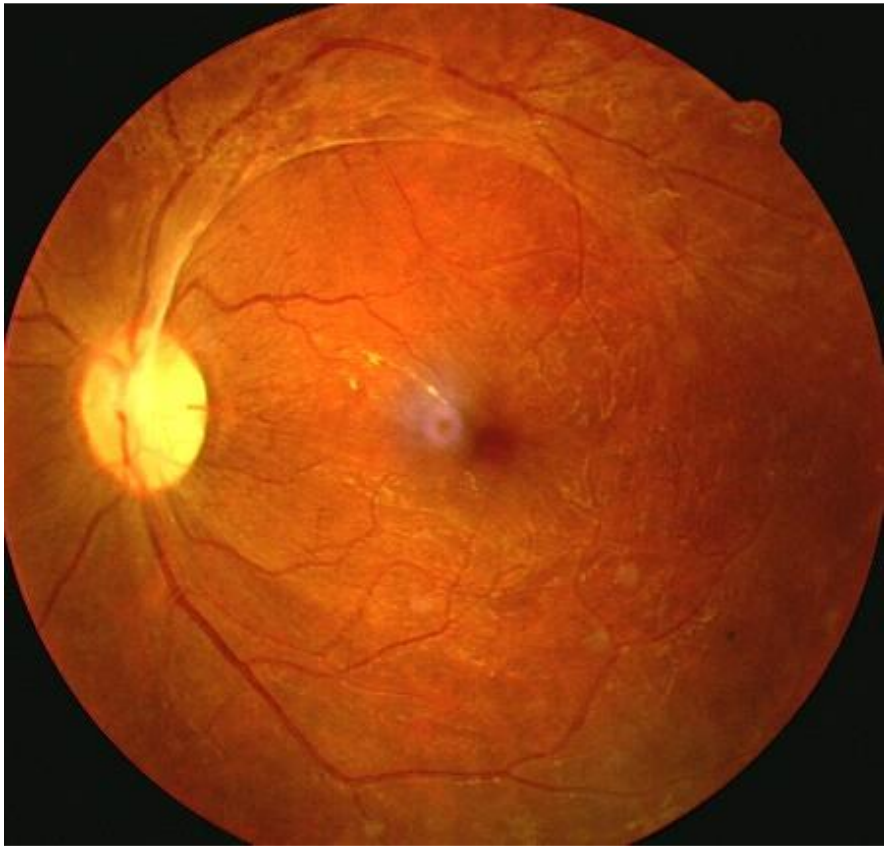
Beyond Retinopathy: 12 Key Factors in Diabetes Wellness





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Who is driving the train ?

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Risk factors for advancement of diabetic retinopathy

#1. **Hb A1C under 7%** ADA, AACE <6.5%
Can be higher in patients with CVD, hypoglycemia, shorter life expectancy and children (7%- 8%)
ACCORD vs. ADVANCE studies

#2. **Hypertensive** patients with diabetes need a BP of 125/80 or better

#3. **Cholesterol** needs to be under control
LDL <100 mg/dl if no history of CVD , Pattern A vs. Pattern B
LDL <70 mg/dl if pre-existing history of CVD
HDL >50 mg/dl in women and >40 mg/dl in men
Triglycerides < 150 mg/dl

#4. **Sleep Apnea** needs to be ruled out
CPAP - reduce nocturnal hypertension, increase oxygen, decrease FBS

#5. **Anemia** needs to be ruled out = hemoglobin needs to be above 11
Procrit (Epoetin alfa) needs to be considered if hemoglobin below 9.
Starts early and has a negative impact on CV morbidity and mortality

#6. Proteinuria (albuminuria) – Starlings Law (hydrostatic vs. osmotic)

30-299 mg = microalbumninuria
300 mg or more = albuminuria
ADA recommends yearly urinalysis followed by GFR
Start ACE inhibitors or ARB = renal protective

#7. Stop smoking

Increases proteinuria, blood vessel wall damage, and vasoconstriction

#8. Vasculitis (R/O gum disease, leg ulcers, gastritis, urinary tract infections)

Daily aspirin decreases CVD in Type 1 and Type 2
ADA 81- 325 mg /day
Not studied extensively for patients under the age of 30

CRP of 3.0 mg / L or higher can triple your risk of heart disease
CRP of 0.5 mg / L or less rarely experience heart attacks

Get some sun

Not too much though

9.Vitamin D

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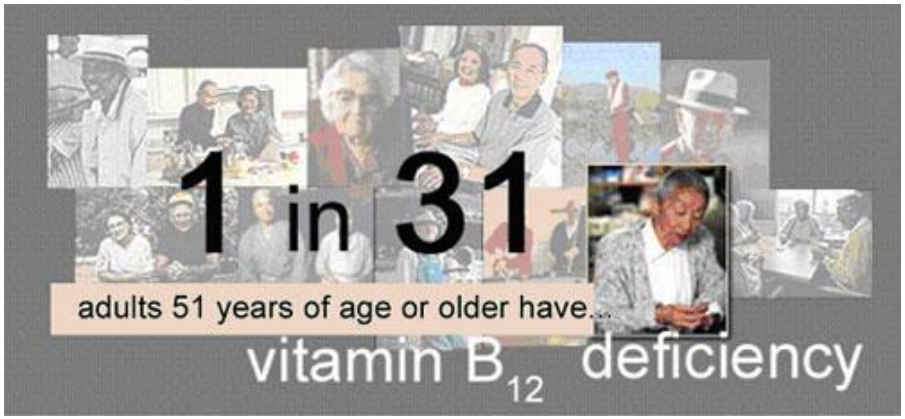
#**10. Obesity** - BMI (body mass index) less than 30 .... better if less than 25

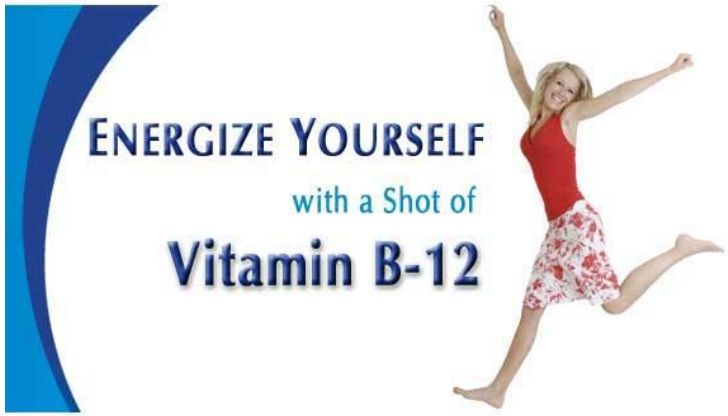
AACE recommends Bariatric surgery Type 2 patients with BMI > to 35 kg/m2.

Surgery is stressed if other conditions are present such as , psuedotumor cerebri, obstructive sleep apnea, hypertension, heart disease, polycystic ovarian syndrome

The American Medical Association voted in 2013 to classify obesity as a disease.

#11.Vitamin B 12 deficiency in diabetics taking metformin





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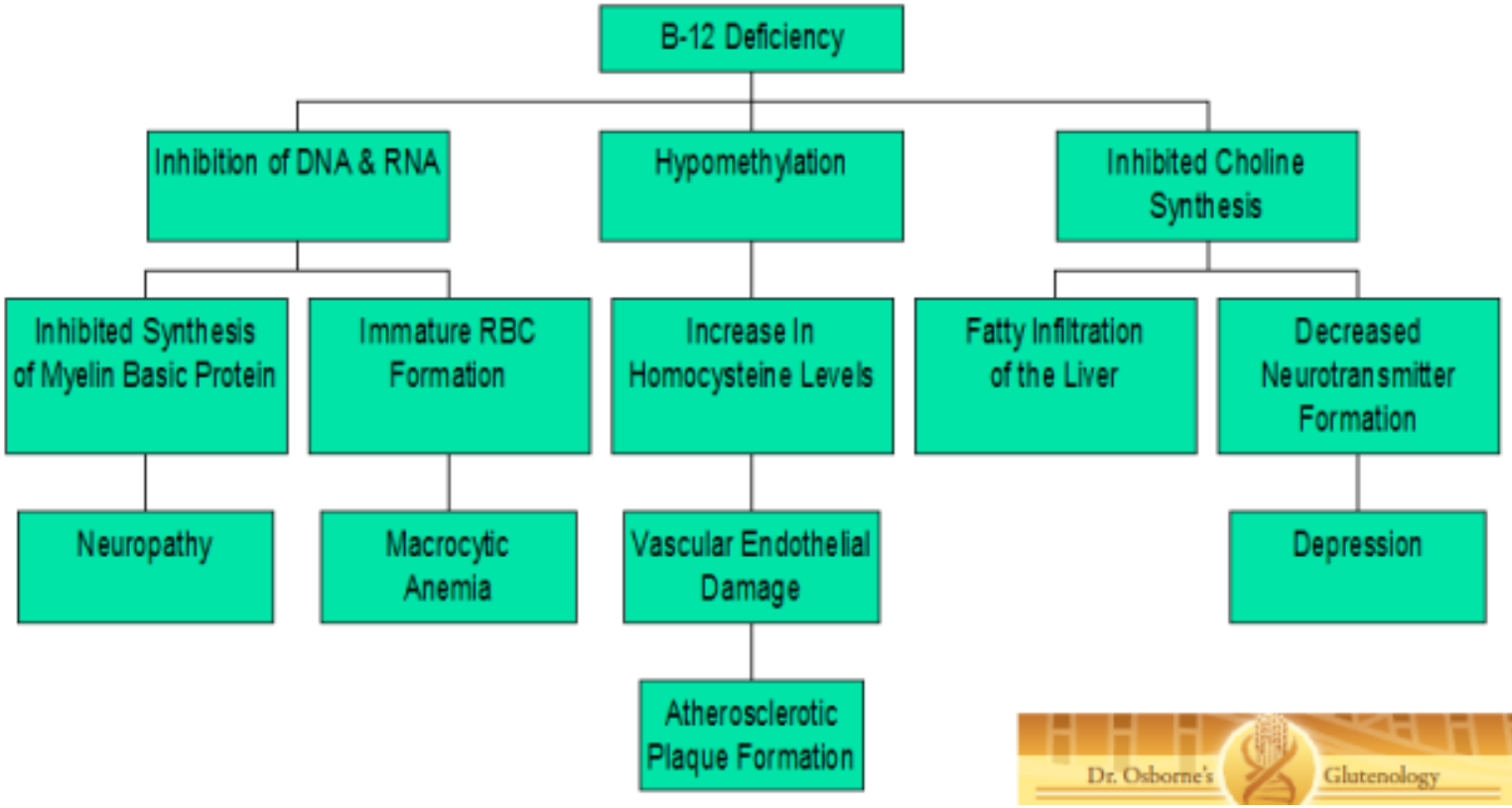
Vitamin B 12 deficiency in diabetics taking metformin



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Vitamin B_{12} deficiency is estimated to be present in up to **30**% of patients with diabetes taking metformin. The risk for vitamin B_{12} deficiency increases with patient age and the dose and duration of metformin use.

The combination of metformin with proton pump inhibitors has been reported to have an additive effect on risk for vitamin B_{12} deficiency.

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#12. **Hyperhomocysteinemia**

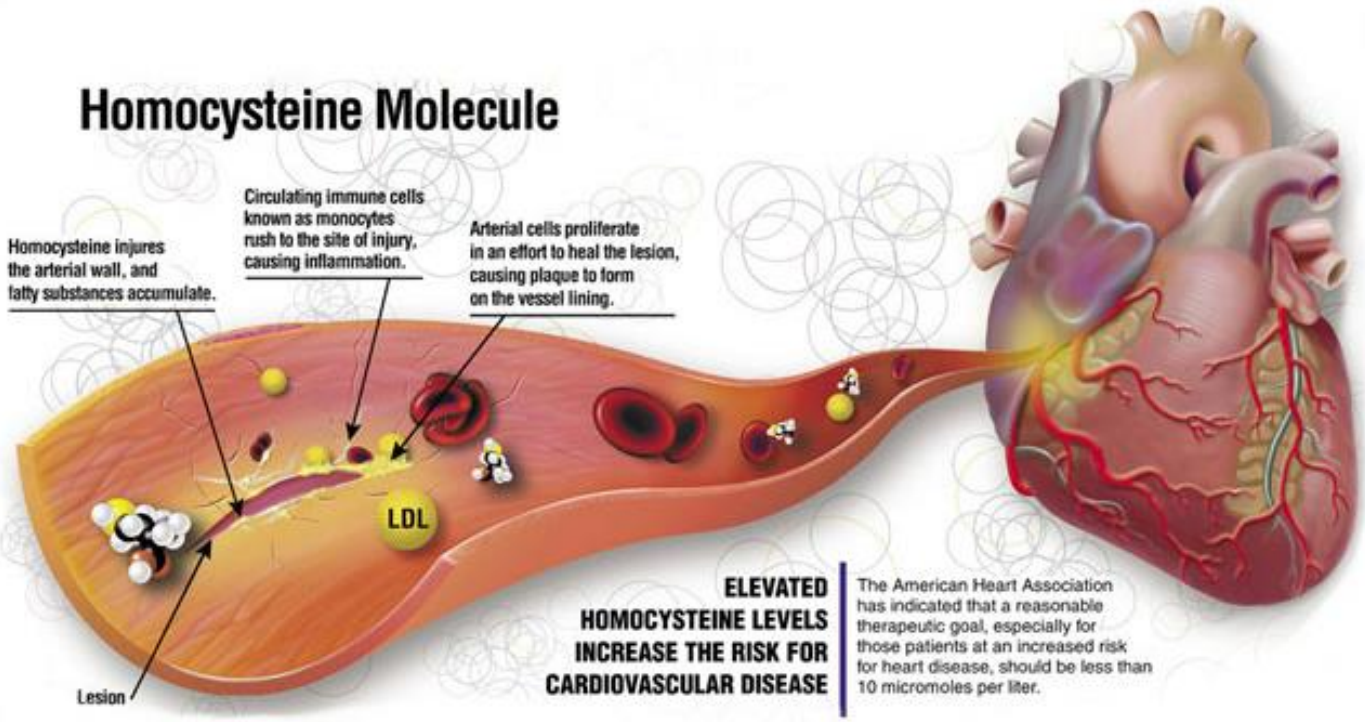
Patients with diabetes mellitus are prone to cardiovascular disease and risk factors presumably unrelated to diabetes, such as **hyperhomocysteinemia**, may be involved in the **atherothrombotic** process in these subjects.

Plasma homocysteine levels are usually normal in diabetes, although both lower and higher levels have been reported. This has been ascribed to hyperfiltration and renal dysfunction or low folate status, respectively.

Insulin resistance does not appear to be a major determinant of plasma homocysteine level.

Hyperhomocysteinemia has been associated with **microalbuminuria** and retinopathy in type 1 and type 2 diabetes.

In patients with **type 2 diabetes**, plasma homocysteine concentration has also been shown to be related to **macrovascular disease and death**. This relation seems to be stronger in diabetics than in subjects without diabetes.



The underlying pathophysiological mechanism of this increased vascular risk remains unexplained but may relate to worsening of endothelial dysfunction or structural vessel properties.

Because homocysteine and diabetes have an apparent synergistic negative vascular effect, patients with diabetes are good candidates for screening and treatment with folic acid until the results of ongoing clinical trials are available.

Aspirin Use in Diabetes

Aspirin use in diabetic patients is not associated with an increased risk of hemorrhage or progression of retinopathy or macular edema !!!

Aspirin use may actually slow the progression of diabetic retinopathy ???

Aspirin Therapy (enteric coated 81-325 mg/day): ADA recommendations

- Family History of coronary heart disease
- Cigarette smoking
- Hypertension
- Obesity
- Albuminuria
- Elevated lipid levels
- Age > 30 years

People with aspirin allergy, bleeding tendency, anticoagulant therapy, recent gastrointestinal bleeding, and clinically active hepatic disease are not candidates for aspirin therapy.

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Proliferative diabetic retinopathy

Sleep Apnea = No "CPAP" use

Anemia = 8 Hb

Albuminuria = >300

BP 145/85

Smoker

Gum Disease

Vitamin D deficiency

HbA1C = 9 %

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Hypertension

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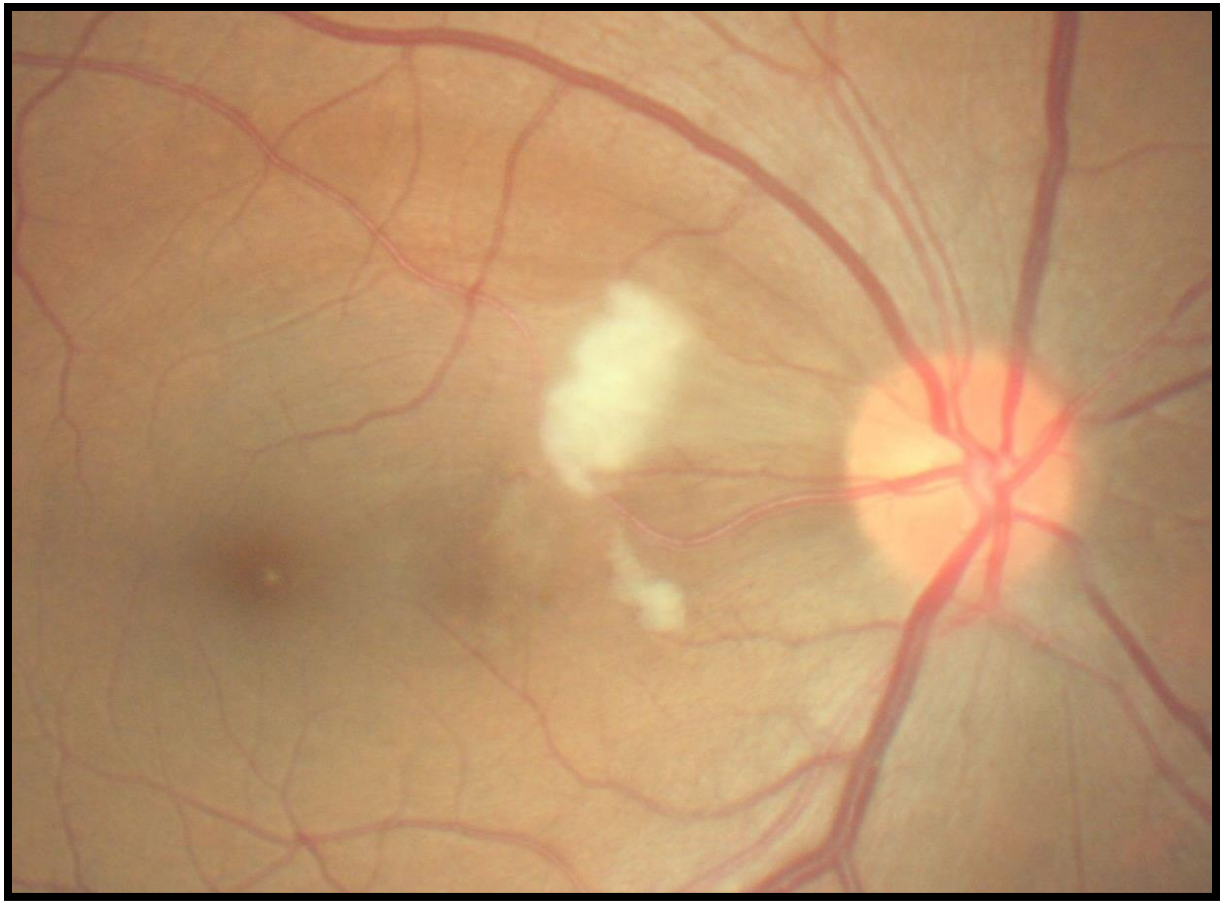
Hypertensive Retinopathy Grade 3



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Most common reason for an office visit in the United States.

30 % of adults in the United States = 95 million people

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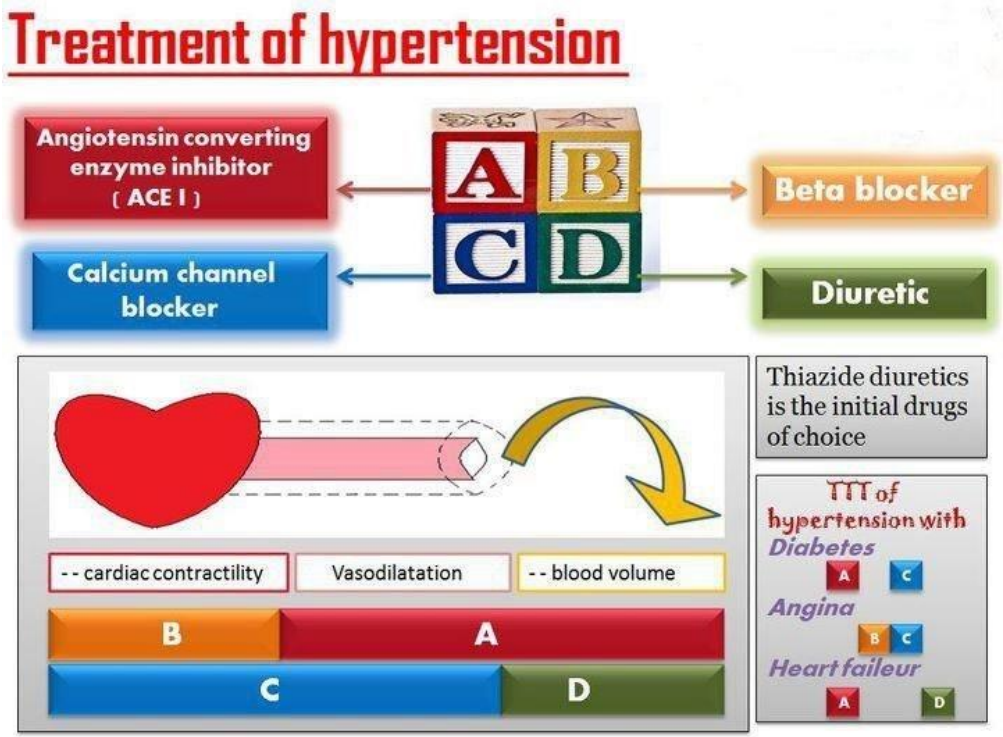
ACE = CHF, DM, Post MI
(30% dry cough, angio-edema of the tongue, neck)

Beta Blockers– Post MI, CHF
(Increase depression, lipids, asthma, decrease HR)

Calcium Channel blocker = AA and the elderly
(Edema and constipation)

Diuretics = AA and the elderly
(Increase lipids, sugar, calcium and uric acid)



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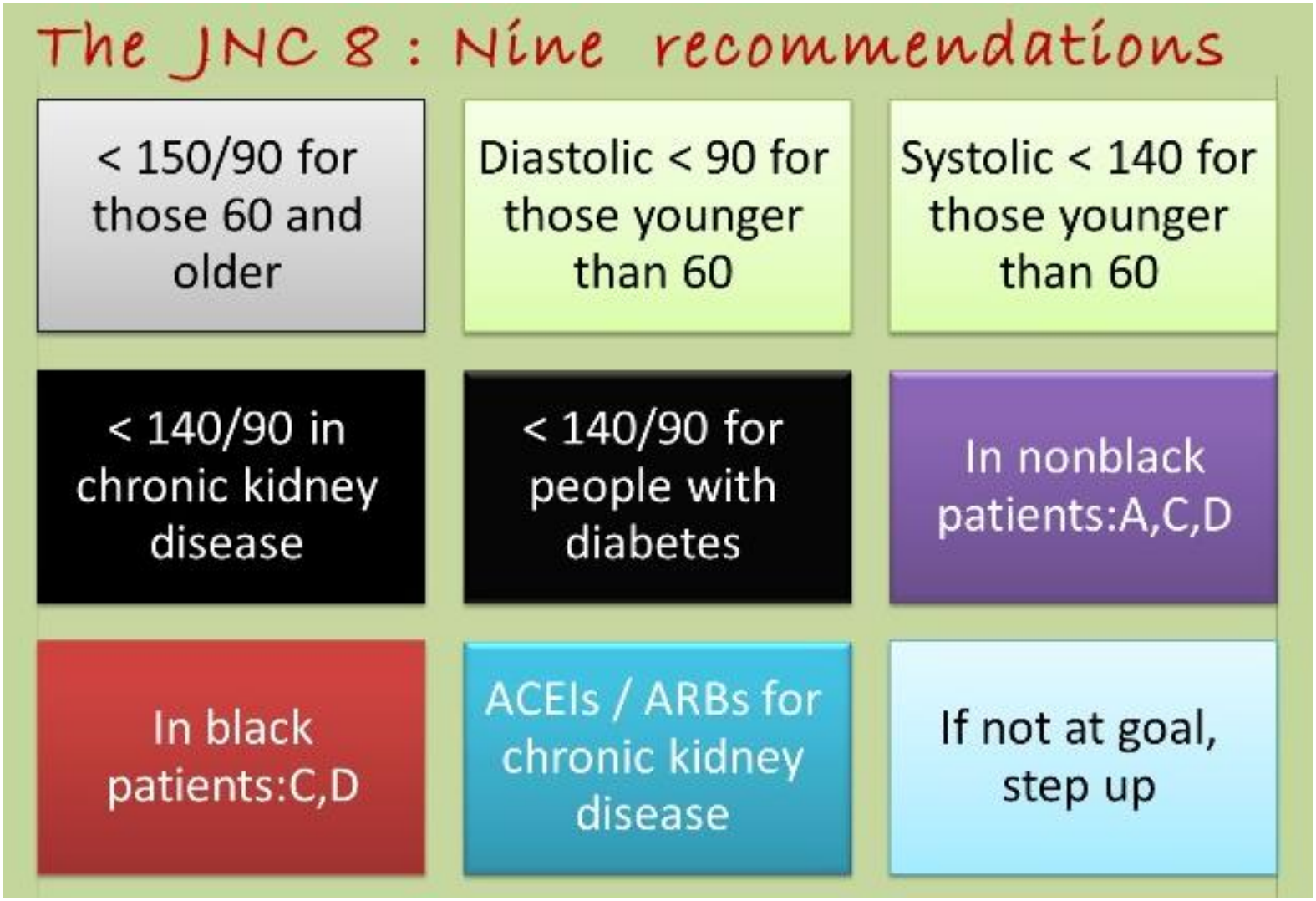
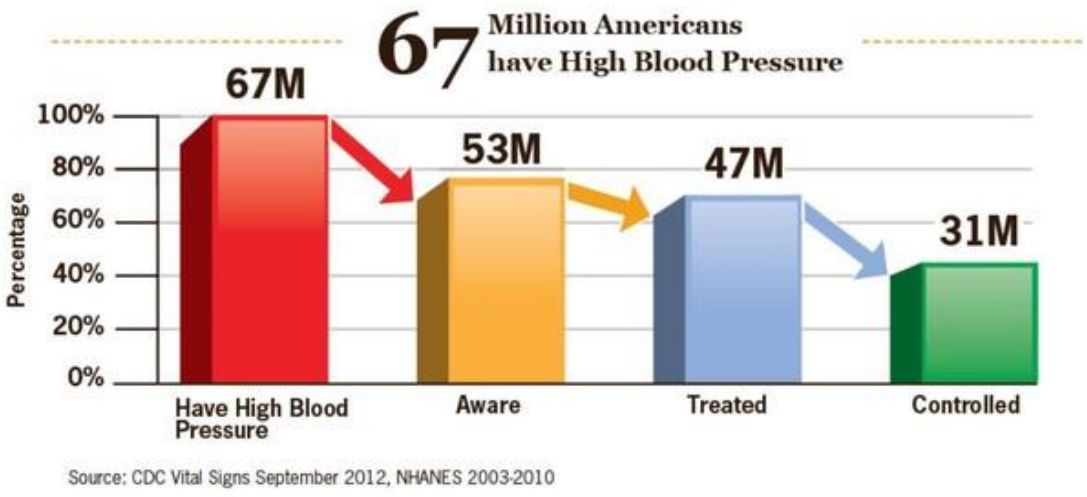
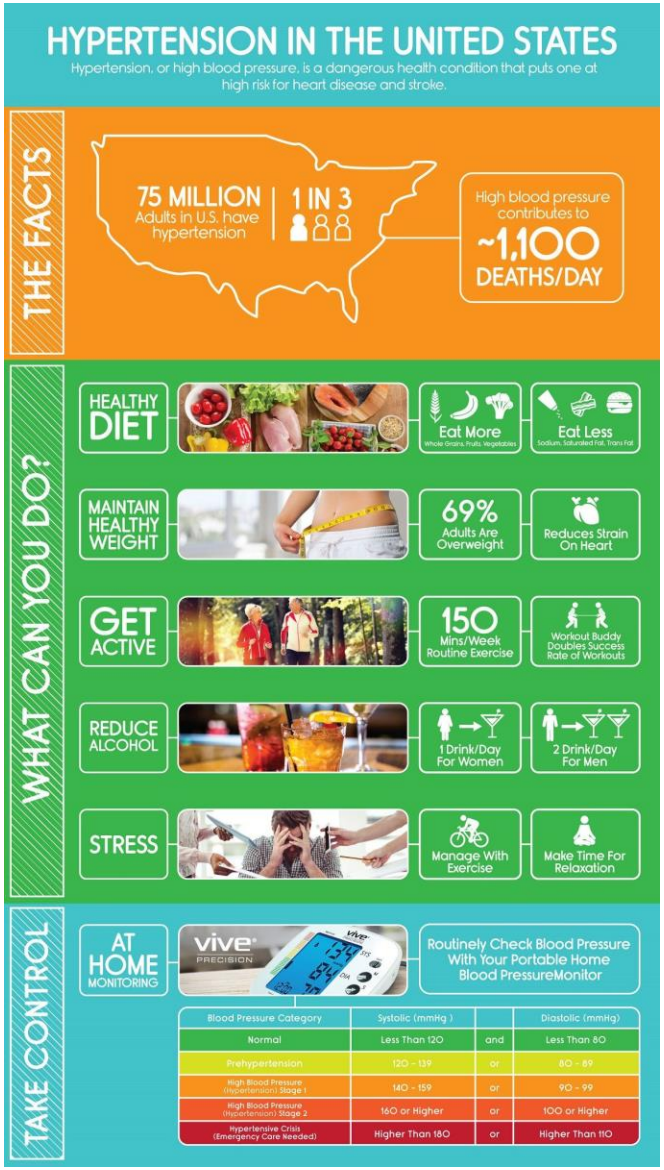

The JNC 8 : Nine recommendations
< 150/90 for those 60 and older
Diastolic < 90 for those younger than 60
Systolic < 140 for those younger than 60
< 140/90 in chronic kidney disease
< 140/90 for people with diabetes
In nonblack patients:A,C,D
In black patients:C,D
ACEIs / ARBs for chronic kidney disease
If not at goal, step up





https://www.visualistan.com

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The definition of hypertension

	Systolic BP		Diastolic BP
Normal	<120 mmHg	AND	<80 mmHg
Elevated Blood Pressure	120-129 mmHg	AND	< 80 mmHg
Stage 1 Hypertension	130-139 mmHg	OR	80-89 mmHg
Stage 2 Hypertentions	>140 mmHg	OR	>90 mmHg
Hypertensive Crisis	≥180 mmHg	AND/ OR	≥120 mmHg
Hypertensive Emergency	Hypertensive Crisis Systolic and Diastolic #s + end organ damage URGENCY!!!		

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Grading of hypertensive retinopathy

Stage	Description	Ocular symptoms	Systemic symptoms
1	Mild to moderate narrowing or sclerosis of arterioles	(-)	(-)
2	Moderate to marked narrowing of arterioles Focal or localized narrowing of arterioles Exaggeration of the light reflex Arteriovenous crossing changes	(-)	(-)
3	Retinal arteriolar narrowing and focal constriction Retinal edema Cotton wool spots Retinal hemorrhages Retinal exudates	(+)/(-)	Cardiac, renal or cerebral dysfunction evident
4	Stage 3 (+) optic nerve swelling Elschnig spots possible	(+)	Severe Cardiac, renal or cerebral dysfunction

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Types of hypertension

Essential Hypertension 90-95%

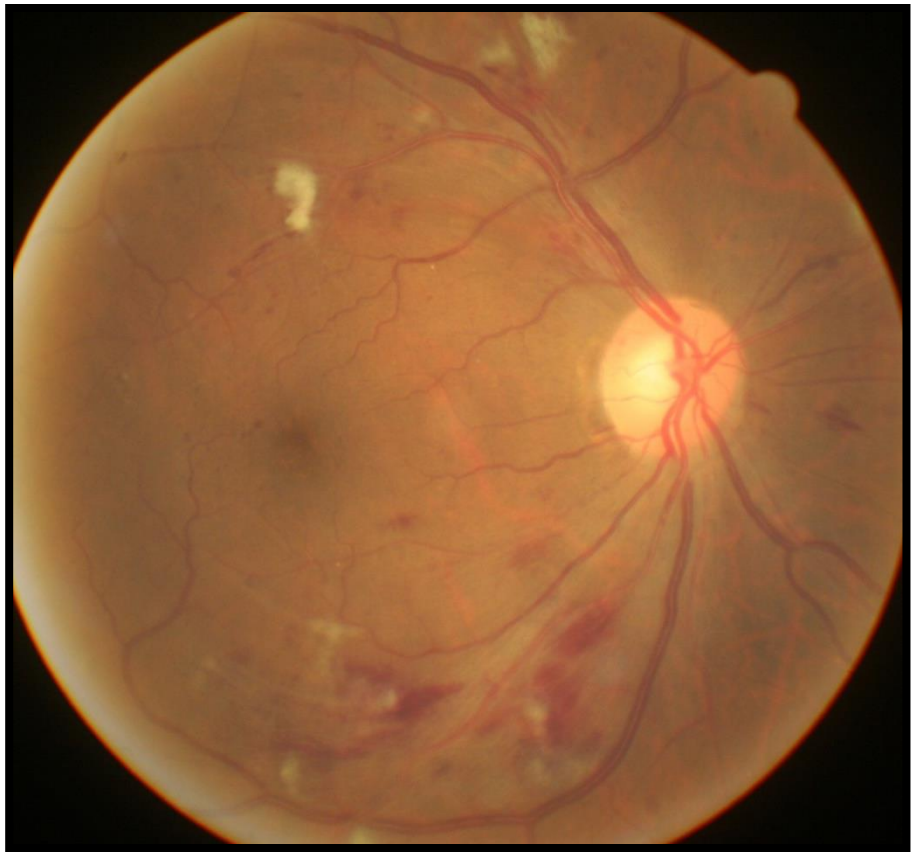
Secondary hypertension 5-10%

Sleep apnea
Medications (i.e., steroids, decongestants, stimulants, birth control)
Endocrine disorder (i.e., Cushing's disease, hypothyroidism, hyperthyroidism)
Adrenal gland (pheochromocytoma)
Renal disease (renal artery stenosis)
Illegal drug use (i.e., cocaine, narcotics, methamphetamine)

Grading of Hypertensive Retinopathy

Grade 1	Retinal vessels narrowed	> 90 and < 110 Diastolic BP
Grade 2	Nicking of retinal vessels	> 90 and <110 Diastolic BP
Grade 3	CWS, Hemes, Lipid exudates	> 110 – 115 Diastolic BP
Grade 4	Grade 3 + Optic disc swelling	> 120 Diastolic BP

Hypertensive Retinopathy Grade 3



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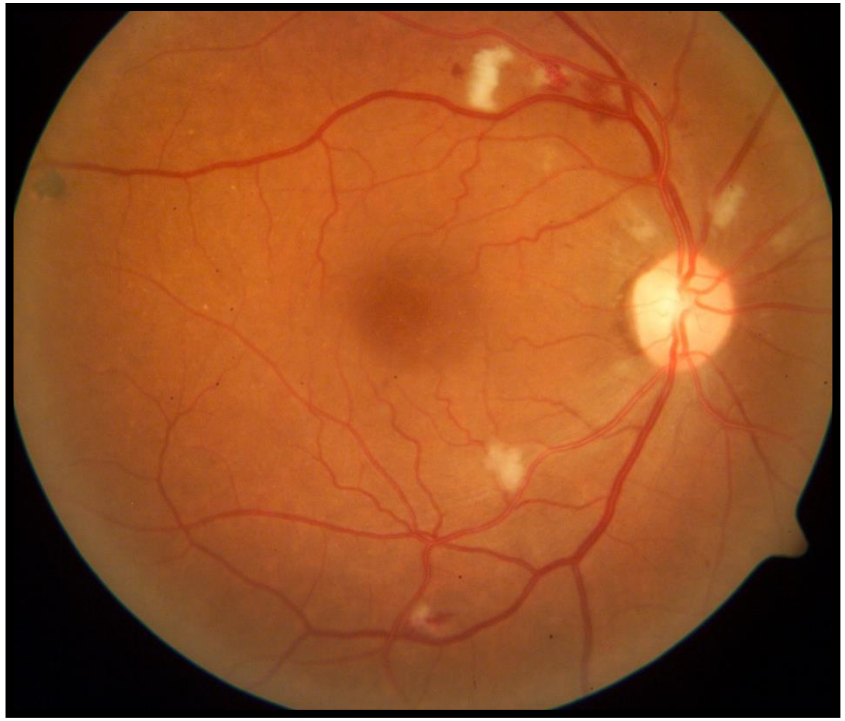
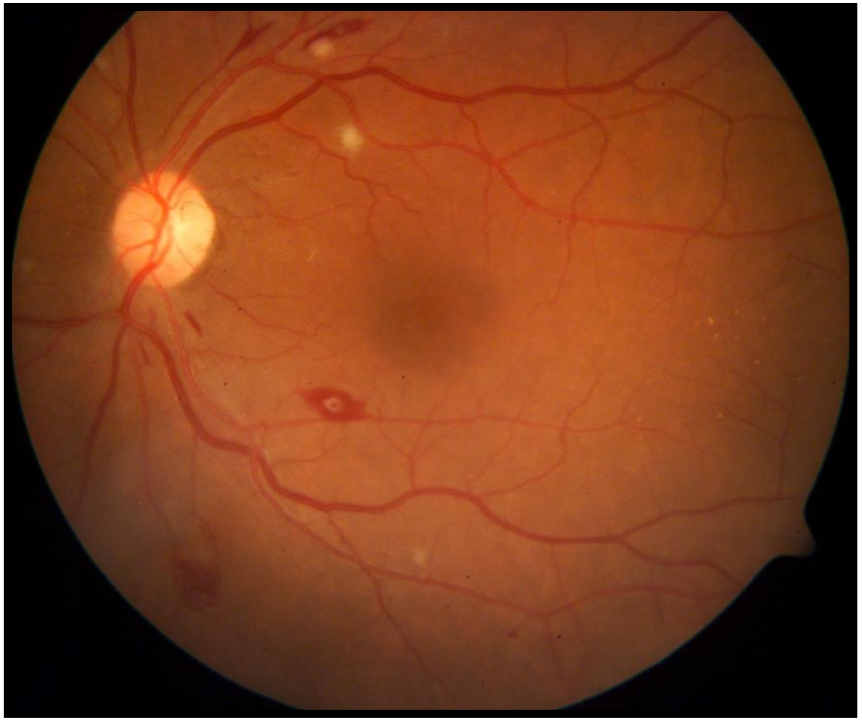
Hypertensive Retinopathy Grade 3





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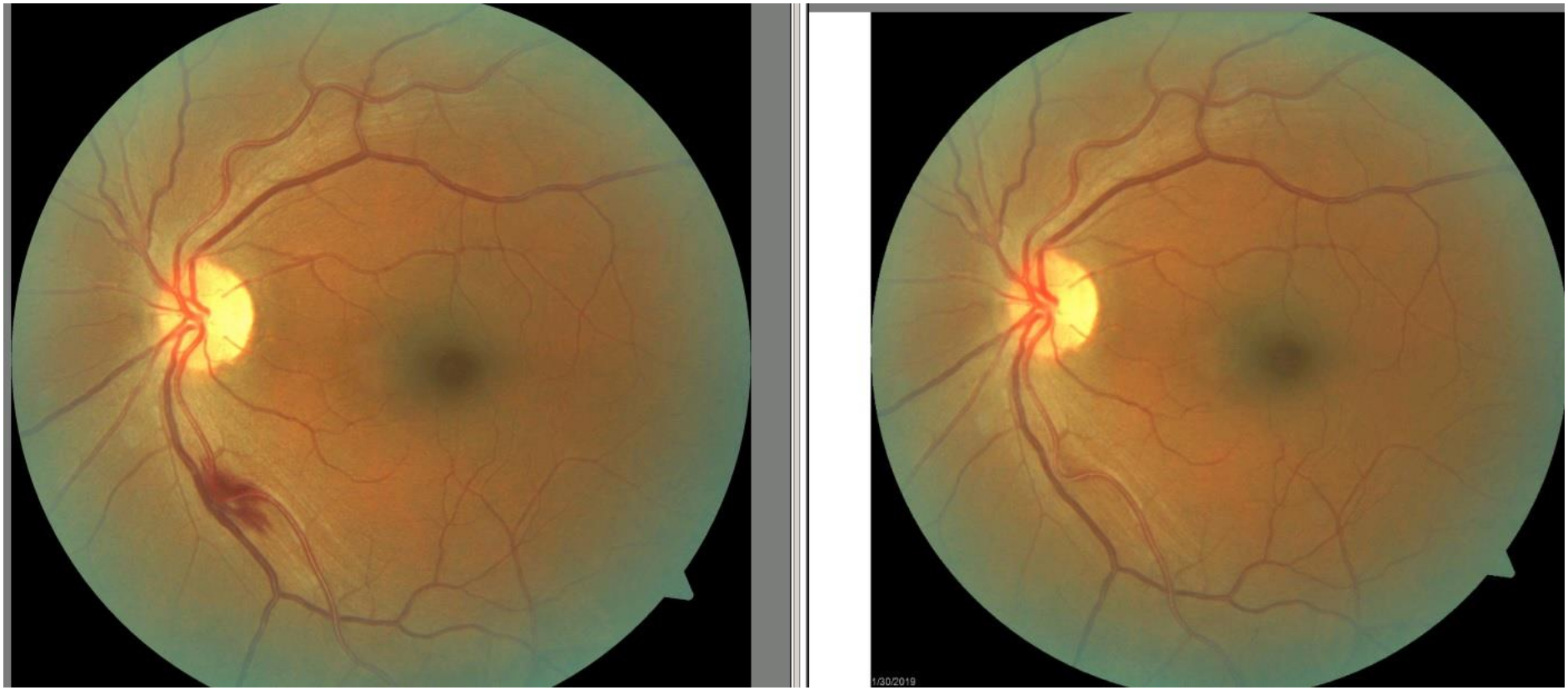
50 year old AA female
November 2018

January 2019



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Malignant Hypertension

Very high pressure with retinal hemorrhages, exudates, CWS or optic nerve swelling

Usually diastolic blood pressure is above 120 mm Hg

Hypertensive <u>Urgency</u>

Severe BP elevation >120 without retinopathy or CNS changes

Hypertensive <u>Emergency</u>

Severe BP elevation >120 with retinopathy or CNS changes

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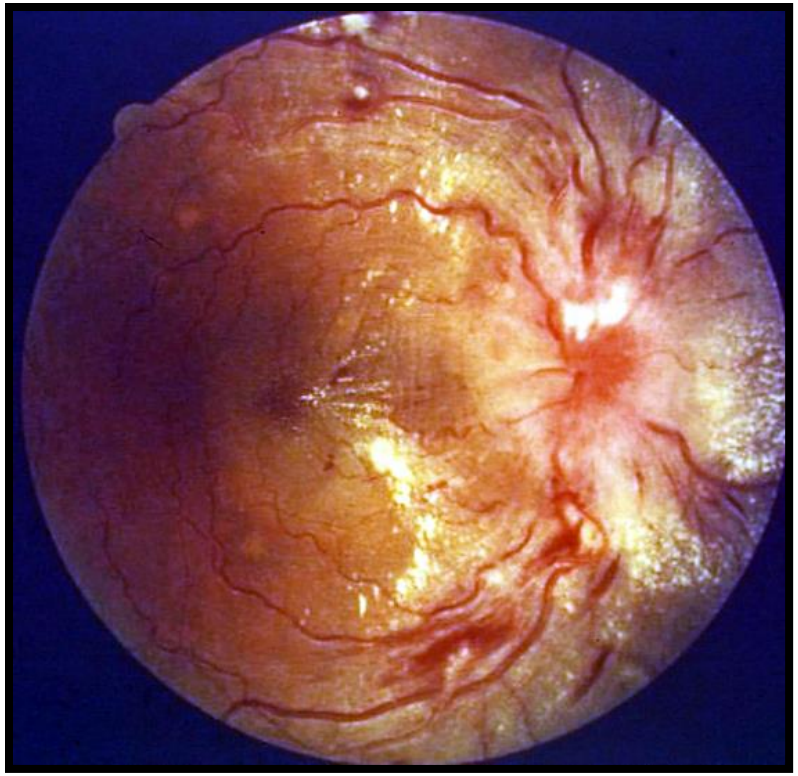
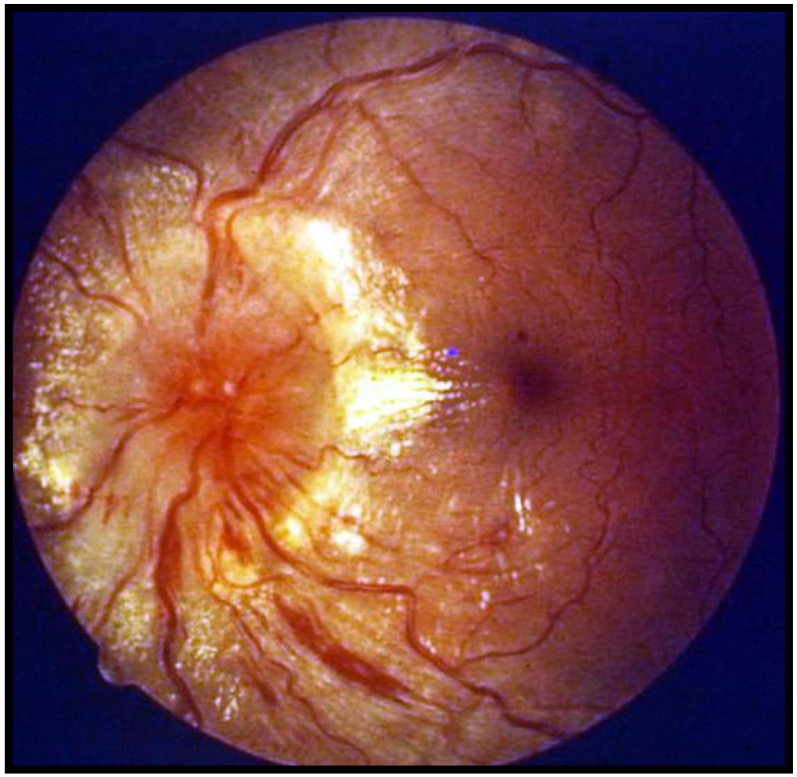
Malignant Hypertension

Immediate attention also if chest pain, cognitive impairment, hematuria, sensory or motor problems



"Malignant hypertension" defined as blood pressure > 180/120



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Malignant Hypertension

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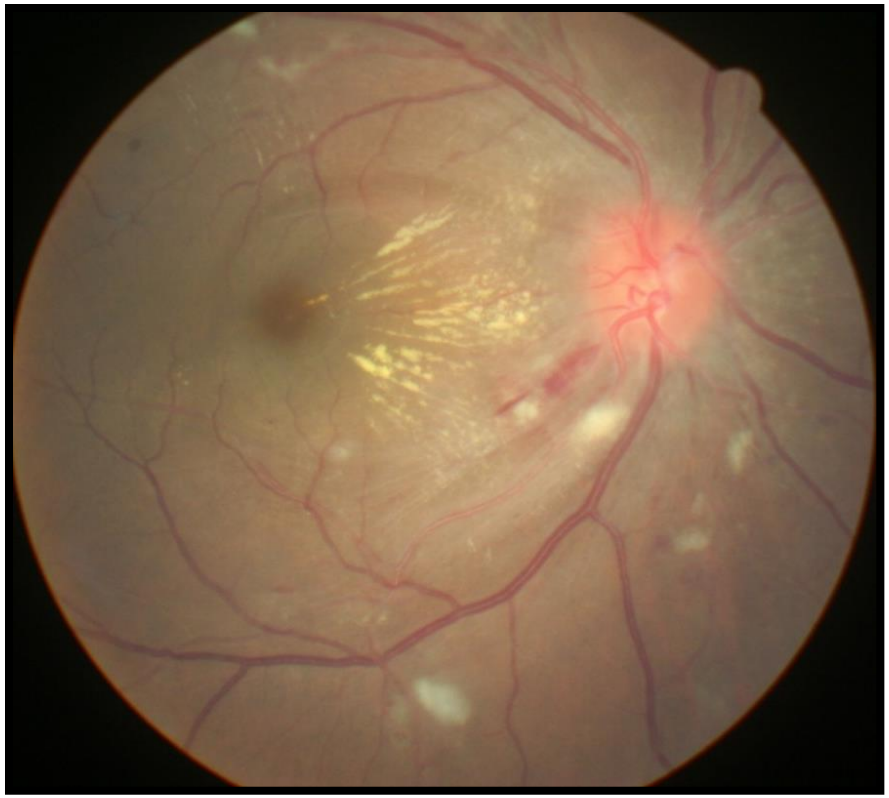
Malignant Hypertension



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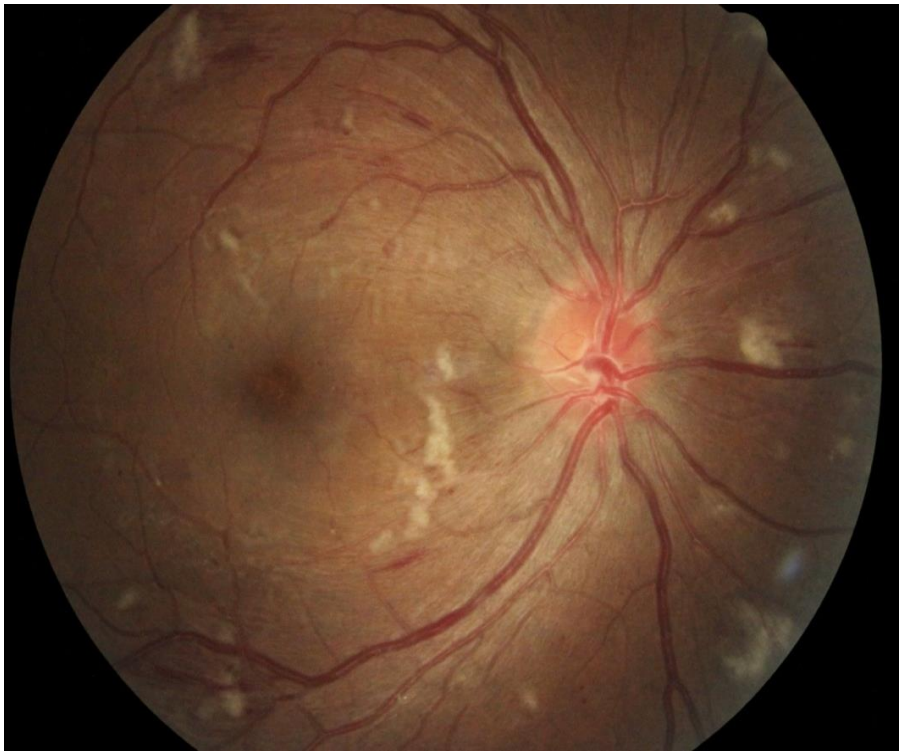
Malignant Hypertension



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Treatment of Malignant Hypertension

Blood pressure measurement

Immediate referral to emergency room or PCP for **slow lowering** of the blood pressure

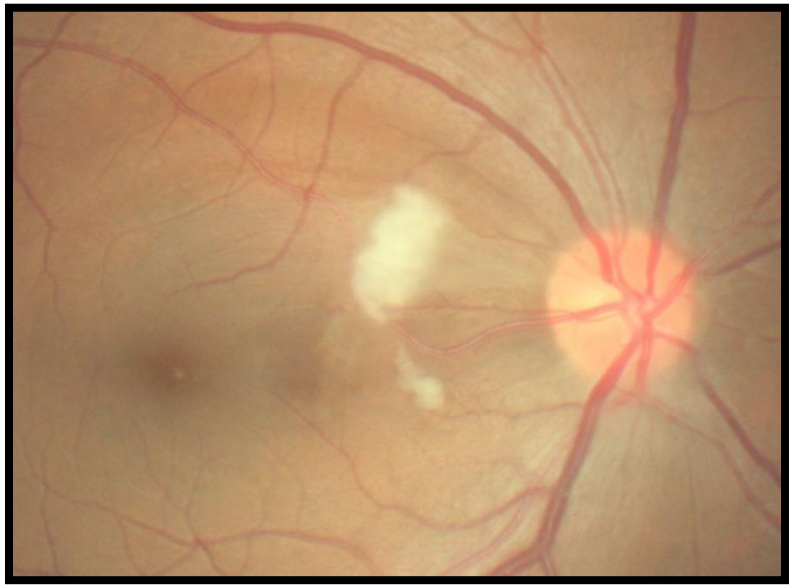
Severe BP elevation >120 without retinopathy or CNS changes **– Hypertensive Urgency**

Severe BP elevation >120 with retinopathy or CNS changes. **Hypertensive Emergency**

Treatment Medications

Vasodilators in the ER

- Clonidine
- Labetolol
- Nitroglycerine
- Esmolol
- Nitroprusside



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Questions for malignant hypertension

Hypertensive encephalopathy

- **Syncope**
- **Seizures**
- **Focal weakness**
- **Speech problems**

Hypertensive renal problems

- **Change in renal volume**
- **Hematuria, abdominal pain**

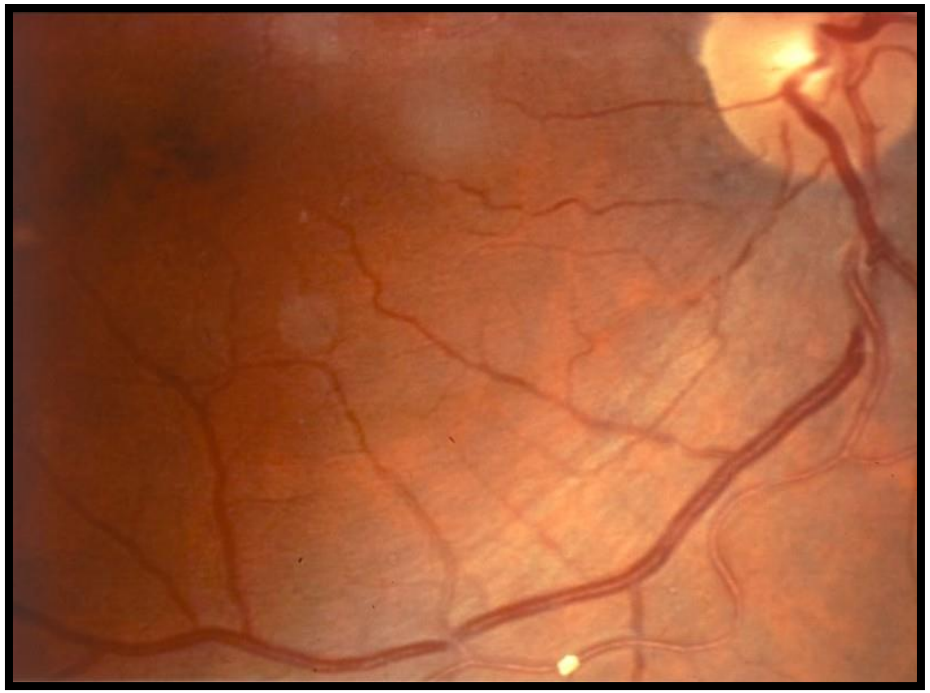
Hypertensive cardiac involvement

- **Chest pain**
- **Palpatations**
- **Cough**
- **Dyspnea**

Organ dysfunction uncommon if DBP is less than 120 mmHg

Beaver Dam Study – Found that the overall prevalence of retinal emboli in a population of 4926 patients was 1.3 % and increased to 3.1 % in patients 75 years or older !!!

It also found an increase in "stroke" and "heart disease" in patients with retinal emboli



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Drug	Common Brands	Amount LDL Lowered	How It Works
Nicotinic Acid		10-20%	Slows the liver's production of certain chemicals needed to produce LDL.
Bile Acid Sequestrants		10-20%	Bind with cholesterol-containing bile acids in the intestines and are then eliminated in the stool.
Cholesterol Absorption Inhibitors		18-20%	Selectively decreases cholesterol absorption from food.
Fibrates	Gemfibrozil		Breaks down particles used to make triglycerides and uses them in other ways. Lower triglycerides, raises HDL.
Statins	Lipitor, Pravachol, Zocor	20-60%	Inhibit production of liver enzyme necessary to produce LDL.

Statins

HMG-CoA Reductase Inhibitors ("statins")

Atorvastatin (Lipitor)
Rosuvastatin (Crestor)

Simvastatin (Zocor)
Fluvastatin (Lescol)
Lovastatin (Mevacor)
Pravastatin (Pravachol)
Pitavastatin (Livalo)

Statins - Muscle problems and liver abnormalities are rare

Order regular liver function tests. Patients who are pregnant or who have active or chronic liver disease should not take statins

Statins

- **MOA:** HMG-CoA reductase is the enzyme responsible for the conversion of HMG-CoA to mevalonate, the early rate-limiting step in cholesterol synthesis = decrease LDL, decrease TGs, increase HDL

- ***** ONLY AGENTS PROVEN TO LOWER THE RISK OF CV EVENTS in patients with high cholesterol.**

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Statins

Side effects:

- < 0.1 % myopathy/myalgia/ myositis/rhabdomyolysis;
  - Including ocular muscles!!
- DM (FDA added warning of increased blood sugar and HgA1C to statin labeling)?
- Memory loss

Niacin (nicotinic acid):Vitamin B3

This drug works in the liver by affecting the production of blood fats. **Increases HDL**

Niacin side effects may include **flushing**, itching and stomach upset. Your liver functions may be closely monitored, as niacin can cause toxicity.

Niacin is used cautiously in diabetic patients as it can raise blood sugar levels and lower blood pressure

Niacin comes in prescription form

Niacin

- Niaspan
  - Only other agent that decreases LDL, TG, and increases HDL
  - Not proven to decrease death
  - SEs:
    - Cutaneous flushing
    - GI
    - Hyperuricemia
    - Loss of glycemic control in DM

Cholesterol Absorption Inhibitor

Selective cholesterol absorption inhibitors

This relatively new class of cholesterol-lowering medications works by preventing the absorption of cholesterol from the intestine.

Selective cholesterol absorption inhibitors are most effective at lowering LDL (bad) cholesterol, but may also have modest effects on lowering triglycerides (blood fats) and raising HDL (good) cholesterol.

The first medication of this class, **ezetimibe (Zetia®)****, was approved in 2002 for the treatment of high cholesterol and certain inherited lipid abnormalities.

Remember: diarrhea

Ezetemibe (Zetia)

- Lowers LDL only
- No mortality data
- Added to statins

Ezetemibe + Simvastatin (Vytorin)

Fibric Acid Derivatives

- Gemfibrozil (Lopid)
- Fenofibrate (Tricor)
- Fenofibric acid (Trilipix)

- Used for high triglycerides only
- No decrease in mortality

Fibrates (fibric acid derivatives):

Fibrates are best at lowering **triglycerides** and in some cases increasing HDL (good cholesterol) levels. These drugs are not very effective in lowering LDL (bad) cholesterol.

Fibrates currently available in the U.S. include:

Gemfibrozil (Lopid®)**
Fenofibrate (Antara®, Lofibra®, Tricor®, and Triglide™)**
Clofibrate (Atromid-S)**

Remember: muscle pain/weakness, gall stones

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Resins (bile acid sequestrant)

This class of LDL-lowering drugs works in the intestines by promoting increased disposal of cholesterol. The body uses cholesterol to make bile, an acid used in the digestive process.

These medicines bind to bile, so it can't be used during digestion. Your liver responds by making more bile. The more bile your liver makes, the more cholesterol it uses. That means less cholesterol is left to circulate through the bloodstream.

Resins currently available in the U.S. include:

Cholestyramine (Questran®, Questran® Light, Prevalite®, Locholest®, Locholest® Light)**
Colestipol (Colestid®)**
Colesevelam Hcl (WelChol®)**

Remember: bad taste, increase triglycerides, gall stones increase

Fish Oil

- Lovaza (prescription product)
  - DHA and EPA
  - Used to treat high triglycerides only
- Many other benefits!
  - Inflammatory diseases
- SEs:
  - Fishy taste
  - Increased bleeding time

Marine-Derived Omega-3 Polyunsaturated Fatty Acids (PUFA)

Referred to as omega-3 fish oils or omega-3 fatty acids, are used in large doses to lower **high triglyceride** levels in the blood.

They help decrease triglyceride secretion and facilitate triglyceride clearance. Because the amount of marine-derived omega-3 PUFAs needed for significant triglyceride lowering (2,000 to 4,000 mg daily) is difficult to attain through diet alone on a daily basis, supplementation with capsules may be needed.

Use of these supplements should only be under the direction and care of a physician because large doses of marine-derived omega-3 PUFA may cause serious side effects, such as increased bleeding, hemorrhagic stroke and reduced blood sugar control in diabetics or interact negatively with other medications, herbal preparations and nutritional supplements.

VASCEPA, along with diet, is clinically proven to lower very high triglycerides in adults by 33%, without raising bad cholesterol (LDL-C).

It's FDA-approved to lower very high triglyceride levels.

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Omega 3 Fish oil vs. Krill oil
Heart brain and eye health

EPA – eicosapentaenoic acid
DHA – docosahexaenoic acid

Increase in longevity, telomeres, HDL

Protects PUFA's in the cell membrane

Decrease inflammation and triglycerides

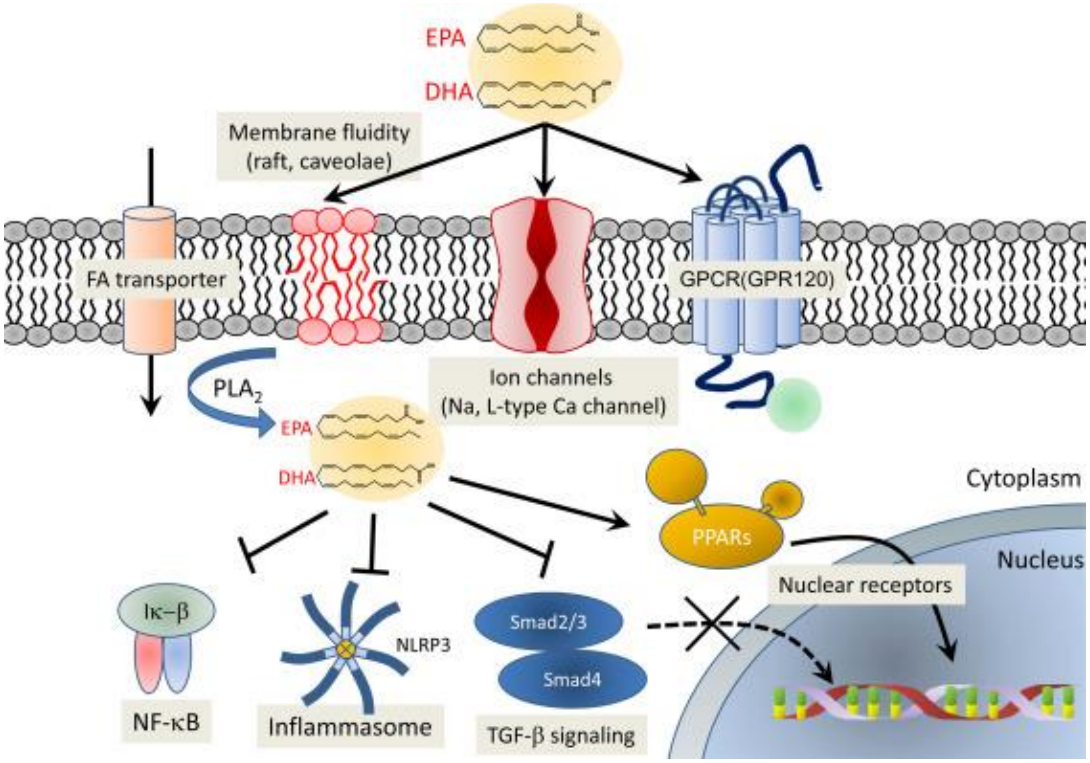
Absorption occurs in the small intestine

DHA most abundant in the brain

Fish oil is in **triglyceride** and **ethyl ester** form

Krill oil is in **phospholipid** form (most bioavailable)

Krill oil contains **astaxanthin** a carotenoid



"Dream" Study – NIH Study (olive oil vs. omega 3)

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Cardio-protective mechanism of omega-3 polyunsaturated fatty acids Author links open overlay panel JinEndo MD, PhD MakotoArita PhD

PCSK9 Inhibitors

Dosing:

- SC injection; once or twice per month
- $10,000 to $14,000 per year (average estimate)

Who might benefit: Certain types of familial hyperlipidemia;

- statin-intolerant patients
- poor response to statins
- contraindications to statins.

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Updated cholesterol guideline released November 13th 2013 by the **American Heart Association and American College of Cardiology** aim to prevent more heart attacks and strokes than ever. How? By increasing the number of Americans who take a cholesterol-lowering statin.

The new guidelines recommend a statin for:

Anyone who has cardiovascular disease, including angina (chest pain with exercise or stress), a previous heart attack or stroke, or other related conditions

Anyone with a very high level of harmful LDL cholesterol (generally an LDL above greater than 190 milligrams per deciliter of blood [mg/dL])

Anyone with diabetes between the ages of 40 and 75 years

Anyone with a greater than 7.5% chance of having a heart attack or stroke or developing other form of cardiovascular disease in the next 10 years.

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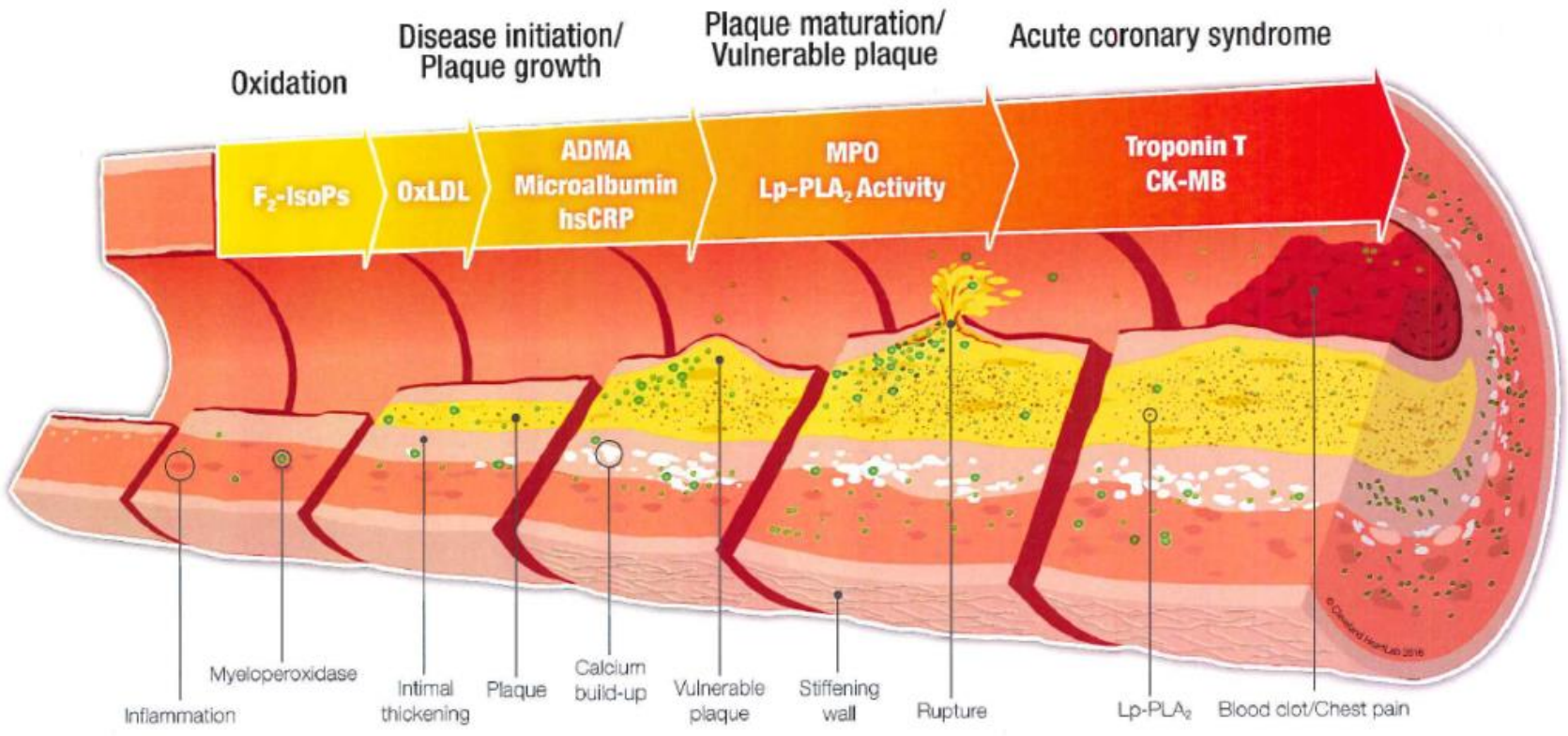

Coronary Artery Calcium Score (CACS) is looking at the arteries around your heart and the carotid intima media thickness (CIMT) is looking at the carotid arteries.

Elevated levels of urinary F2-IsoPs are seen in conditions associated with increased risk for atherosclerosis and certain forms of cancer

Hs CRP should not be > 3 , Myeloperoxidase (MPO) increase

Lp-PLA2, or lipoprotein-associated phospholipase-A2, measures disease activity within the artery wall below the collagen or calcified cap due to the activation of macrophages.

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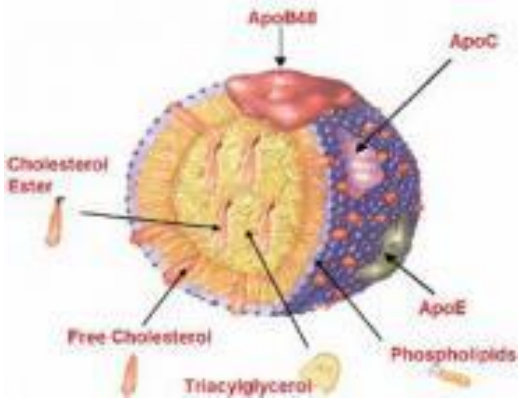
What APO-E Means for Your Health

APO E GENOTYPE CORRELATION TO TREATMENT RESPONSE

	Apo E2		Apo E3		Apo E4	
Genotype	*2/2*	*2/3*	*3/3*	*2/4*	*3/4*	*4/4*
Population Frequency	*1%*	*10%*	*62%*	*2%*	*20%*	*5%*

Genotype	E2/E2	E2/E3	E2/E4	E3/E3	E3/E4	E4/E4
Disease Risk	40% less likely	40% less likely	2.6 times more likely	Average risk	3.2 times more likely	14.9 times more likely



http://alzdiscovery.org

http://dpbheartdisease.homestead.com

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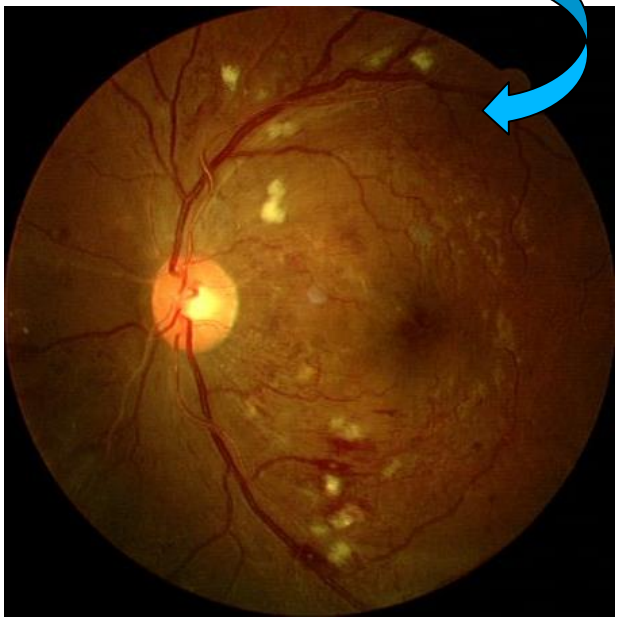
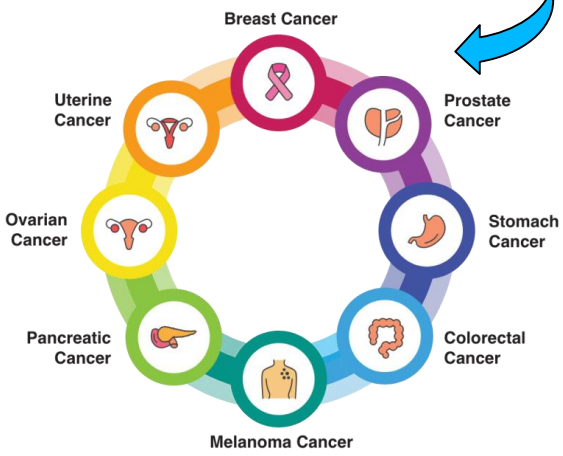
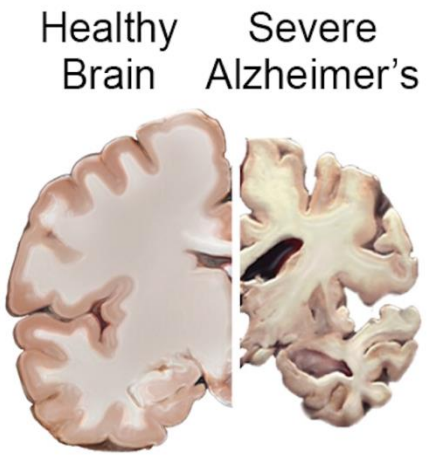
So when you see this:



Think this:





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Thank You!

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