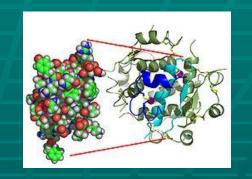


Insulin binding to Cell Receptors



Hyper-Insulinemia

1) A condition in which there are excess levels of pancreatic insulin circulating in the blood relative to the level of glucose.

2) Associated with HTN, Dys-lipidemia (High TG & sdLDL & Low HDL), IR & Obesity

"Metabolic Syndrome"

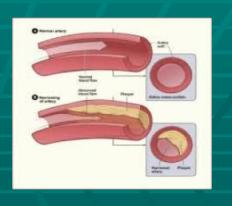
Insulin Resistance (IR)

1) A pathological condition in which cells fail to respond to insulin.

2) A useful adaptive condition in pregnancy & acute illness.



Type 2 Diabetes Spectrum (Diabesity)



- Elevated insulin-> Abdominal Obesity
 ->Inflammation → IR → Metabolic
 Syndrome → Pre-diabetes → type 2 DM
- Mild sugar imbalances---- full blown DM
- Different stages of the same disease
- Negatively impacts blood vessels
- All treated the same

Purpose of insulin

- 1) Stores energy as Glycogen (lasts 1 day), very little can be stored (muscle, liver) and remainder is stored as fat.
- 2) Lowers sugarSugar lowering hormone

Insulin is affected by + and – health behaviors

- Insulin is the main driver of obesity.
- Many things and habits can increase Insulin
 - Simple sugars 168 types in food chain
 - Refined grains
 - Carbohydrates
 - Animal proteins
 - Cortisol is also a major player in stimulating insulin secretion.
 - Fructose increases insulin resistance directly which indirectly leads to increased insulin levels.

Insulin Resistance (IR) Pathophysiology

- Increased insulin receptor resistance
- Increases circulating insulin
- Insulin is a storage hormone
 - storage of fat in viscera
- It results in the inability to mobilize fat for energy production
- It results in the burning of muscle for energy needs

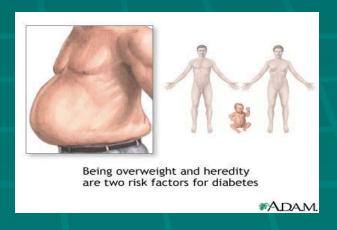
Type 2 DM cause is too much insulin, not too little



High insulin first sign of problems



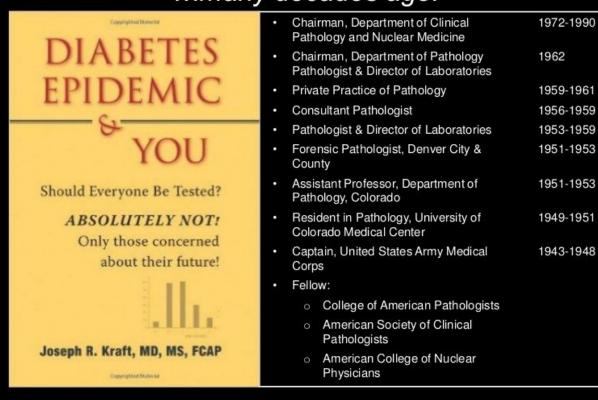
Isolated abdominal obesity (VAT) w/o equal obesity in buttocks (SCAT)



Joseph Kraft MD (1911-2017) Father of the Insulin Assay



KRAFT: The man who decoded Diabetes and Heart Disease ...many decades ago.



fasting serum glucose

Two Phases of Diabetes

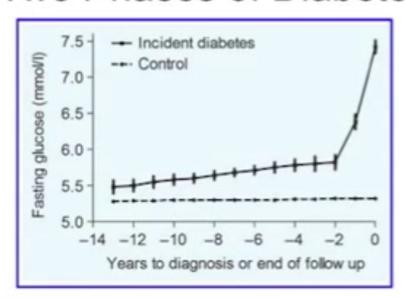
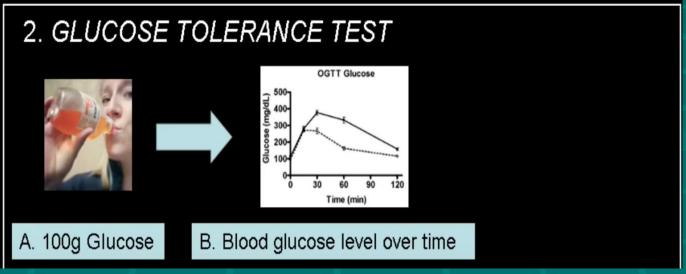


FIGURE 1 Change in fasting plasma glucose during the 13 years prior to onset of Type 2 diabetes. These data from the Whitehall II study demonstrate the elevation of plasma glucose within the normal range

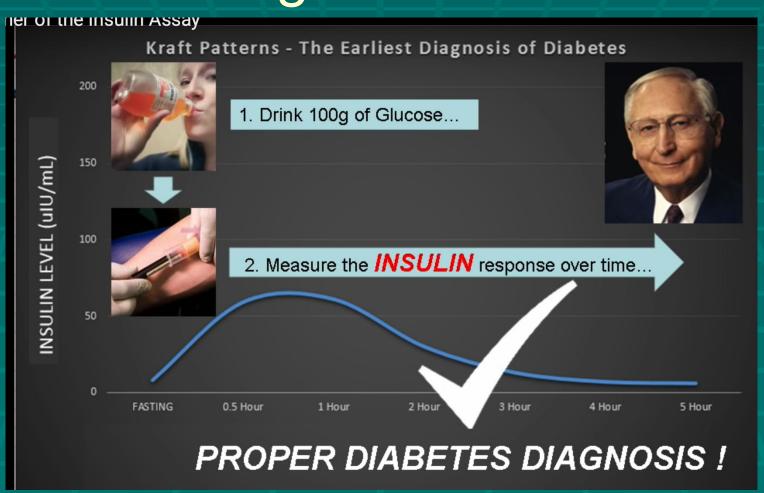
Trajectories of glycaemia, insulin sensitivity, and insulin secretion before diagnosis of type 2 diabetes: an analysis from the Whitehall II study. Lancet 2009; 373: 2215–2221.

PROPERLY DIAGNOSING *DIABETES*

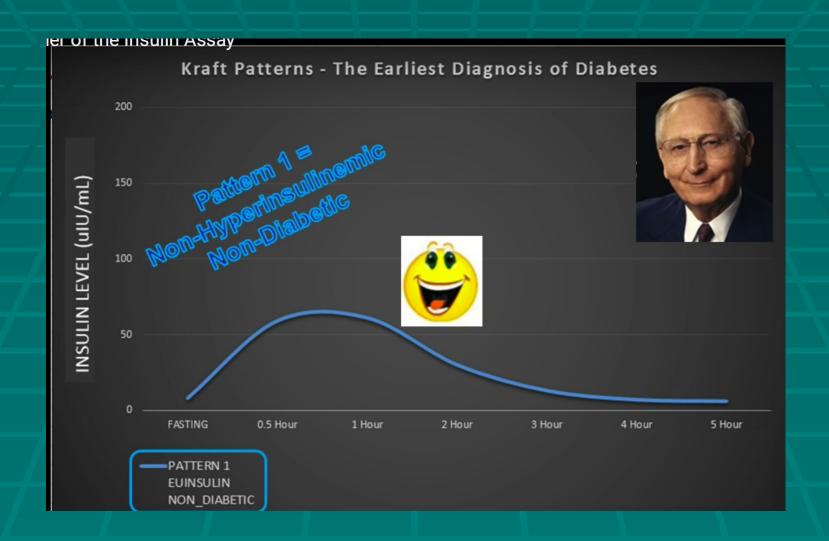




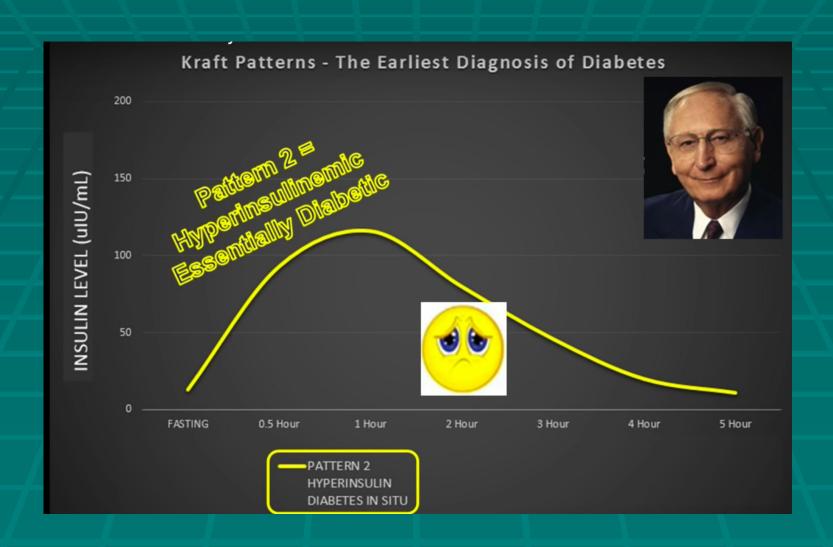
Kraft Test Earliest Diagnosis of Diabetes



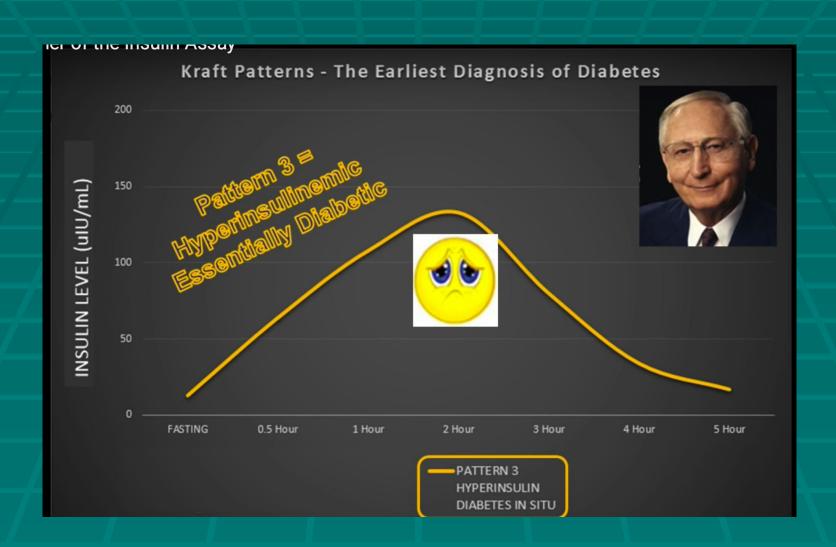
Euinsulin



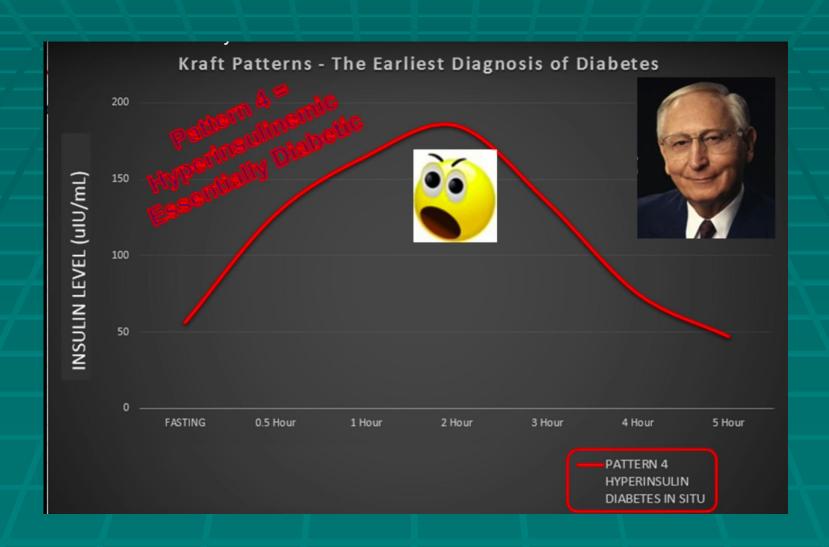
Pattern 2 Insulin



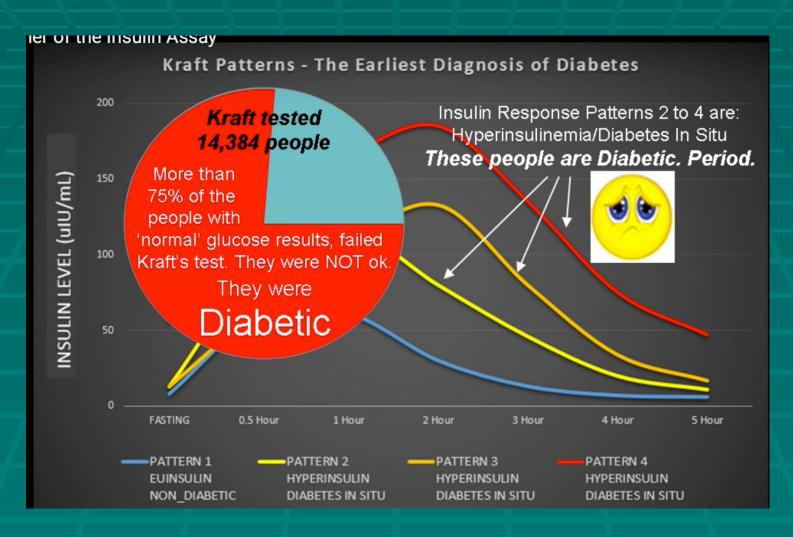
Pattern 3 Insulin



Pattern 4 Insulin

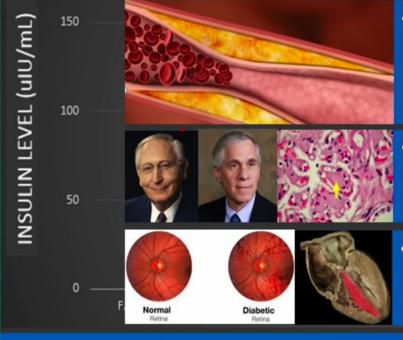


Insulin = "The Most Important Health Test You Can Get"



Kraft Patterns - The Earliest Diagnosis of Diabetes

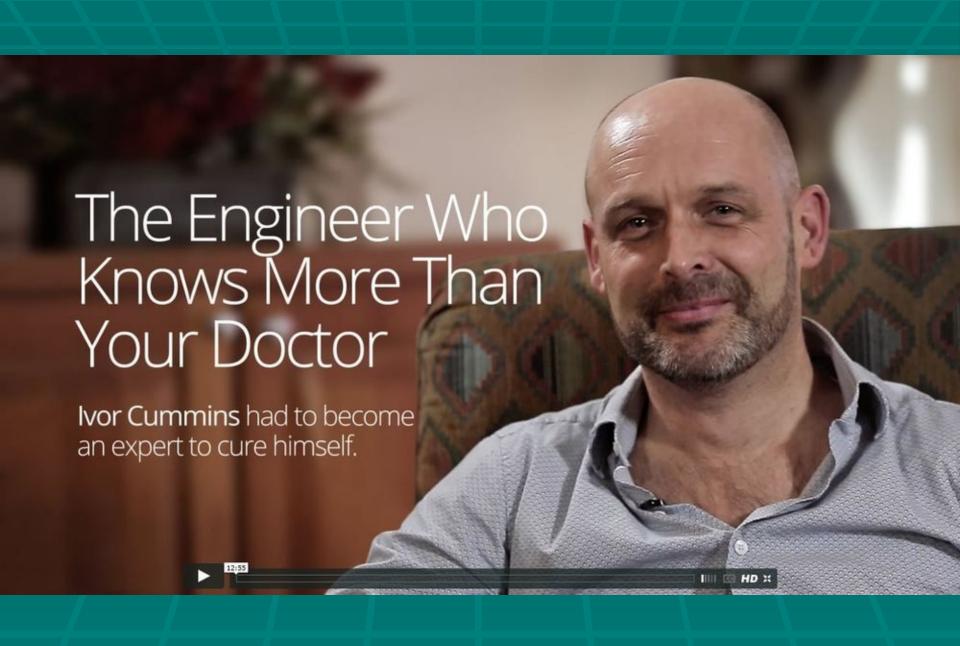
Critically, Kraft's research and >3,000 autopsies (personally conducted) led him to infer that:



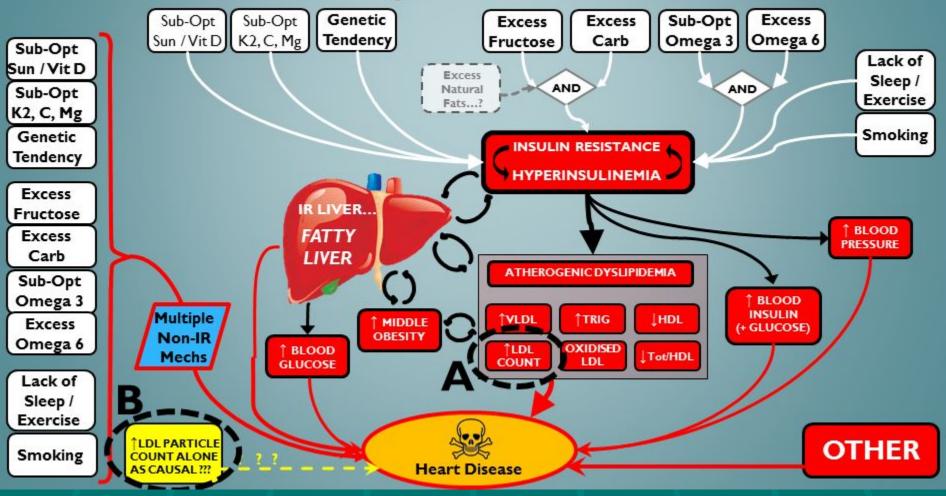
- The damage of diabetes is vascular: you must assume diabetes is the root cause, unless Pattern 1 demonstrated!
- The damage **precedes** the point where the glucose becomes elevated (ref: Kimmelsteil's work)
- This diabetic-driven disease is observed in all vessels, incl. micro vessels of the heart's IV Septum

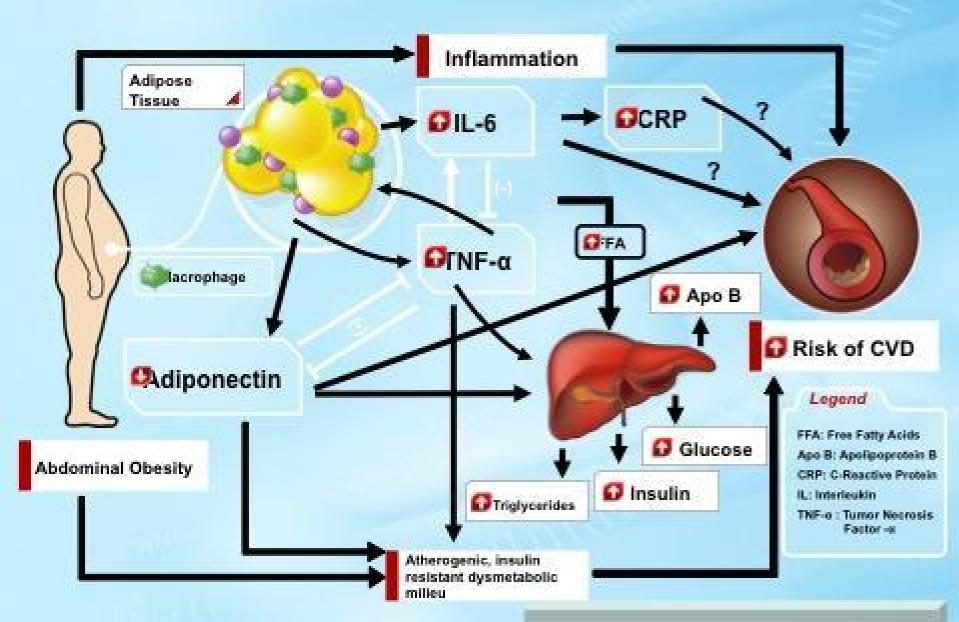
In summary, Kraft concluded that:

"Those with cardiovascular disease not identified with diabetes...are simply undiagnosed."



Draft Root Cause Diagram for Cardiovascular Disease





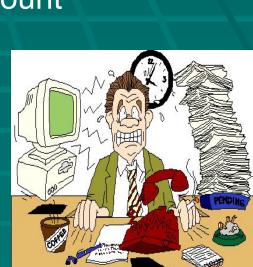
Hyperinsulinemia / IR and smoking



- Smoking has been shown to increase the risk of developing diabetes as well as diabetic retinopathy. Xie Xt, Liu Q, Acta Pharmacol. Sin. 2009
- Women whose mothers smoked while pregnant (1800 women)
 - Journal of Developmental Origins of Health and Disease)
 - 2 3 times more likely to develop diabetes as adults regardless of weight
 - Second hand smoke from fathers also increase risk of DM

Hyperinsulinemia / IR and Quality Sleep (affects 70% of Americans)

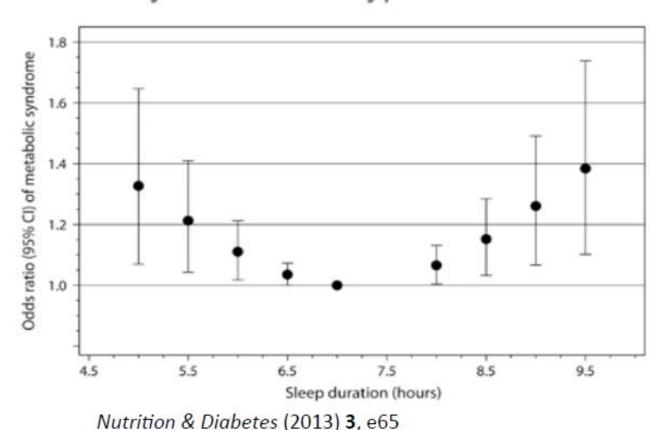
- Increases cortisol & lack of sleep increases insulin and cytokines
 - Can lead to wt gain, IR and type 2 DM
- Elevates cortisol (C), the stress hormone
 - C is Anti-inflammatory, but need correct amount
 - Raised BS causing abdominal fat gain
 - Increases BP
 - Causes liver to incease glucose (gluconeogenesis)
 - Decreases bone formation and loss of collagen in skin



Impairs memory: DM II have 4x inc risk of AD

Sleep and Diabetes Risk

Both long and short sleep duration, as well as napping, are associated with increased risk of Metabolic Syndrome and type 2 diabetes



More Bad News with Light At Night (LAN)

- Increased blue light exposure during the evening meal increases hunger & decreases insulin sensitivity x 2 hours
 Am Acad Sleep Med 2014
- Increased light at night exposure significantly elevated BP 4/3 mm Hg in Japanese subjects
 - —6% increased mortality -10K additional deaths

Chronobiol Int. 2014 Jul;31(6):779-86

 Increased LAN also significantly associated with increased rates of obesity and dyslipidemia independently of melatonin levels

J Clin Endocrinol Metab. 2013 Jan;98(1):337-44

Grave Yard Shift CDC reports shift work is known carcinogen

- Those working the night shift for one to two years had a 17 % higher risk for diabetes.
- Graveyard shift for 10
 years, jumps risk for
 diabetes to 42 %.
 nightsMedicineNet.com January 12, 2015



Obstructive Sleep Apnea

- Seniors who snore or suffer with sleep apnea
 - Are 27 and 50 % more likely, respectively, to develop type 2 diabetes compared to those who sleep well. (Diabetes Care September 17, 2015)
- "Getting good sleep is as important as nutrition and exercise to remain healthy during the aging process," Eve Van Cauter, a sleep and metabolism researcher at the University of Chicago

w3 / w6 ratio US Physicians Health Study

 People who consumed one fish meal per week reduced risk of sudden cardiac death by 52%



		Farm Raised	Wild Caught
	Nutrition	Lower levels of protein, omega 3's and found to contain more fats	Higher levels of Omega 3's and less fats
	Feed	Fed fishmeal consisting of conventionally grown crops most likely containing pesticides, herbicides and GMOs	Wild caught fish find their own natural food in the wild
	PCBs {Polychlorinated Biphenyls}	These highly toxic compounds are 8 times more present in farm raised fish	Very low levels of PCBs
	Mercury	Usually lower levels of mercury found in farm fish, however the fish being farmed in the ocean have the same levels of mercury as the wild caught	Some fish, especially Salmon, may contain mercury. This is why it is recommended no to eat fish everyday but instead maybe 2 times a week.
	Disease	Diseases, lice and pests are usually present. Fish usually given dose after dose of antibiotics to control the diseases. Also, pesticides and herbicides are present due to the fishmeal	Extremely low levels of diseases, no antibiotics, pesticides, herbicides or GMOs
	Environmental	Disease and excess waste pollute ecosystem and environment.	Farm fish that escape can wipe out a whole population of wild fish due to the disease it

Omega-3 Study

 People with history of heart disease who consumed 1 g omega-3 fats daily for 3.5 years had 25% decrease in myocardial infarctions and 33% decrease in sudden

(Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarcto Miocardico

(GISSI)-Prevention trial)





Higher omega-3 levels are associated with lower rates of

Death from any cause

Mozaffarian D, et al, Plasma Phospholipid Long-Chain omega-3 Fatty Acids and Total and Cause-Specific Mortality in Older Adults: A Cohort Study. Annals of internal medicine 2013;158:515-25.

Pottala JV et al, Blood Eicosapentaenoic and Docosahexaenoic Acids Predict All-Cause Mortality in Patients With Stable Coronary Heart Disease: The Heart and Soul Study. Circulation Cardiovascular quality and outcomes 2010;3:406-12.

Sudden cardiac arrest

Albert CM et al, Blood levels of long-chain n-3 fatty acids and the risk of sudden death. N Engl J Med 2002;346:1113-8.

Slower rates of cellular aging

Farzaneh-Far R et al, Association of marine omega-3 fatty acid levels with telomeric aging in patients with coronary heart disease. JAMA: the journal of the American Medical Association 2010;303:250-7.

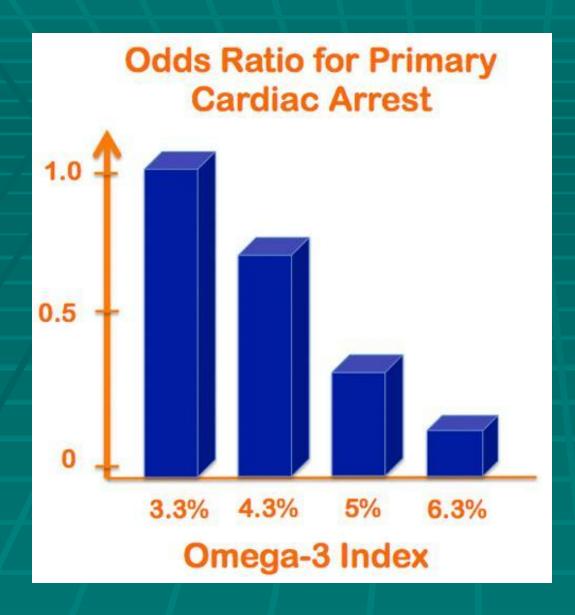
CA in several studies

The risk benefit for fish oils remains

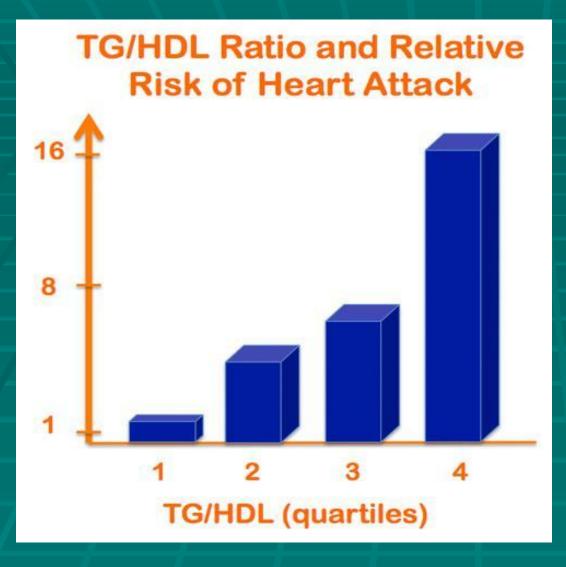


5-05-19 The Importance of Maintaining Eye Health as We Age Omega-3 Is Associated With Reduced Risk of AMD



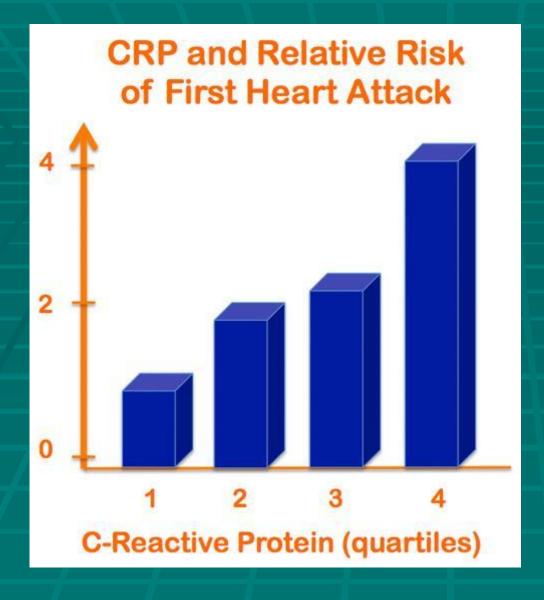


Omega-3 Index and risk for cardiac arrest. Several studies have linked 70 to 90% risk reduction in people with the highest Omega-3 index. Source: Harris, 2008.



Triglyceride to HDL ratio is a reliable predictor of heart attacks. People with the highest levels are 16-times more likely to suffer heart attacks than those with the lowest. Source: Gaziano et al.,

www.Omega3via.com



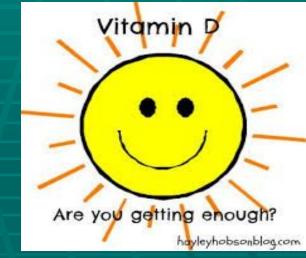
www.Omega3via.com

C-Reactive Protein and relative risk of first heart attack.
People with the highest CRP have a 4-fold increased risk for heart attacks.
Source: Ridker et. al., 1997.

Vitamin D3 and Omega III, vitamin C / polyphenols are all anti-inflammatory

Hyperinsulinemia / IR and Vitamin D

- Lowers systolic BP 14 mm/Hg
- Increases pancreatic output of insulin
- Increases peripheral insulin sensitivity
- Reduces inflammation
- Colds and Flu
 - Among 19,000 Americans, those with the lowest vitamin D levels had significantly more colds or cases of the flu.(Arch Intern Med. 2009)
 - At least five additional studies show an inverse association between lower respiratory tract infections and vitamin D levels

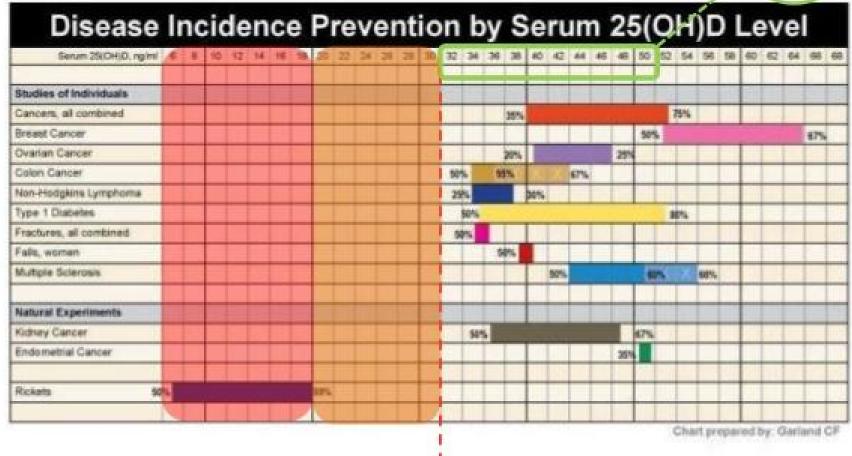


Hypovitaminosis D

- 70%--80% of Americans deficient in Vitamin D
- Every cell in body has Vitamin D receptors
- Low D → abnormal immune response
- Partly responsible for <u>fat cell growth</u>
- Optimal vitamin D levels decrease your risk of cancer by MORE THAN HALF
- Low D → Increases Insulin Resistance

Prelude – The Implications of Low...





References:

All Cancers: Lappe JM, et al. Am J Clin Nutr. 2007;85:1586-91. Breast: Garland CF, et al. J Steroid Biochem Mol Biol. 2007;103:706-11. Colon: Gorham ED, et al. Am J Prev Med. 2007;32:210-6. Diabetes: Hypponen E, et al. Lancet 2001;358:1500-3. Endometrium: Moltr SB, et al. Prev Med. 2007;45:323-4. Falls: Broe KE, et al. J Am Geriatr Soc. 2007;55:234-9. Fractures: Bischoff-Ferrari HA, et al. JAMA. 2005;293:2257-64. Multiple Scienosis: Munger KL, et al. JAMA. 2006;296:2832-8. Non-Hodgkin's Lymphoma: Purdue MP, et al. Cancer Causes Control. 2007;15:989-99. Ovary: Tworoger SS, et al. Cancer Epidemiol Biomarkers Prev. 2007;16:783-8. Renal: Moltr SB, et al. Int J Cancer. 2006;119:2705-9. Rickets: Arnaud SB, et al. Pediatrics. 1976 Feb;57(2):221-5.

Vitamin D in the body is inversely associated with the risk for developing type 2 diabetes in adults."

- 5,200 Australian adults, "high serum levels of 25-hydroxyvitamin D (25OHD) levels, but not dietary calcium, were associated with a significantly reduced risk for developing type 2 diabetes during five years of follow up
- Those w/ highest concentration of 25 hydroxy D
 - Reduced progression from prediabetes to diabetes
- With each 25 nmol/l increase in serum 25OHD...associated with a 22% to 29% decreased diabetes risk

Journal Diabetes Care 2011

Hyperinsulinemia / IR and W3

- Omega-3 oils (most people are deficient)
 - Affects cellular circulation
 - Affects Cell membrane fluidity →
 increases insulin receptor sensitivity –
 Glut 4 receptor migration to cellular
 membrane.
 - Vitamin E added→ prevents oxidation of fragile Omega-3 oils

Hyperinsulinemia / IR and Environmental Toxins

- People should not take environmental toxins lightly as we are surrounded by over 80,000 environmental toxins
- increase IR and the risk of diabetes. Lancet Jan 26

2008 and J Med Toxicol 2010.

· 1-Heavy metals role:

- Four metals, namely lead, arsenic, cadmium and mercury, are of particular concern in food because of their toxicity, especially for long term (chronic) intake since they may accumulate in the body and cause organ damage particularly to susceptible groups such as foetuses and young children.
- Although acute poisoning from these metals is possible, it is more likely that it happens through non-food route. Each of these metals also forms numerous compounds with other elements, which vary in properties and levels of toxicity to humans when ingested.
- Other than through exposure in workplace, some of these metal contaminants enter our body mainly through the food we eat while others mainly enter our body through other means like from the air we breathe or from direct skin contact.

The "Dirty Dozen"

aldrin 1
chlordane 1
dichlorodiphenyl trichloroethane (DDT)1
dieldrin1
endrin1
heptachlor1
hexachlorobenzene 1,2
mirex1
toxaphene1
polychlorinated biphenyls (PCBs) 1,2
polychlorinated dibenzo-p-dioxins2(dioxins)
polychlorinated dibenzofurans2 (furans)

- 1-Intentionally Produced.
- 2-Unintentionally Produced Result from some industrial processes and combustion.

For more information, see table below.

Environmental Toxins

- The average US women uses 12 personal care products and/or cosmetics a day, containing 168 different chemicals Environmental Working Group (EWG)
- About 80 percent of the women who develop breast cancer:
 - Have no family history
 - Environmental chemicals, including those that disrupt your body's hormone systems (endocrine-disrupting chemicals) are thought to play a significant role. Idaho Mountain Express July 29, 2015



"Environmental medicine" is no longer fringe

- Several studies have linked high dioxin burdens to increase risk of diabetes (POP = Persistent Organic Pollutants)
 - Almost all human have DCL stored in fat tissues (Env health perspectives 2001)
- A strong dose –response between serum concentrations of 6
 POP's and the prevalence of diabetes (diabetes care 2006)
 - 37X greater risk of diabetes in highest quintile vs lowest (dioxin, oxychlordane)
 - These 6 were detectable in 80% of participants
- Prediabetes and diabetes had higher serum concentrations of several POPs compared with normoglycemic individuals. (J Clin Endocrinol Metab, September 2012)
 - 2), dioxin-like polychlorinated ,biphenyls (PCB) , non-dioxin-like PCB (4 –7), and or-ganochlorine (OC)

Environmental Toxins,Diabetes and obesity

- Coexposure of both obesity and POPs was a strong determinant of diabetes, with a 9 fold increase odds of having diabetes
- Toxins cause diabetes by several different mechanisms
 - decrease pancreatic insulin production
 - impair insulin receptors
 - disrupt intracellular glucose metabolism.







Mancozeb

- A toxic chemical that is used in research to induce Parkinson's disease in experimental animals.
- 104 studies show a two-fold increased risk for developing diabetes.



Chemicals have been found to promote hyper-insulinemia / IR

 A number of chemicals have also been found to promote obesity by disrupting your hormones.

- This includes but is not limited to include
 - bisphenol-A (BPA),
 - PCBs,
 - phthalates,
 - triclosan,
 - agricultural pesticides,
 - fire retardants.
 - agricultural chemicals,
 - glyphosate in particular, may also affect your weight by healthy gut bacteria.









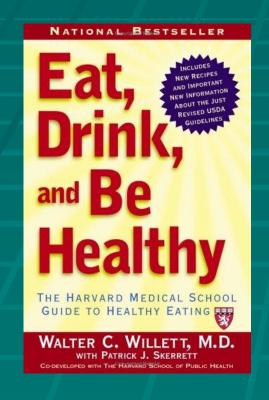
Nutrigenomics

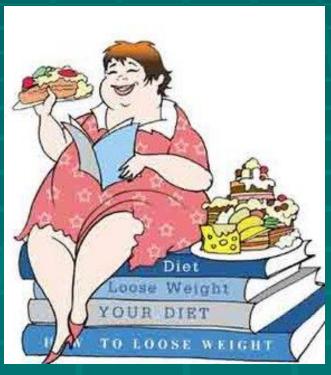
How nutrition affects your genes

- Genetic predisposition may play a small role
- However, Lifestyle & environment modulate genes to create changes moment to moment in biological functioning
 - Creates health and disease
 - Changes gene expression



Walter Willett M.D. Eliminate 90% type 2 DM 70% CVA & Colon CA & 82% MI







DMII is 90 % curable -- Archives of Internal Medicine May 2009

Diabetes is an environmental disaster

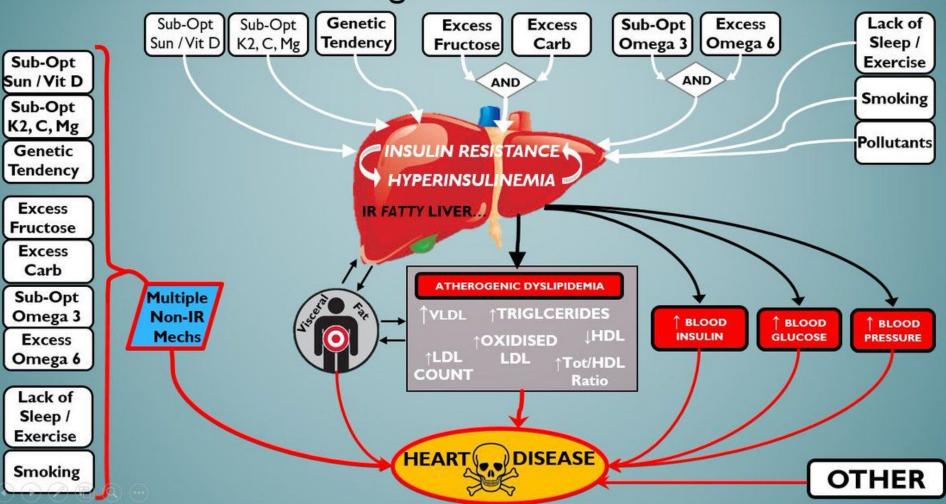
- 38%-50% of Pima Indians living in US have diabetes
- Only 6% living in Mexico have diabetes





Obese in 1 generation

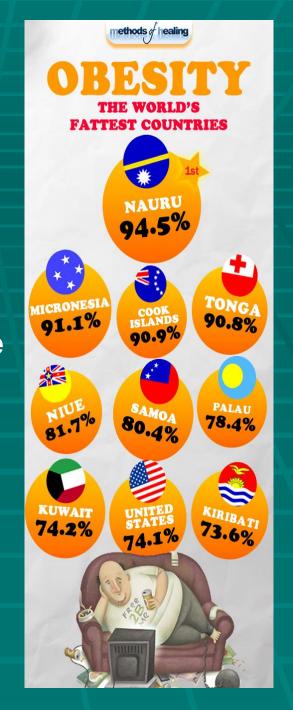
Draft Root Cause Diagram for Cardiovascular Disease



SummaryFactors Affecting Your Weight

Factors contribute to hyper-insulinemia / IR and poor health, and *all* of them need to be considered if we are to successfully address the Diabesity epidemic:

- 1. Stress & Lack of sleep & exercise
- 2. Processed food
- 3. Omega III & Vitamin D & micronutrient deficiencies
- 4. Chemicals (in food, environment, and everyday household products)
- 5. Antibiotics (in medicine and in food production) microbiome



Measuring Fasting Insulin and 2 hour insulin is key

Patterns 2,3,4 - Hyperinsulinemia

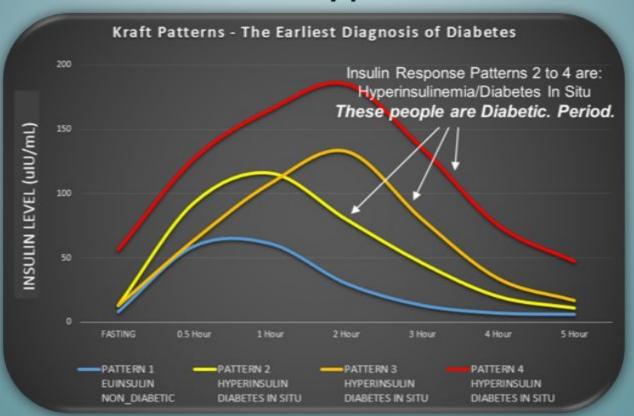


Image curtesy Ivor Cummins BE(Chem) CEng MIEI

Elevated Insulin Causes (Hyperinsulinemia)

- Cancer
 - Decrease apoptosis, growth promoter
- Weight gain
- Atherosclerosis→ hyperinsulinemia is primary driver
 - Hyperinsulinemia Makes all stages of atherosclerosis worse
 - Increased adhesion molecules expression on endothelial cells
 - Increased trans-endothelial migration of leukocytes (wbc cells get into blood vessel wall)
 - Stimulation of smooth muscle proliferation
 - Pro-inflammatory cytokines

Elevated Insulin Causes (Hyperinsulinemia)

- The fundamental pathology of diabetes is vascular
 - This involves every capillary, every small artery, every major artery, all have potential for involvement
 - When degree of involvement is excessive certain things will happen
 - Diabetic Retinopathy
 - Need Fasting and 2 hr insulin tested
 - ED patient are at least pre-diabetic or diabetic
 (20 million people in US) need Kraft test
 - Heart Kidney Brain etc. All INVOLVED

Elevated Insulin Causes vascular tree destruction

Thrombosis (plaques have insulin receptors)

Insulin inhibits fibrinolysis Diabetes 2006

Hyperglycemia stimulates coagulation increase of thrombotic event Diabetes 2006

MI and Stroke

Stimulates sympathetic nervous system

MI 2x-3x more likely after high carb meal vs. high fat inc Insulin constrict arteries

Calcified arteries

Elevated blood platelet adhesiveness

Retinopathy

Increase Blood pressure

Loss of magnesium→ vasocontriction

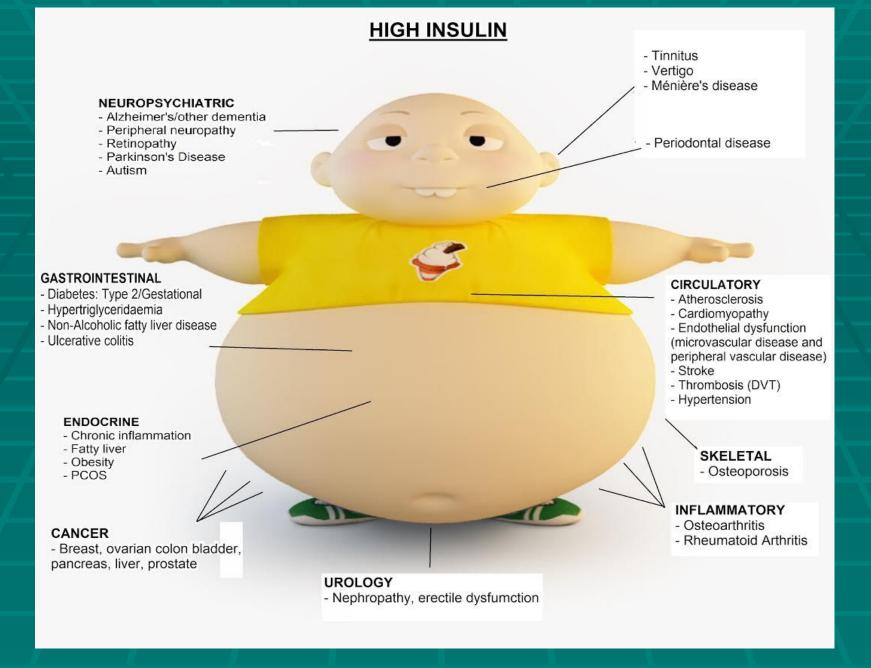
Causes fatigue need MG++ for energy production

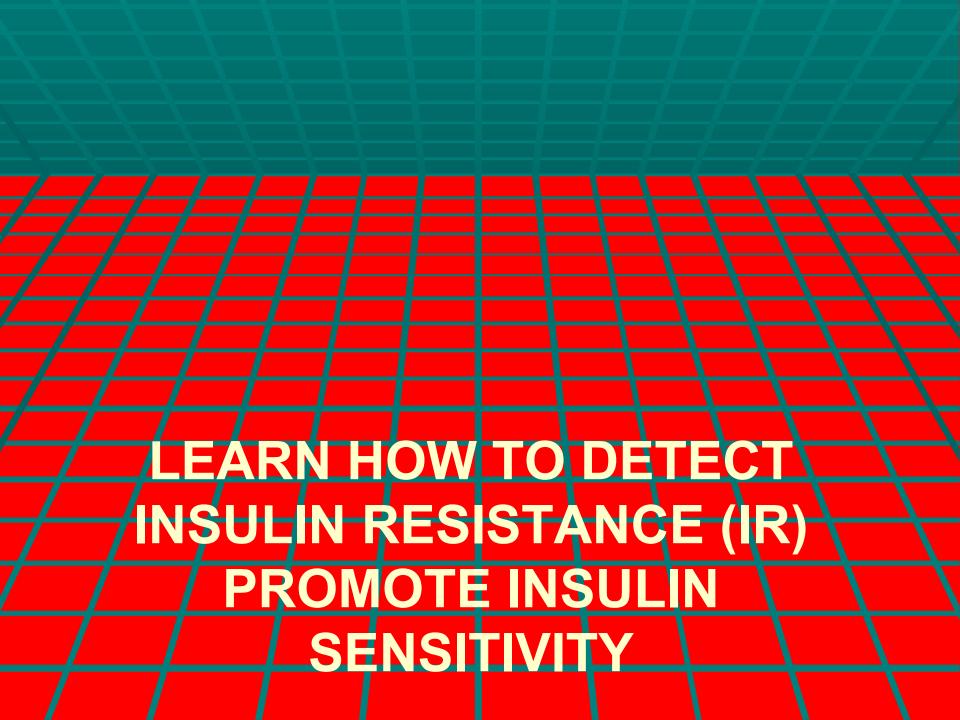
Lowers NO

Impairs sodium balance at level of proximal tubule causing HTN and edema

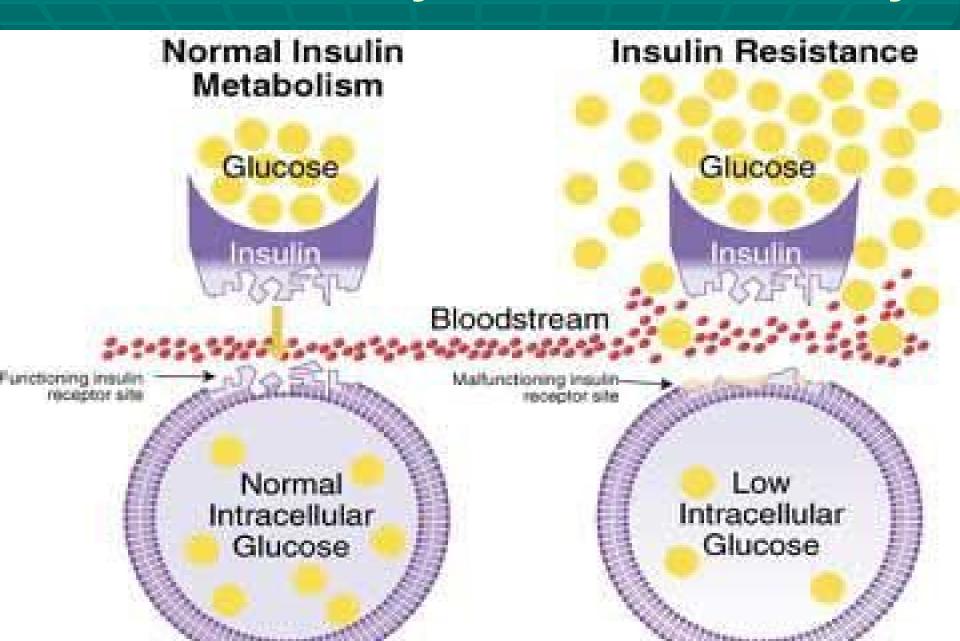
Elevated Insulin Causes other diseases

- Alzheimer's
 - promotes formation of beta-amyloid in brain
- Kidney damage
- Hypothyroid (Hashimotos) worsened
 - (BUT RULE OUT Hypothyroid as-looks like METABOLIC SYNDROME)
- Abnormal lipids
 - Increase liver production of TG
 - Increased liver production of small dense LDLparticles
 - Almost direct correlation of triglyceride levels with Insulin levels
- Increase estrogen in men and increase testosterone in women





IR / Metabolic Syndrome / Diabesity



Insulin Resistance

- Liver → muscles → fat (order of resistance)
 - Liver resistance.... liver makes sugar when sleeping→ Fatty liver → inc fasting insulin
 - Muscle resistance...can't burn sugar made by liver→ blood sugar goes up
 - Fat cells store fat until become IR (takes long time to become fat resistant)
 - Weight goes up until plateau
 - Pancreas keeps making insulin until it poops out

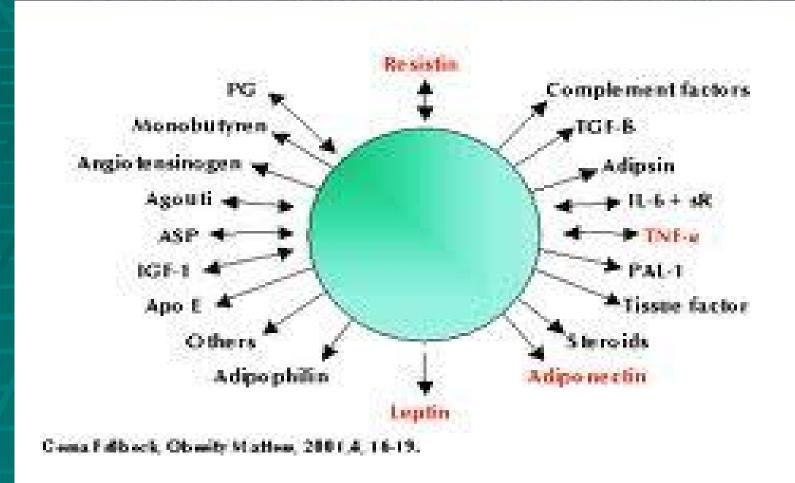
Blood sugar Rise from IR

Initially after meals

Then in fasting state

Now type 2 DM

Adipose Tissue as an Endocrine Organ



Fat cells release adipokines (cytokines) inducing inflammation.

Elevated insulin or Hyperinsulinemia

- It is the elevated levels of insulin that cause
 - High blood pressure
 - angiotensin
 - Abnormal cholesterol
 - Inflammation
 - higher CRP
 - Not high blood sugars.

Metabolic Syndrome consists of excess abdominal body fol, high triglyoerides, low HDL, and often hypertension.

Risk for premature death

Glucose Tolerance Factor

Chromium III (i.e. from Brewers Yeast)

- Cr complex of nicotinic acid and three amino acids (glycine, cysteine and glutamic acid)
- Potentiating insulin-like effect by acting on cellular signals (phosphorylation and enzyme activation) downstream of the insulin receptor.
- Plasma chromium inversely associated w pre-DM and type II DM.
- RDA lowered in 2001 from 50–200 μg for an adult to 30–35 μg (adult male) and to 20–25 μg (adult female).
- 2 Meta-analysis studies
- 0.6 HbA1c drop in DM II patients

Nutr Hoen 16:33/1):27 2016

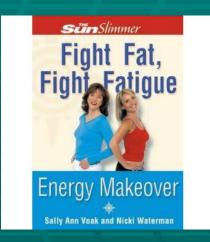
- Diabetes Care 30:2154–2163, 2007 ---
- 29.26 mg/dL drop in BG, p = 0.01, CI 95% = -52.4 to -6.09

The Biochemical Role of Macro and Micro-Minerals in the Management of Diabetes Mellitus and its Associated Complications: A Review.

Int J Vitam Nutr Res. 2015;85(1-2):88-103

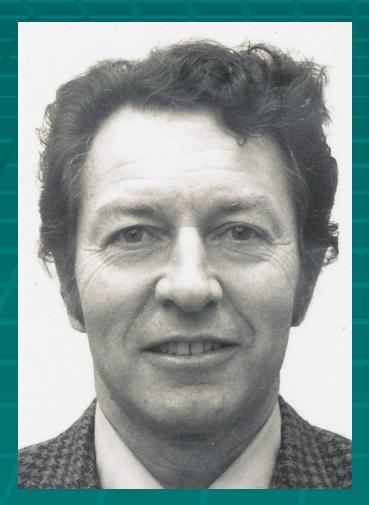
"Chromium, vanadium, zinc, molybdenum and magnesium can enhance insulin activity while molybdenum, manganese and zinc stimulate lipogenesis. Zinc and iron can modulate glucose, metabolizing enzymes in the gastrointestinal tract and limit oxidative stress, respectively"

IR Effects (common)



- Hunger, Lethargy & Brain fog
 - Carb craving, sleepiness
- Weight gain, abdominal fat storage and difficulty losing weight
- Increased cholesterol, high TG, low HDL
- Increased BP
- Increased uric acid
- Rising blood sugar

The "glucose – ascorbate antagonism theory"



1923 - 2011 Dr John Ely

In 1973, Dr John Ely related to Linus Pauling a theoretical reason why the clinical trials of oral vitamin C (IV Vitamin C is effective) against cancer may have failed because of the high blood sugar levels in the affluent nations. The GAA was described in over a dozen peer reviewed publications, as well as, several articles in the Journal of Orthomolecular Medicine. http://orthomolecular.org

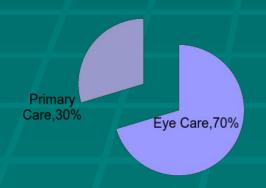
THE PROACTIVE **OPTOMETRIST**

Primary Eye Care is the Ideal Channel to Screen for IR / Early Diabetes

Eyecare Professionals see more patients Consider in 2011 there were:

- 40 million visits to primary care / family care providers where they might have had a blood draw
- 95 million visits to primary eyecare providers (More than 2 times the number of visits)

Patient Visits for Annual Exam



Bottom line: One is more likely to see an eye care provider than a primary care provider

Implications of Pre-diabetes and the Relevance of Early Intervention

 1 out of 12 patients with pre-diabetes have some form of diabetic retinopathy.

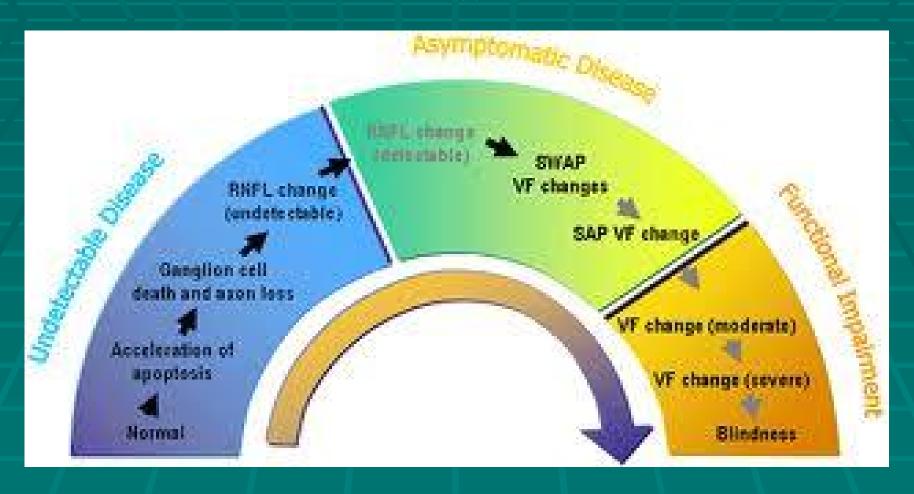
(Diabetic Retinopathy Without Diabetes. Chous, P. (August 16, 2005) http://www.diabetesincontrol.com/articles/64-/3019-)

If these patients are diagnosed early, almost 100% can prevent full blown diabetes with proper lifestyle modifications

(National Diabetes Education Program http://ndep.nih.gov/diabetes-facts/)

GLAUCOMA OFFERS A MODEL

Figure: The Glaucoma Continuum: Adapted from Weinreb et al. Am J Ophthalmology. 2004;138:458-467.



Hyperinsulinemia / IR and the Eye (recurrent chalazions!)

 Up to 1/3 of diabetics manifest a skin disorder during there lifetime. Styes, boyles, carbuncles are some examples.





Pre DM II- Visible During Eye Exam Dermatologic signs of hyperinsulinemia

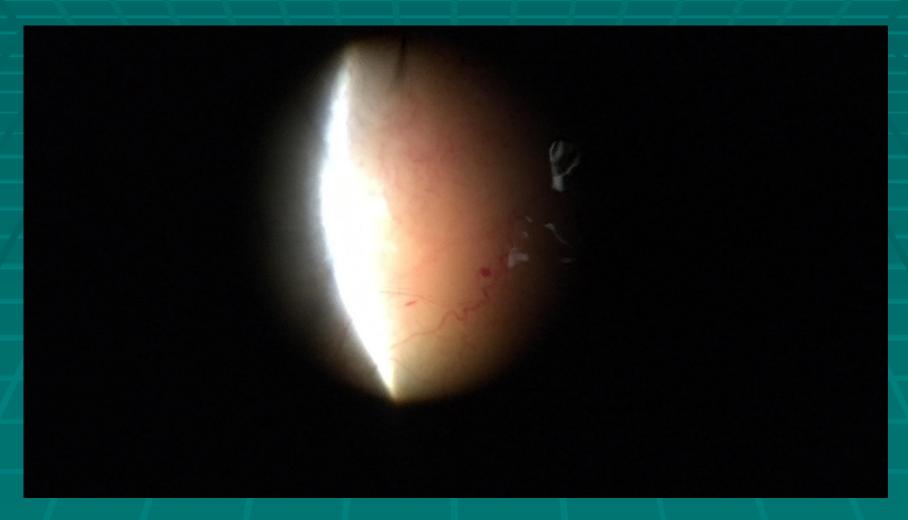








Conjunctival Microaneurysms (glucose-ascorbate antagonism)



Pre- DM II

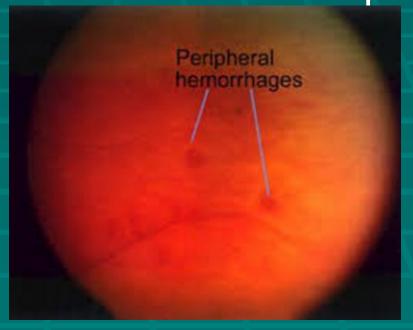
- 86 Million people older than 20 y/o
 - Unfortunately most are unaware
 - Ther have Pre Diabetes
 - 93% of people with prediabetes are undiagnosed (CDC)
 - Blood glucose levels higher than normal but not above classification for diabetes
 - A1C in 5.7%-6.4% range
 - Fasting blood sugar of 100-125 mg/dL and/or;
 - 2 hour glucose tolerance of 150-199 mg/dL

Pre DM II - Peripheral Retinal Heme is <u>Highly Predictive</u>

3-fold increased risk of DR progression

Nearly 5-fold increased risk of developing

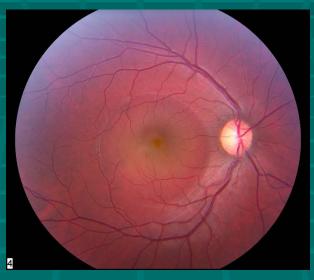
proliferative DR

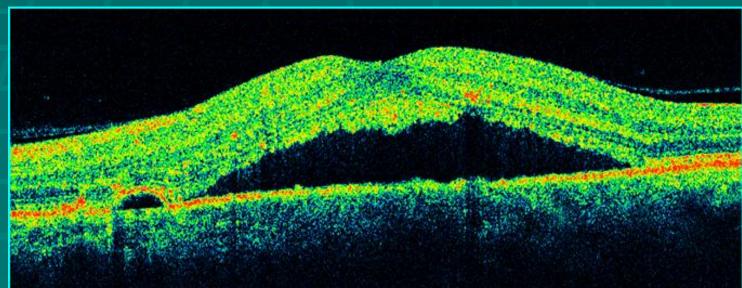


Silva PS, Cavallerano JD, Haddad NM, et al. Peripheral lesions identified on ultrawide field imaging predict

increased risk of diabetic retinopathy progression over 4 years. Ophthalmology. 2015;122(5):949-956 .

What Retinal Condition comes from Elevated Cortisol?





EBM = Statistical Medicine



Prescription Drug Use

Ignore science, Promote commerce

- 59% of American adults now use at least one prescription drug
 - 50 percent increase from a decade ago
- Harvard's T.H. Chan School of Public Health
- About 15 percent of adults now take more than 5 drugs,
 - Researchers suggest this rise in drug use may be related to an increase in obesity.
- Nearly 1 in 5 Baby Boomers have diabetes, 40% are obese and more than half take prescription drugs. Medscape May 7

Diet, Nutrition and Lifestyle are the most scientific way to head off aging and degenerative disease.

- Add nutrient dense food
 - Supplement with comprehensive multi-mineral
- Minimize individual toxic foods / ingredients
 - Sugar / HFCS / Vegetable oils / Harmful GMOs
- Correct digestive issues
 - Address individual dysbiosis, gluten, candida, fat and protein digestion, etc.
- Lifestyle Issues
 - Increase parasympathetic activity i.e. deep breathing
 - Individualize mental / emotional / spiritual dimension
 - lymphatics / circulation exercise



Alternative- Preventive Ocular Medicine

Functional medicine

leverage our training in physiologic optics

1) AMD center of excellence

- Beyond AREDS, AREDS II high risk supplements
- Beyond heroic anti-VEGF rescue treatments
- Early diagnosis and mitigation of risk factors

2) Low tension glaucoma

- . 40 % of all glaucoma
- . Aligns with primary care, internal medicine / cardiology

3) Scheie 3 decision point retinopathy

- Precocious retinal disease and / or arcus seniiis
- Often minority patients
- Aligns with primary care, internal medicine and cardiology

4) Age related cataract

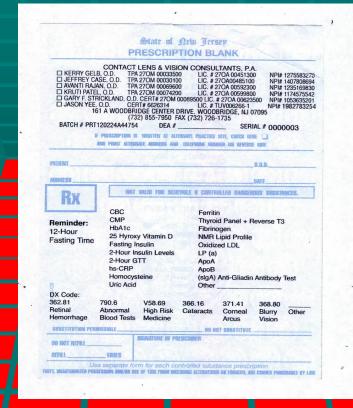
Measurement and topical / oral treatment(s)

Where will optometry (your practice) find itself in the year 2025?

- Competing with on-line refractions and internet eyeglasses?
- Competing with and adopting Academic & Clinical Ophthalmology as "our model"
 - Yes, but only 15 20 % profession writes 90 % of all pharmaceutical Rxs
 - Yes, Laser & minor surgical procedures by legislation i.e. Refractive surgery co-management
 - Yes, Glaucoma management

Leptin Resistance

- Constant & Poor Quality Foods
 - High CHO and fructose, HFCS
 - High Protein
 - Gluten
 - GMO
 - Poor quality oils
 - Low Vegetable & Fruit Consumption



LAB TESTS

EVALUATING IR AND ADVANCED CARDIOVASCULAR PARAMETERS

57 y/o WM ... RX shift +150 D AC Δ's Retina unremarkable Meds Niaspan, lipitor, Folic Acid, Benicor



Case 1

FBS 108 BP 142/96 2h glucose 105 HbA1c 6.4 Fasting insulin 26.3 2hr Insulin 41.6 25 (OH)D 18.5 Lp(a) 37 Hs-CRP 1.48 TCHOL 153 TG 160 **LDL 81 HDL 36**

Lab Tests to evaluate IR / CVDz Health



BASIC

Also good predictors

- 1. Fasting, 2hr Insulin . homocysteine,
- 2. Triglyceride / HDL 2. apoB (sdLDL)

3.

ratio

CRP (C Reactive

Protein)

1. Omega 3 Index

- 4. ferritin,
- 5. TSH r/o thyroid

oxLDL,

6. GGT / ALT want low

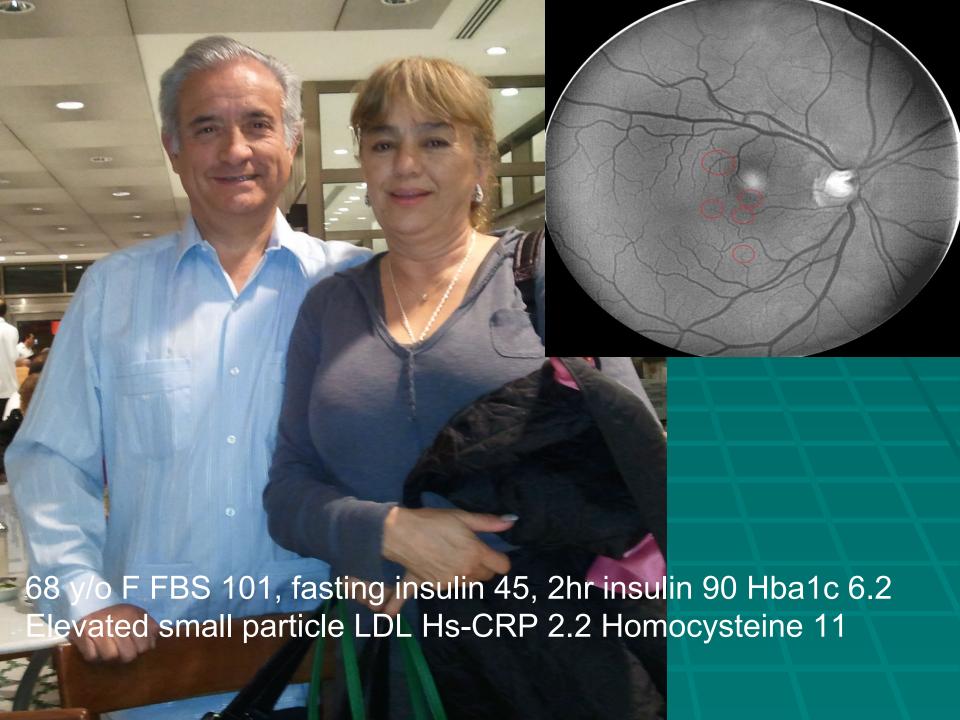
coloium cooro CAC

7. * Coronary artery

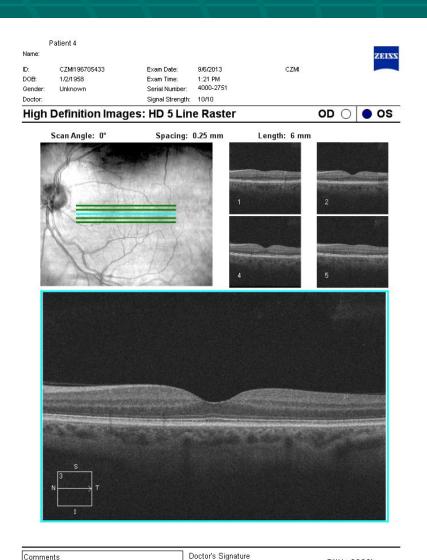
INSULIN

- Fasting Insulin < 5 ul/ml ideal
- Fasting Insulin >10 ul/ml = IR
- Postprandial > 30 ul/ml =IR

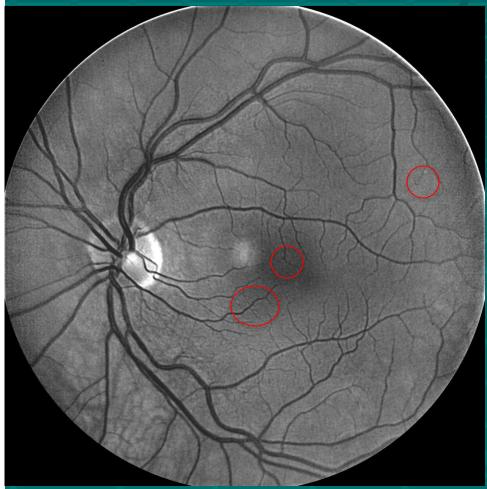
Should not be > 3x fasting Insulin levels



Patient #5 OS OCT and MSI Yellow



Copyright 2012 Carl Zeiss Meditec, Inc All Rights Reserved Page 1 of 1

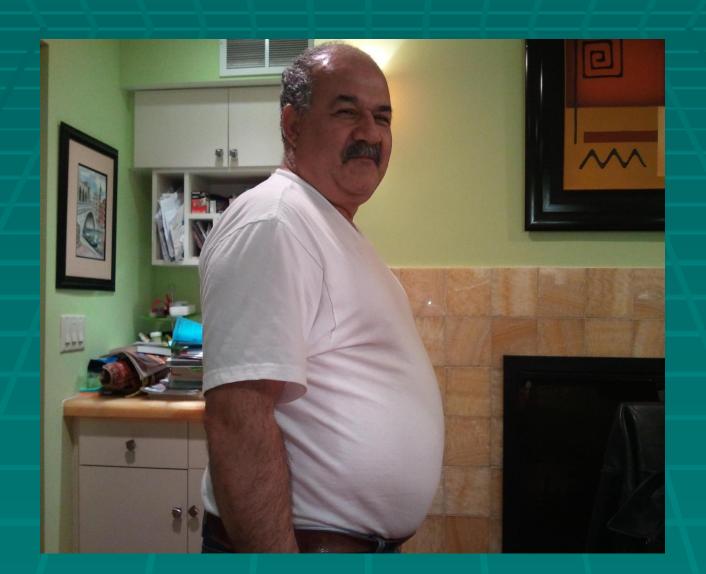


Polypharmacy

- BF 57 y/o overweight W/M +DM +HTN high cholesterol gout (uric acid)
 - Meds
 - Metformin
 - Actos
 - Byetta
 - Linsinipril
 - HCTZ
 - Norvasc
 - Bystolic
 - Asprin
 - lipitor
 - Allopurinol
 - Viagra



3 Weeks on 10 Point Plan Diet



MAGING TECHNOLOGY FOR IYPERINSULINEMIA & IR



The ALLDocs Study

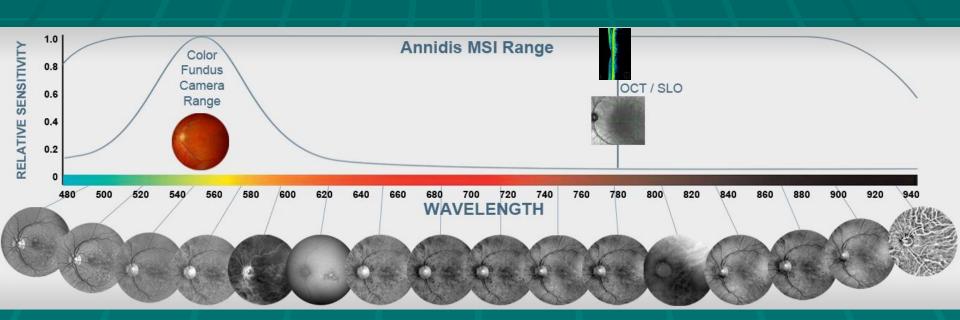


Multi-Spectral Imaging of Subclinical Microaneurysms is Correlated with Insulin Resistance Parameters and Vitamin D Liver Reserve Status

- Kerry M. Gelb, OD
- Stuart Richer, OD, PhD, FAAO
- Jerome Sherman, OD, FAAO
- Jeffrey M. Gold, DO, FACC
- Cheryl N. Zimmer, OD*

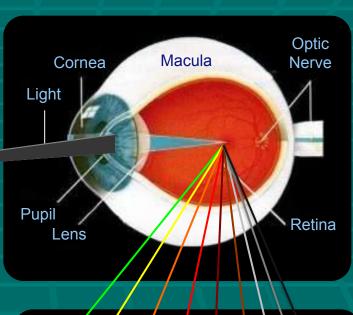
^{*}Conflict of Interest: Dr. Cheryl N. Zimmer is an employee of Annidis Corporation.

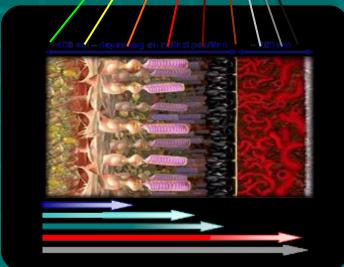
Unlike traditional white light fundus cameras, the Annidis RHATM Multi-Spectral Imaging (MSI) Platform consists of 12 LED spectral channels



The Annidis RHATM



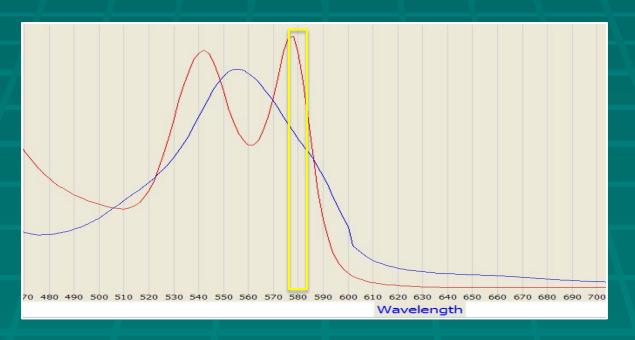






The Annidis RHATM

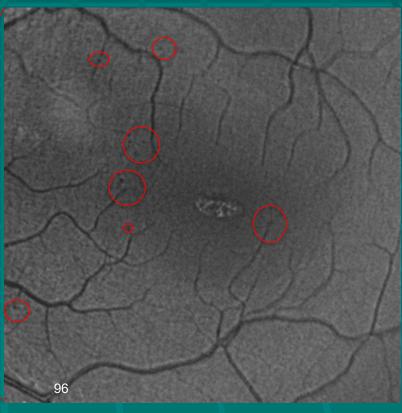
MSI 580mn yellow wavelength highlights oxygenated hemoglobin, making the retinal vasculature highly visible



Retinal Vasculature

- outpouchings/capillary dilations/microaneurysms
 - Are easily visible using the Annidis RHATM 580 nm channel





The ALLDocs Study

The Concept

 Investigate if the number of small blood vessel outpouchings (MA) seen with MSI-580 correlate with insulin resistance screening blood tests and computed values.

methods 1

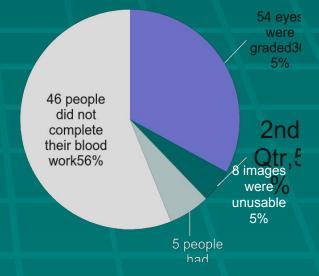
assemble n = 30 busy eye care professionals and/or their significant others who were imaged on the Annidis RHATM

and agreed to complete their lab work, including a 2 hour insulin test



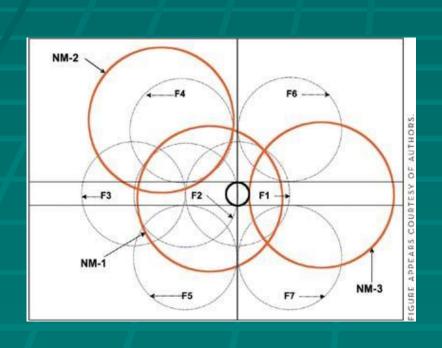
Marco Island, Florida October 2014,

There was grading of n= 54 eyes of 30 subjects who completing their imaging + lab work



methods 2

 Use Early Treatment Diabetic Retinopathy study (ETDRS) 7 standard field overlay to count the number of small blood vessel outpouchings seen in the central 30 degrees (Black circle).

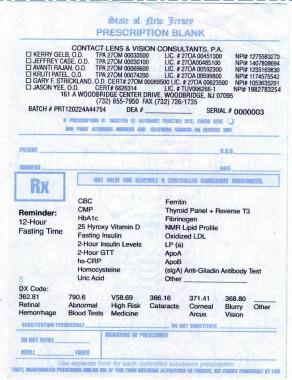




methods 3

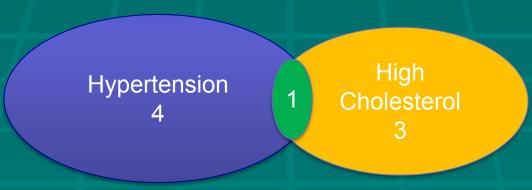


- Demographics: Brief medical history weight, height and current medications
- Requisition for <u>6 blood tests</u> and asked to complete ASAP but no later than <u>3 months</u>:
 - HbA1c
 - fasting glucose
 - 2 hour glucose
 - fasting insulin
 - 2 hour insulin
 - vitamin D



Demographics

- Mean age 53.5 ± 7.58 years
- 19 of the 30 participants were male
- Mean body mass index (BMI) of 26.00 ± 4.44 kg/m²
 - 25.0-29.9 is considered overweight
 - 30.0 or more is considered obese
 - <u>Disease burden</u>: "these eye care professionals relatively healthy by conventional measures"



methods 4 calculations

HOMA-IR is the Homeostasis Model Assessment

- It estimates the steady state beta cell function (%B) and insulin sensitivity (%S) as a percentage of the normal reference population using fasting glucose and insulin.
- It was originally described in 1985
 - Fasting glucose (mmol/l) X Fasting insulin (mU/l) / 22.5 or
 - Fasting glucose (mg/dL) X Fasting insulin (ulU/mL) / 405

HOMA -IR2

- Established in 1998
- Is a computer generated value
- It accounts for variations in hepatic and peripheral glucose resistance, increases in the insulin secretion curve for plasma glucose concentrations above 10 mmol/L (180 mg/dL) and the contribution of circulating proinsulin [Diabetes Care 1998; 21: 2191-92].

methods 5 STATISTICS / correlation coefficient assumptions

- Correlation Coefficient
 - Illustrates a quantitative statistical relationships between two or more observed data values with a linear strength and direction
- 1.0 is a perfect correlation
- 0.0 means that the two variables do not vary together linearly.
- Anything in between shows a degree of correlation
- A negative value indicates an inverse correlation, meaning as one value increases, the other decreases.
- A value of:
 - 0.3 is weak
 - 0.5 is moderate
 - 0.7 is strong

Overall Results

Table 1: Correlation Coefficients for Blood Test Results and Computed Values Relative to Retinal Vessel Outpouching/MA Quantity

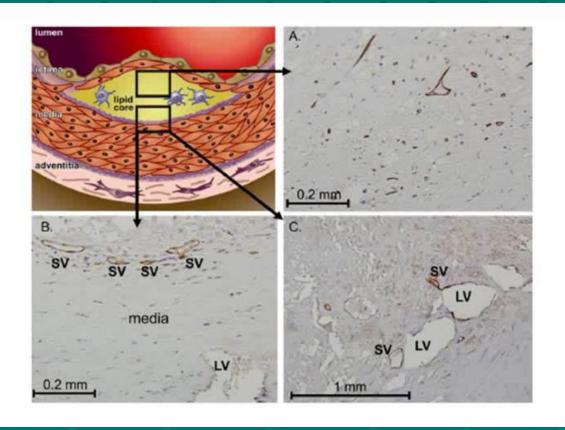
Laboratory Blood Test and Computed Values	Correlation Coefficient (p value) Note: p value < 0.05 was considered statistically significant Note n=54 unless otherwise indicated
Insulin sensitivity (%S)	-0.509 (0.00008)
QUICKI	-0.469 (0.0004)
HOMA2-IR	0.408 (0.002)
Insulin resistance (100/%S)	0.407 (0.002)
Fasting insulin	0.403 (0.003)
HOMA1-IR	0.399 (0.002)
Beta cell function (%B)	0.323 (0.02)
Fasting blood glucose	0.318 (0.02)
25 hydroxy vitamin D	-0.318 (0.02), n=53
2 hour insulin	0.291(0.08), n=38
Body Mass Index (BMI)	0.178 (0.3), n=33
2 hour glucose tolerance test	-0.124 (0.4), n=49
HbA1c	-0.027 (0.8)

Prediabetes, Insulin Resistance, Metabolic syndrome & the OD

"Few people know they have pre-diabetes, and yet they could prevent or postpone diabetes by making some basic lifestyle changes," says Dr. Ann Albright, director of the CDC's diabetes division. "This should be shouted from the rooftop."

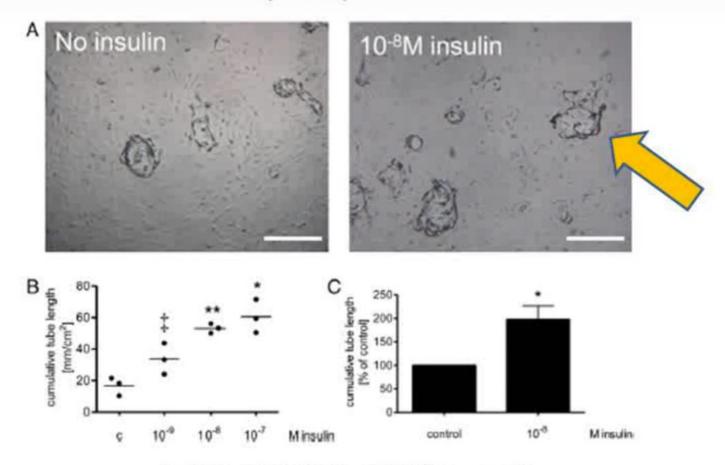


Biopsied Human Atherosclerotic Plaques



Small vessels have insulin receptors where large vessels do not

Insulin stimulates angiogenesis in human plaque



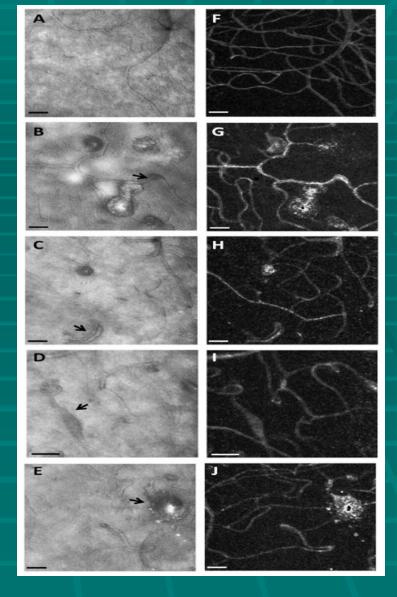
In vitro angiogenic sprouting assay.

Endothelial insulin receptor expression in human atherosclerotic plaques: Linking micro- and macrovascular disease in diabetes?

Atherosclerosis 222 (2012) 208–215, Rensing KL

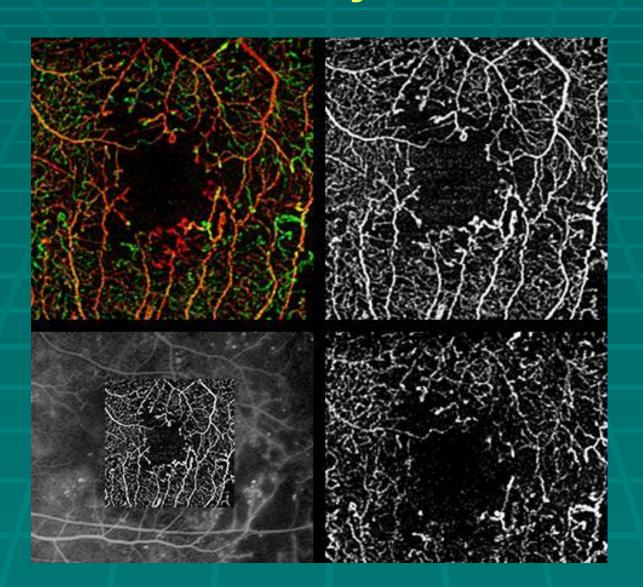
With adaptive optics, diabetics show extensive capillary remodeling w/only mild or moderate NPDR

Corkscrew-shaped
capillaries observed in
patients with very
early disease
Larger Perifoveal
capillary diameters in
diabetic subjects



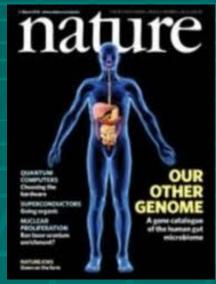
In vivo adaptive optics microvascular imaging in diabetic patients without clinically severe diabetic retinopathy Stephen A. Burns, Biomed Opt Express. 2014 Mar 1; 5(3): 961–974. Published online 2014 Feb 27. doi: 10.1364/BOE.5.000961

OCT Angiography now can view 3 layers of the FAZ

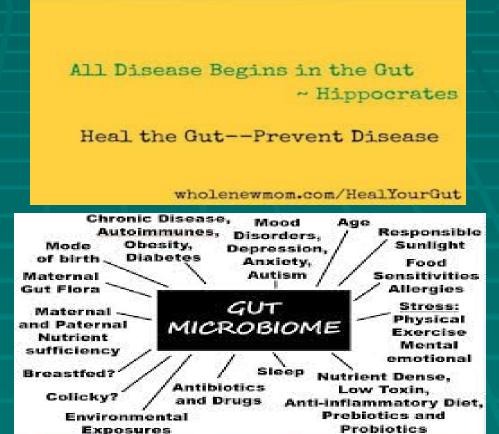


GUT MICROBIOME FASTING DETOXIFICATION NEW CONCEPTS

Gut Microbiome







While it's long been said that "you are what you eat," a more accurate description might be "you are what your microbes eat.

Obesity and type 2 diabetes (T2D) are associated with a profound dysbiosis

- New research has shown that patients can lose weight simply by changing their gastrointestinal microbial balance
- There are pro-inflammatory microbes that lead to diabetes and obesity and anti-inflammatory microbes that can help to reverse it
- Your gut is your gatekeeper for your inflammatory response
 - KEY Inflammatory pathways are critically involved in the evolution of insulin resistance

Gut bacteria play a fundamental role in diseases such as obesity, diabetes and cardiovascular disease......

- Your gastrointestinal tract houses some 30-40 trillion bacteria
 - About two to three pounds worth
 - Collective genome is MANY times larger than our own.
 - > 5 TIMES the number of cells you have in your entire body. (does not include virus, protozoa fungi)
 - Ideal ratio in your gut is 85 percent "good" and 15 percent "bad" bacteria.
 - 80 percent of your immune system (GALT)
 - 70%-80% antibody producing cells are located in intestine
- Microbiome should be properly balanced and cared for if you want to be healthy. Weintraub, P. 2013 Exp. Life Mag

Gut bacteria play a role in helping numerous bodily functions

- Benefits your mood and mental health
- Boosts weight loss
- Produced vitamins, absorbing minerals and eliminating toxins
- Digesting and absorbing certain carbohydrates
- Keeps bad bacteria under control
- Modulates your immune response and reduce inflammation

Symptoms of Dysbiosis and Intestinal Permeability

- Gas and bloating, fatigue, sugar cravings, nausea, headaches, constipation or diarrhea.
- Difficulty losing weight
 - Firmicutes helps your body to extract calories from complex sugars and deposit those calories in fat
- Leaky Gut
 - fatigue, cardiovascular diseases, autoimmune diseases, rash, eczema, psoriasis, depression, anxiety.



Which Factors are Driving This Autoimmunity Epidemics?

Microbiome
Composition

Maturation
GALT

H
Genetic
Predisposition

Immune-Mediated
Diseases



autoimmune diseases

- 50 million Americans suffer from autoimmune disease (AARDA
- 80-100 different autoimmune diseases
 - Suspect at least 40 additional diseases of having an autoimmune basis including Type 1 DM.
- 75% are women
- These diseases are chronic and can be life-threatening.
 - Top 10 leading causes of all deaths among U.S. women age 65 and younger.
- Specialists are generally unaware of interrelationships among the different autoimmune diseases or advances in treatment outside their own specialty area.

What causes gut bacteria be become compromised

- Sugar feeds pathogenic bacteria
- Processed foods
- Gluten → changes in the bacteria
- Casein
- Antibiotics, PPI's, NSAIDS
- Chlorinated water
- Agricultural chemicals (glyphosate) GMO's
- Pollution
- Sucralose
 - In a study in PLOS One when rats were fed aspartame it shifted the gut microbiota causing it to produce sugar producing short term fatty acid which in turn leads to elevation in blood sugar.
- CAFO beef
 - CAFO animals are routinely fed low-dose antibiotics, plus genetically engineered grains, which have also been implicated in the destruction of gut flora

type 2 diabetes & antibiotics

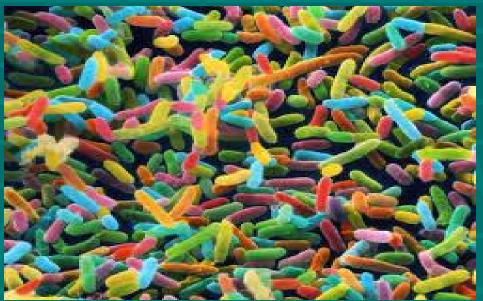
- Tracked 170,404 patients with type 2 diabetes and 1.3 million who did not have the disease.
- Those given 5 or more prescriptions of antibiotics over a period of up to 15 years are up to 53 per cent more likely to develop Type 2 diabetes than those given antibiotics just once or never
- Journal of Clinical Endocrinology & Metabolism 2015

Ways to Treat Dysbiosis Improve Gut Bacteria Balance

- Metformin
- Fermented foods
 - Lassi (an Indian yoghurt drink, traditionally enjoyed before dinner)
 - Fermented milk, such as kefir
 - Fermented vegetables cabbage, turnips, eggplant, cucumbers, onions, squash and carrots
 - Added benefit great source of vitamin K2
 - Natto (fermented soy)
- Probiotic supplement and prebiotics
 - Probiotics; useful to help repopulate the gut microflora
 - Animal studies show that probiotics and prebiotics I
 - Inulin (soluble fiber) is naturally present in many different foods such as garlic, leeks, onions, asparagus, bananas, herbs, dandelion root, chicory root
- Berberine can be helpful b/c it is an antimicrobial herb that helps correct GI dysbiosis

Summary - Living in Harmony with your Microbiome

 Living in harmony with your microbiome instead of assaulting it – is of critical importance for disease prevention and optimal health



Many things can increase Insulin, the main driver of obesity

- Refined grains
- Carbohydrates
- Animal proteins
- Cortisol is also a major player in stimulating insulin secretion.
- Fructose increases insulin resistance directly which indirectly leads to increased insulin levels.

Centenarians

- Centenarians common factor
 - Have low insulin levels and highly insulin sensitivity

- Calorie Restriction (w/ optimal nutrition)
 depending on species live longer including primates
 - Lifespan increases 30%-200%

Treatment

- We need to reduce insulin without increasing blood sugar because as you decrease insulin your sugars will increase and you avoid gluco-toxicity
 - Metformin
 - Acarbose
 - Gastric Bypass
 - Fasting/ intermittent fasting
 - Glucose goes down but remains stable
 - Insulin reduces significantly
 - Lose weight w/o muscle loss unlike other diets
 - Spike in growth hormone
 - Preserves muscle mass
 - Helps body burn fat for fuel
 - Free fatty acids increase because feeding your body thru your own fat
 - Increase energy because norepinepherine levels increase

intermittent fasting



Jason Fung, MD nephrologist

6 ways to <u>Decrease Insulin</u> Address Insulin Resistance / Not sugar Jason Fung, MD nephrologist www.kidneylifescience.com

- 1. Intermittent Fast = all major religions
- 2. Decrease Refined Carbs
- 3. High Fat Diet (natural fats)
- 4. High Fiber Diet
- 5. Vinegar
- 6. Spices & Herbs (i.e.

Detoxification

- Avoid exposure
- Detox



- Promote plant based diet making urine alkaline
 - Example: when hospitals give IV sodium bicarbonate for toxin overdose like aspirin
- Probiotics ,B6, MG, NAC, chlorella (after meals)
- Niacin
- Infrared sauna
- Exercise





General principles to decrease DM 2 and Metabolic Syndrome

- Fasting/ intermittent fasting
- Wheat; promotes inflammation directly. Klement. Nutrition & Metabolism 2011)
 - Cause SIBO (Olesen, Am J Clin Nutr)
- Low carbohydrate diets (Paleo Mediterranean diet)
 - Reduce inflammation. Decreases CRP by 47% (Pereira, JAMA 2004)
 - Improves the quality of the intestinal bacteria
 - When we change the diet we change the microbes in the gut.
 - Plant based diets are the best for improving bacterial SIBO
 - Low Carb diet (30% Carb diet) decrease A1c 3% beats drugs equal to insulin in severe diabetics (10.9 dec to 7.8 in 6 mo)
 - Diet treatment of choice
- Paleo more satiating than Med diet Jonsson 2010 Nut and Metobolism
- High nutrient dense diet
 - Decreases hunger even though less calories
- Multivitamin/multi-mineral supplements.
 - Most people do not consume and optimal amount of vitamins by diet alone. Fletcher, JAMA 2002.
 - Decrease risk of infections in Diabetics because diabetics often have nutrient deficiencies
 Barringer ANN Internal Med 2003



1. Avoid

- a) Smoking
- b) Weight gain
- c) High glycemic index foods- the white fluffies
- d) High fructose corn syrup
- e) Soda and sweetened drinks
- f) Artificial sweeteners including ingredients Aspertane, Sucralose, Saccharine
- g) Dairy
- h) Grain Fed Meat
- i) Trans Fats
- j) Prolonged sitting
- k) Toxins

2. Eat Foods with Omega-3 and/or take supplements

- a) Wild salmon, sardines, mackerel
- b) Omega 3 Fish oil Supplements DHA + EPA = (1000 mg 2000mg 3000mg 4000mg)



3. Anti Inflammatory Diet/Paleo Diet

- a) Organic vegetables and organic fruits (3:1 Vegetable to fruits)
- b) Raw unsalted nuts & seeds, grass fed hormone & antibiotic free meat, avocado, olive oil, coconut oil (best for cooking), eggs including yolk

4. Spices

c) Cinnamon, rosemary, oregano, garlic powder, curcumin, ginger and paprika

5. Green Tea and Freshly Squeezed Lemon





- 6. Vitamin D3 / K2... Optimal Blood Levels
 - a) 25 hydroxy vitamin D levels 50-80 ng/ml
 - b) 1000 IU 2000IU 3000IU 4000IU 5000IU
- 7. Stress Reduction and Regular Exercise

8. Sleep 7-8 Hours Every Night

9. Supplements That Help

- a) Chromium, Brewers Yeast w niacin
- b) Magnesium Citrate
- c) Cinnamon Powder
- d) Alpha-Lipoic Acid
- e) Fenugreek
- f) Resveratrol, Quercetin and Lonegvinex ®
- g) Probiotic & Enzymes
- h) IP6 (against labile iron)
- i) High Quality Multi-Vitamins like Life Extension, Garden of Life or Zeavision DVS

10. Recommended Reading

- j) Paleo Diet by Loren Cordian, PhD, the new edition
- k) Paleo Cookbook by Dr. Loren Cordian



Improve Vision & Neuropathy

Supplement Facts

Serving Size: 2 Softgels / Servings per Container: 30

Amount Per Serving		%DV
Vitamin C (Ascorbic Acid)	60 mg	100%
Vitamin D3* (Cholecalciferol)	2,000 IU	500%
Vitamin E* (d-alpha Tocopherol)	60 IU	200%
Vitamin B12 (Cyanocobalamin)	6 mcg	100%
Zinc (Zinc Oxide)	15 mg	100%
Fish Oil EE* 70%	320 mg	t
Total Omega-3 A%	240 mg	†
EPA 40% (Eicosapentaenoic Acid) A%	128 mg	†
DHA 30% (Docosahexaenoic Acid) A%	96 mg	†
Alpha Lipoic Acid	150 mg	†
Coenzyme Q-10 (Ubidecarenone)	20 mg	†
Mixed Tocotrienols/Tocopherols*	20 mg	†
Zeaxanthin*	8 mg	†
Lutein*	4 mg	†
Proprietary Blend*	530 mg	+

Benfotiamine, N-Acetyl Cysteine, Grape Seed Extract, Resveratrol (Polygonum Cuspidatum), Turmeric Root Extract (curcuminoids), Green Tea Leaf, *Pycnogenol*® (French Maritime Pine Bark Extract).

† Daily Value not established * From natural sources

Other Ingredients: Gelatin, glycerin, soybean oil, purified water, beeswax, colors (annatto extract, titanium dioxide), lecithin oil.



Gluten Free
Contains
NO Yeast
Contains soy
& fish (cod,
pollack,

whiting)



Conclusion "Pre-diabetes"

- Prediabetes is not pre anything.
 - It is a deadly disease driving our biggest killers;
 - Heart attacks, strokes, dementia, retinal bleeding and cancer as well as AMD
- 2/3rds of all patients admitted to the ER with heart attacks had prediabetes or undiagnosed diabetes.(Jessani; Int J Clin Pract; 2007)
- Prediabetes can cause pre-dementia or mild cognitive impairment.
 - Think of it as early Alzheimers

Conclusion – be proactive, not reactive

- Most people with prediabetes remain undiagnosed with standard testing of fasting blood sugar
- The take home message is not only to get your blood sugar tested but also test your insulin levels







Q & A
5
minutes

A Society Focused on Ocular Nutrition Education 目の栄養教育啓発 www.ocularnutritionsociety.org