



# How to Counsel Patients on Lifestyle Modifications for Ocular Health

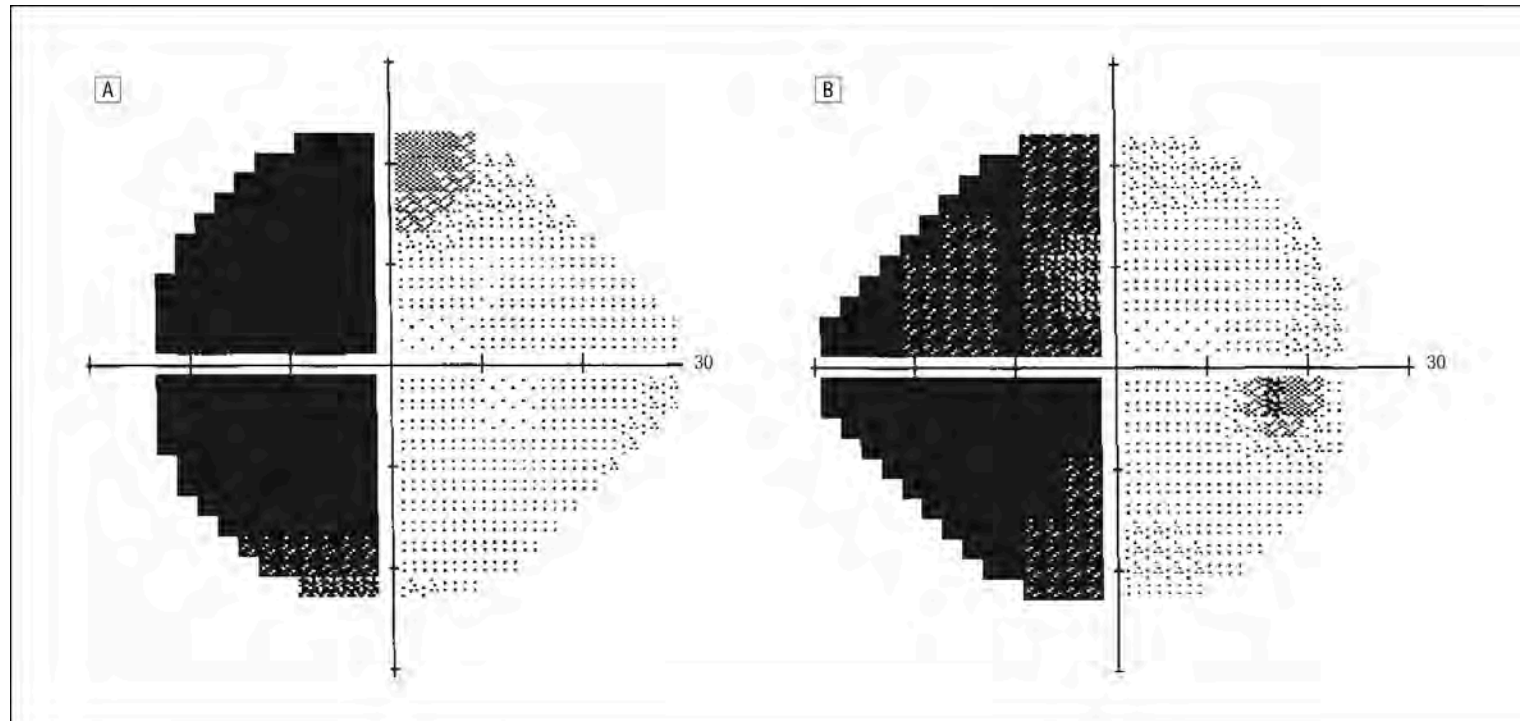
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Fort Lauderdale, Florida USA

# Case 1

- 49 year old female
- Referred by local primary care physician for diabetes
- PMHx: Diabetes, hypertension, 2 strokes, high cholesterol
- **Medications: Atorvastatin 10 mg (Lipitor), Lisinopril 20 mg, Metformin 500 mg BID, Plavix 75 mg, women's multivitamin gummies 200 mcg , Xarelto 20 mg**
- Social: Non-smoker, **drinks 3 glasses wine per night**
- **BP 145/90 RAS**
- Height 5'6" (167.64 cm) Weight 215 lb. (97.5 kg) **BMI 34.7**
- **FBS 273**, A1C unknown
- Other: Does not like taking medications, **poor compliance with follow-up visits.**

## Case 1

- Corrected visual acuity 20/25 OD, OS (6/7.5)
- IOP 13 mm Hg OD, 15 mm Hg OS
- Visual field:







## Diagnoses

Essential (primary) hypertension

Left homonymous hemianopsia 2<sup>o</sup> to stroke

T2DM with ophthalmic complications

Moderate NPDR OU

Hyperlipidemia, unspecified

Obese due to excess calories with BMI 34.7

**What is the ocular management for this patient?**

**What are the medication considerations?**

**What are the nutritional and lifestyle considerations?**

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Monitor for DME and progression to proliferative

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How about intravitreal injections Lucentis for NPDR?

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April 2017 Lucentis (ranibizumab) approved in US for treatment of all types of NPDR - even in absence of DME

Ocular Management

# Medication Considerations

## Multivitamin “chewable gummies”

## Atorvastatin (Lipitor)

- Statin – lowers LDL’s (LDL’s transport carotenoids)
- Liver problems, may increase blood sugar levels.

## Lisinopril

- ACE inhibitor lowers BP by reducing the production of angiotensin II, relaxing arterial muscle and enlarging arteries
- Kidneys: narrowing of the arteries by angiotensin II decreases blood flow and damages the kidneys.
- **Can deplete zinc levels.\***



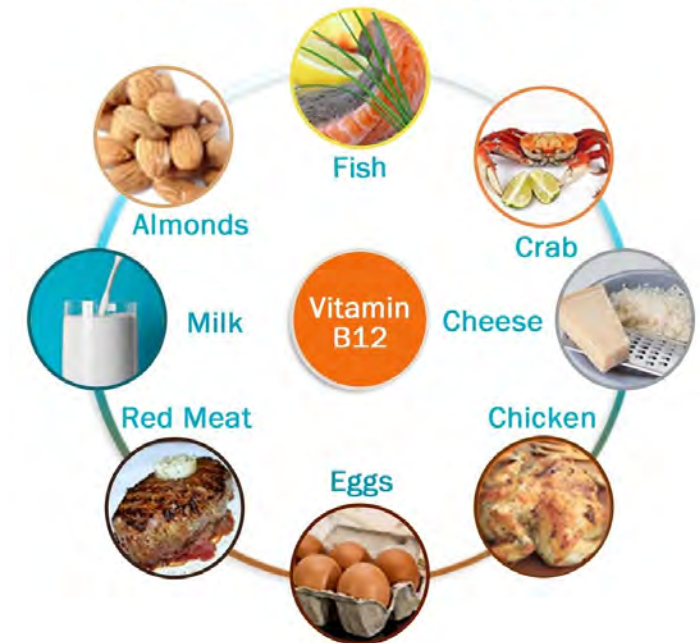
# Medication Considerations

**Metformin** – Glucophage (500 mg BID typical dosing)

- Acts by increasing the sensitivity of liver, muscle, fat, and other tissues
- The most serious side effect metformin can cause is lactic acidosis.
  - Boxed warning: most severe warning FDA
- Digestive problems\*
- Chronic metformin use results in **vitamin B12** deficiency in 30% of patients.
  - May present without anemia and as a peripheral neuropathy
  - Often misdiagnosed as diabetic neuropathy, although the clinical findings are usually different.



## Vitamin B12 Rich Foods



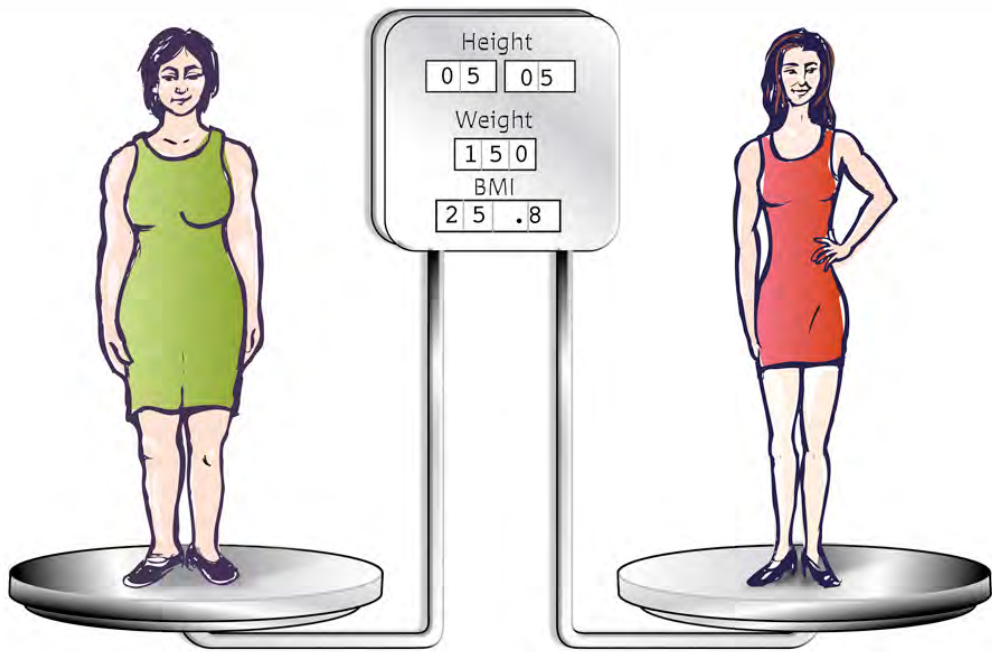
# Medication Considerations

## Xarelto

- Prevents clotting; blood thinner
- Targets Factor Xa (FXa), inhibiting formation of blood clots.
- Factor Xa is the active form of Factor X, an enzyme that is synthesized in the liver and assists in coagulation.
- Selective anticoagulant - only interferes with the one factor, Factor Xa, thereby interacting with less of the body's natural functions.
- Doesn't interact with **vitamin K** like warfarin – can eat leafy green vegetables and other foods rich in **vitamin K**.

## Plavix

- Inhibits platelet function
- No known interactions with **vitamin K**



BMI	Classification
< 18.5	underweight
18.5–24.9	normal weight
25.0–29.9	overweight
30.0–34.9	class I obesity
35.0–39.9	class II obesity
≥ 40.0	class III obesity

# Discussing Weight Loss

A close-up photograph of a person's arm being measured with a skinfold thickness caliper. The caliper is white with black markings and is being held by a hand. The measurement is taken on the upper arm. The background is a light gray.

# Metabolic Health?

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- Normal FBS, BP, blood lipids
- Less visceral fat, smaller fat cells
  - Hyperplasia vs. hypertrophy of fat cells
- Lack of physical activity
- Insufficient diet
  - Variety or substance




# Blood Pressure Categories

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

# Obesity and Diabetes

- Hyperinsulinemia leads to insulin resistance and impaired glucose tolerance
- Obesity is the greatest risk factor for type 2 diabetes

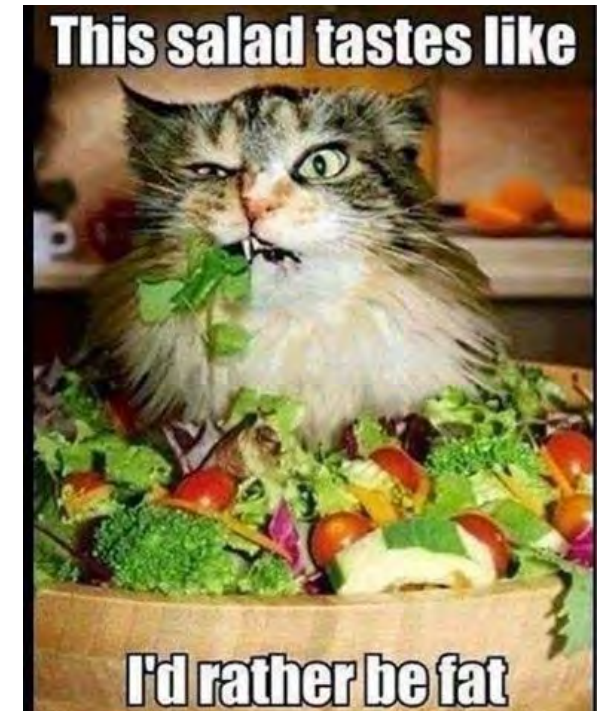
BLOOD GLUCOSE CHART				
	Mg/DL	Fasting	After Eating	2-3 hours After Eating
Normal		80-100	170-200	120-140
Impaired Glucose		101-125	190-230	140-160
Diabetic		126+	220-300	200 plus





# Diabetes and Weight Loss

- Reducing energy intake while maintaining a healthful eating pattern
- Ten (10%) weight loss improvement in diabetic control
- Central obesity\*\*
- Modest weight loss correlates with clinical benefits; improved glycemic control, blood pressure and lipid profiles
- May be able to remove or reduce medications



# Diabetes and Macronutrients

- Carbohydrate intake has a direct effect on postprandial glucose levels and is the primary macronutrient of concern.
- GI and GL
- No ideal/prescriptive percentages, but on average:
  - Carbohydrates 45%
  - Protein 16%-18%
  - Fat 36%-40%
- Mediterranean eating pattern reported with largest improvement in A1C at 1 year





# Mediterranean “Diet”

- Primarily plant-based foods, such as fruits and vegetables, whole grains, legumes and nuts
- Replacing butter with healthy fats (olive oil and canola oil)
- Using herbs and spices instead of salt to flavor
- Limiting red meat to no more than a few times a month
- Eating fish and poultry at least twice a week
- Enjoying meals with family and friends
- Drinking red wine in moderation (resveratrol)
- Getting plenty of exercise



Esposito K, et al. Ann Intern Med. 2009 Sep 1;151(5):306-14. **Effects of a Mediterranean-style diet on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes: a randomized trial.**



# Exercise Works!

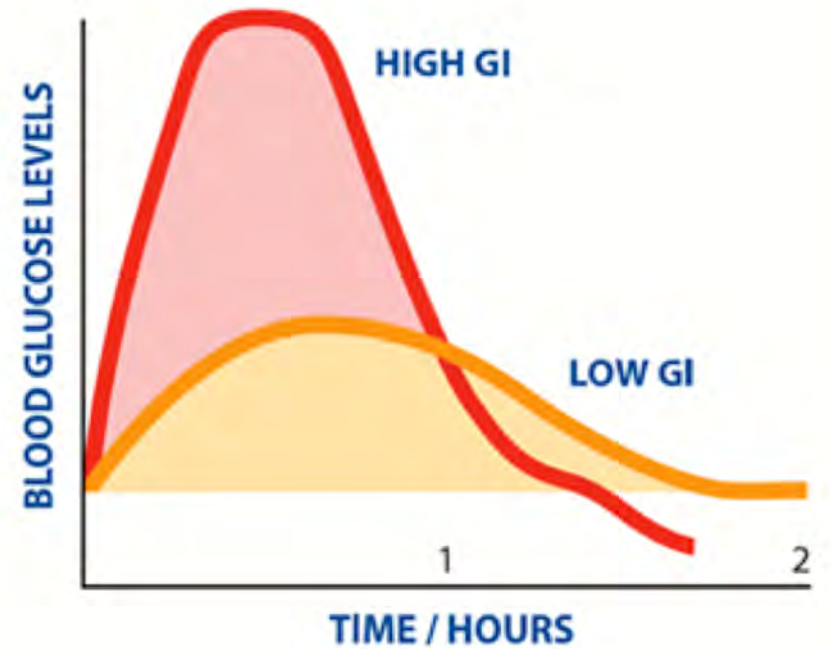
- Insulin action in muscle and liver can be modified by exercise
- Acute state: aerobic exercise increases muscle glucose uptake 5-fold
- After exercise:
  - Glucose uptake remains elevated up to 48 hours following prolonged bouts
  - Shorter bouts of exercise (high intensity) glucose uptake remains elevated for up to 24 hours
  - Low intensity 60 minutes enhances insulin action in obese, insulin resistant adults.





# Carbohydrates and Glycemic Index

- GI measures **how rapidly consumption of a carbohydrate increases plasma glucose levels.**
- Values range from 1 (slowest increase) to 100 (fastest increase, equivalent to pure glucose).
  - Incremental area under blood glucose curve after ingestion of 50 g carbohydrates compared to glucose (or white bread).





# Glycemic Load

Considers GI AND amount consumed

- GL = GI (decimal) x carbohydrate (grams)
- Useful for diabetics to determine how quickly the sugar will rise
  - High GL  $\geq 20$
  - Intermediate GL 11-19
  - Low GL  $\leq 10$

GI of watermelon is 76 and GI of a doughnut 76 BUT  
One serving of watermelon 11 g of carbohydrate  
One doughnut 23 g of available carbohydrate.

Food	GI	Serving Size	Net Carbs	GL
Peanuts	14	4 oz (113g)	15	2
Bean sprouts	25	1 cup (104g)	4	1
Grapefruit	25	1/2 large (166g)	11	3
Pizza	30	2 slices (260g)	42	13
Lowfat yogurt	33	1 cup (245g)	47	16
Apples	38	1 medium (138g)	16	6
Spaghetti	42	1 cup (140g)	38	16
Carrots	47	1 large (72g)	5	2
Oranges	48	1 medium (131g)	12	6
Bananas	52	1 large (136g)	27	14
Potato chips	54	4 oz (114g)	55	30
Snickers Bar	55	1 bar (113g)	64	35
Brown rice	55	1 cup (195g)	42	23
Honey	55	1 tbsp (21g)	17	9
Oatmeal	58	1 cup (234g)	21	12
Ice cream	61	1 cup (72g)	16	10
Macaroni and cheese	64	1 serving (166g)	47	30
Raisins	64	1 small box (43g)	32	20
White rice	64	1 cup (186g)	52	33
Sugar (sucrose)	68	1 tbsp (12g)	12	8
White bread	70	1 slice (30g)	14	10
Watermelon	72	1 cup (154g)	11	8
Popcorn	72	2 cups (16g)	10	7
Baked potato	85	1 medium (173g)	33	28
Glucose	100	(50g)	50	50

# Recommendations

- Focus on **quality** of carbohydrate (GI/GL)
  - Replace sucrose (table sugar) for nutrient dense starches.
- Fructose in fruit results in better glycemic control compared to sucrose and starch without affecting triglycerides
  - Obesity and diabetes rates were low when total fructose intake was in the range of 25–40 g/d.
- Add **fiber and whole grain**



# Recommendations

- No specific vitamin or supplement recommendations by ADA for diabetics.
- Use general population recommendations for vitamin and essential fatty acid intake.
- Fats
  - **Increase monounsaturated fats** (Mediterranean diet)
  - **Increase EPA and DHA** (fatty fish) and ALA for beneficial effects on lipoproteins, prevention of heart disease
  - Decrease saturated and trans fats

# Dietary Approaches to Stop Hypertension (DASH Diet)

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Requires no special foods but **daily and weekly nutritional goals**.

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Vegetables, fruits, and whole grains.

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Fat-free or low-fat dairy products, fish, poultry, beans, nuts, and vegetable oils

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Limiting foods high in saturated fat (fatty meats, full-fat dairy products, and tropical oils (coconut, palm kernel, and palm oils)).

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Limiting sugar-sweetened beverages and sweets.



# DASH-Sodium Trial

- Combination of reduced sodium intake AND the DASH diet lowered SBP throughout the range of pre- and stage 1 hypertension, with progressively greater reductions at higher levels of baseline SBP.
- SBP reductions in adults with the highest levels of SBP ( $\geq 150$  mm Hg) were greater and reinforced the importance of both sodium reduction and the DASH diet in this high-risk group.
- **Blood pressure decreased with each reduction of sodium.**
- **Conclusion: Reducing sodium intake and following the DASH diet is more beneficial for lowering blood pressure than following the DASH diet alone or reducing sodium alone.**

# DASH Diet

- **Standard DASH diet:** Can consume up to 2,300 mg of sodium
- **Lower sodium DASH diet:** Can consume up to 1,500 mg of sodium
- 1,500 milligrams (mg) sodium lowers blood pressure even further than 2,300 mg sodium daily.
- Low in saturated and *trans* fats
- Rich in potassium, calcium, magnesium, fiber, and protein
- Lower in sodium





## Clinical Perspective

1 tsp salt

6 g salt

2400 mg sodium

104 mmol

## Case 2: Swollen Nerves

21 year old female

CC: blurry vision since she broke specs

LEE: 3 years ago

PMHx: unremarkable

FHx: Diabetes (mother and grandmother)

Meds: None (no birth control)



# Case 2

- Social Hx: No smoking, denies alcohol intake, caffeine occasionally
- BP 115/70
- POHx: optic nerve swelling OU
  - Discovered at CEE 3 years earlier
  - Reports MRI was 'normal' and lumbar puncture was performed and 'high' (no report available).
  - Rx's acetazolamide – D/C due to metallic taste in mouth
  - Educated on weight loss

# Case 2

- Gained 20 pounds in past 2 years (9.07 kg)
- Height 5'4" (164 cm)
- Weight 220 lbs. (99.8 kg)
- BMI 37.8 (obese)



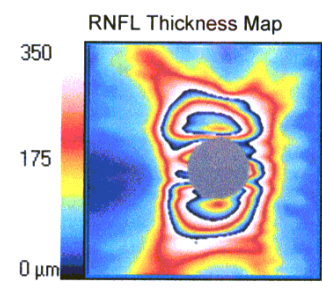
"No, that doesn't make any difference either, Miss Jones."



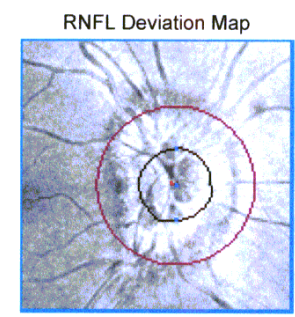
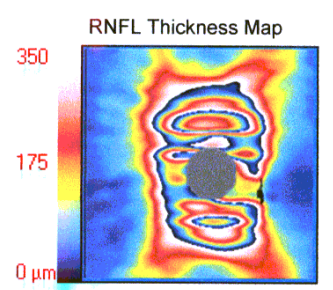






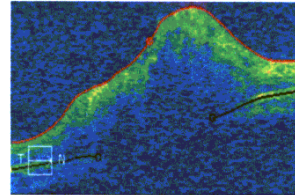


	OD	OS
Average RNFL Thickness	287 $\mu\text{m}$	354 $\mu\text{m}$
RNFL Symmetry	89%	
Rim Area	2.10 $\text{mm}^2$	1.69 $\text{mm}^2$
Disc Area	2.05 $\text{mm}^2$	1.42 $\text{mm}^2$
Average C/D Ratio	0.06	0.07
Vertical C/D Ratio	0.06	0.07
Cup Volume	0.000 $\text{mm}^3$	0.000 $\text{mm}^3$

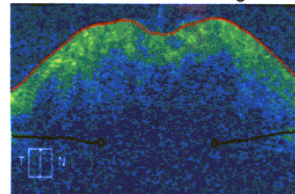


Disc Center(0.39,-0.18)mm

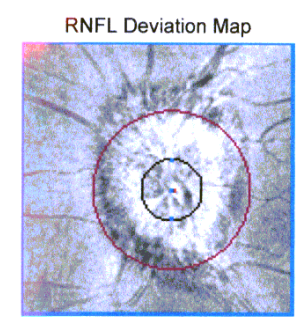
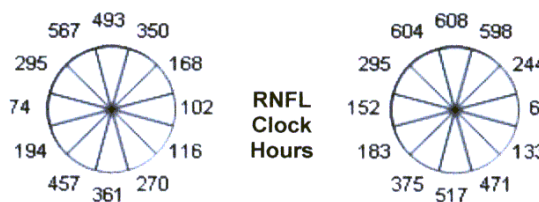
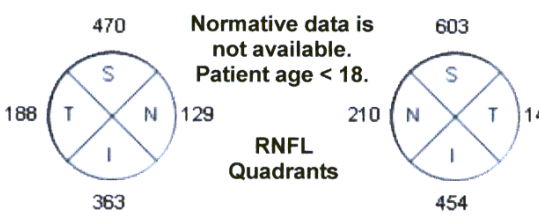
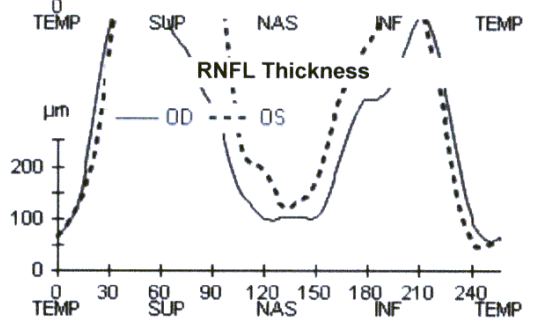
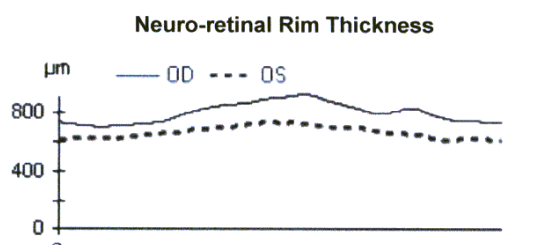
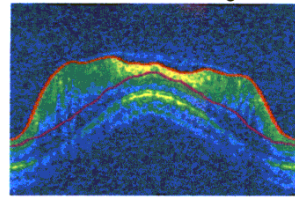
Extracted Horizontal Tomogram



Extracted Vertical Tomogram

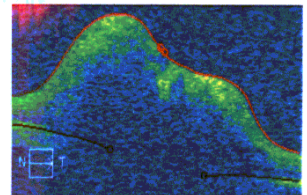


RNFL Circular Tomogram

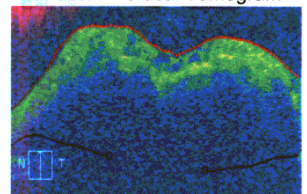


Disc Center(0.27,-0.21)mm

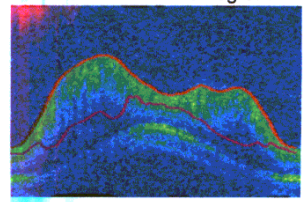
Extracted Horizontal Tomogram



Extracted Vertical Tomogram



RNFL Circular Tomogram



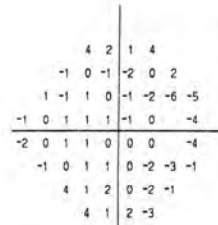
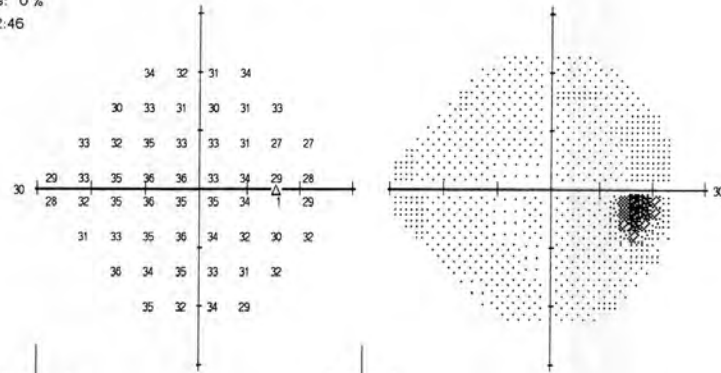
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 Fixation Target: Central  
 Fixation Losses: 2/11  
 False POS Errors: 13 %  
 False NEG Errors: 0 %  
 Test Duration: 02:46

Stimulus: Ill, White  
 Background: 31.5 ASB  
 Strategy: SITA-Fast

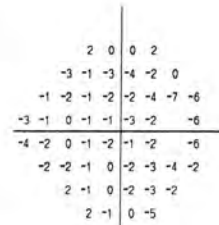
Pupil Diameter: 6.4 mm  
 Visual Acuity:  
 RX: +0.00 DS DC X

Date: 06-23-2015  
 Time: 8:42 AM  
 Age: 17

Fovea: OFF

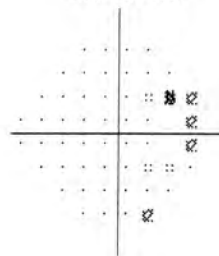
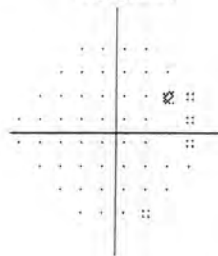


Total Deviation



Pattern Deviation

GHT  
 Within normal limits  
 VFI 99%  
 MD -0.03 dB  
 PSD 1.95 dB P < 5%



:: < 5%  
 :: < 2%  
 :: < 1%  
 ■ < 0.5%

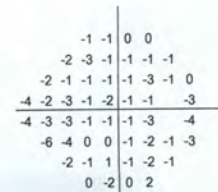
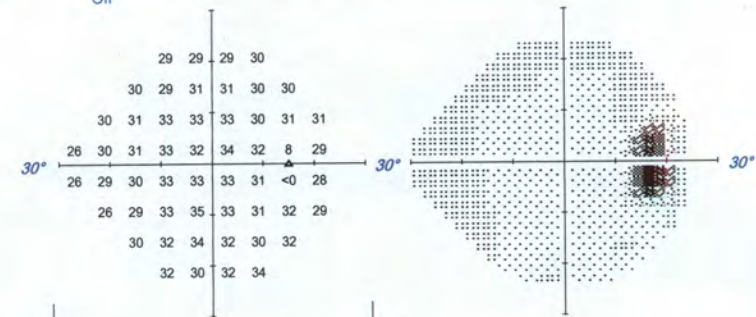
## OD Single Field Analysis

## Central 24-2 Threshold Test

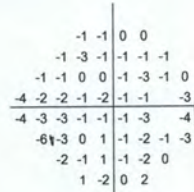
Fixation Monitor: Gaze/Blind Spot  
 Fixation Target: Central  
 Fixation Losses: 3/10 XX  
 False POS Errors: 0%  
 False NEG Errors: 0%  
 Test Duration: 02:57  
 Fovea: Off

Stimulus: Ill, White  
 Background: 31.5 asb  
 Strategy: SITA Fast  
 Pupil Diameter: 6.4 mm \*  
 Visual Acuity:  
 Rx: +0.00 DS

Date: Sep 18, 2018  
 Time: 11:20 AM  
 Age: 21



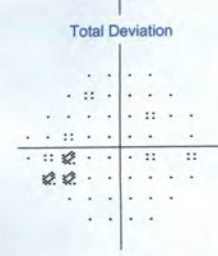
Total Deviation



Pattern Deviation

GHT: Within Normal Limits

VFI: 99%  
 MD24-2: -1.59 dB P < 10%  
 PSD24-2: 1.41 dB



\*\*\* Low Test Reliability \*\*\*

:: P < 5%  
 :: P < 2%  
 :: P < 1%  
 ■ P < 0.5%



# Central 24-2 Threshold Test

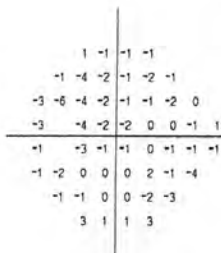
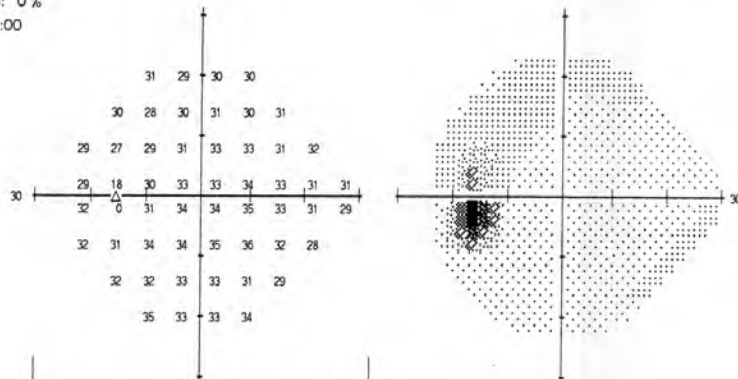
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 Fixation Losses: 1/10  
 False POS Errors: 6 %  
 False NEG Errors: 0 %  
 Test Duration: 03:00

Stimulus: III, White  
 Background: 31.5 ASB  
 Strategy: SITA-Fast

Pupil Diameter: 5.2 mm  
 Visual Acuity:  
 RX: +0.00 DS DC X

Date: 06-23-2015  
 Time: 8:46 AM  
 Age: 17

Fovea: OFF



Total Deviation



Pattern Deviation

GHT

Within normal limits

VFI 98%

MD -1.05 dB

PSD 1.72 dB P < 10%

•• < 5%  
 • < 2%  
 • < 1%  
 ■ < 0.5%

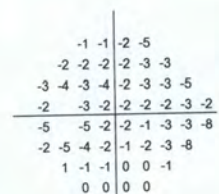
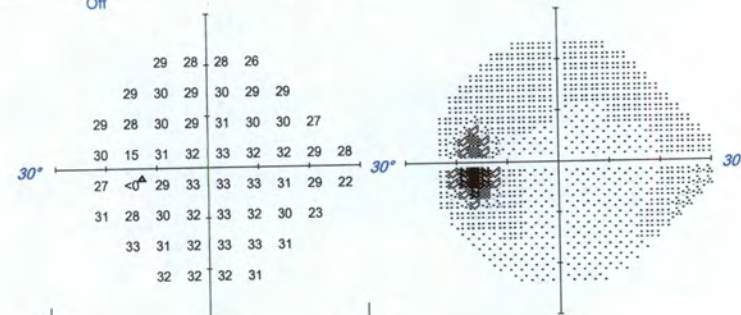
## OS Single Field Analysis

## Central 24-2 Threshold Test

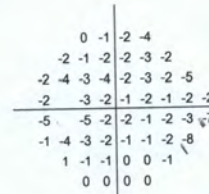
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 Fixation Target: Central  
 Fixation Losses: 0/10  
 False POS Errors: 0%  
 False NEG Errors: 0%  
 Test Duration: 03:03  
 Fovea: Off

Stimulus: III, White  
 Background: 31.5 asb  
 Strategy: SITA Fast  
 Pupil Diameter: 6.0 mm \*  
 Visual Acuity:  
 Rx: +0.00 DS

Date: Sep 18, 2018  
 Time: 11:27 AM  
 Age: 21



Total Deviation



Pattern Deviation

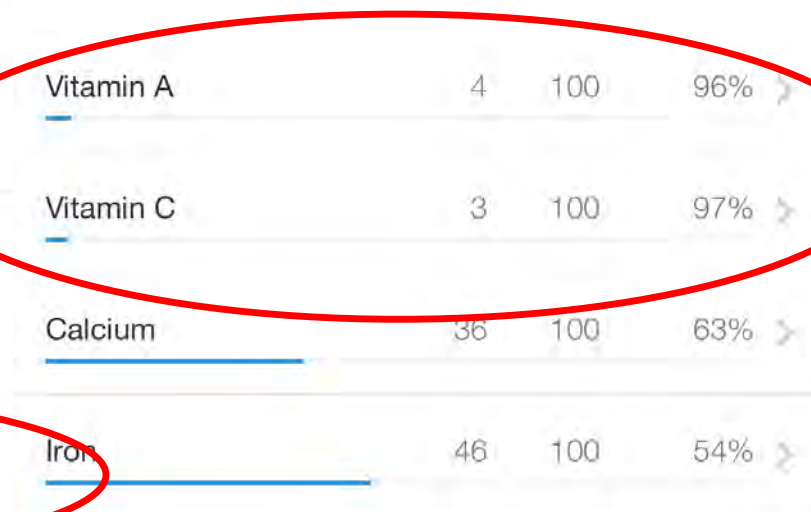
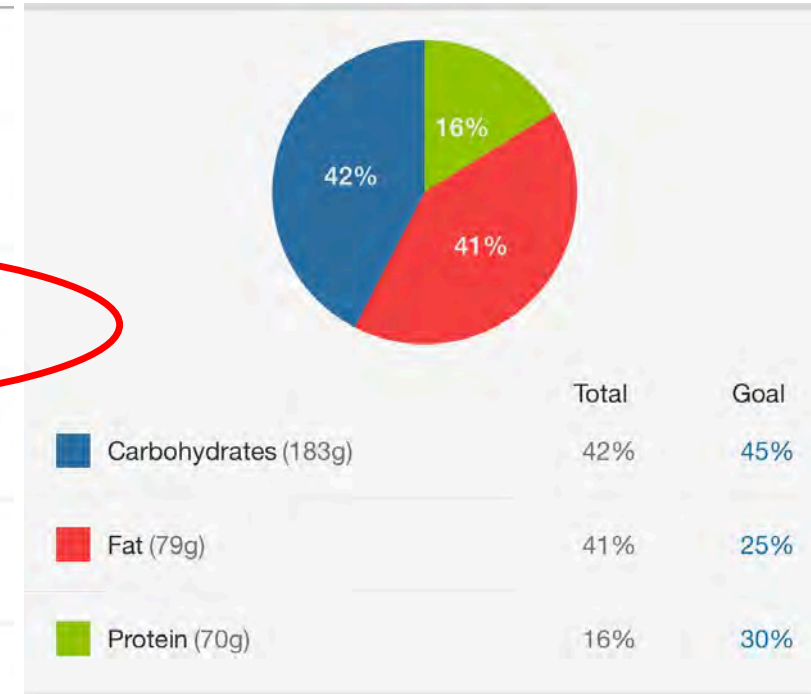
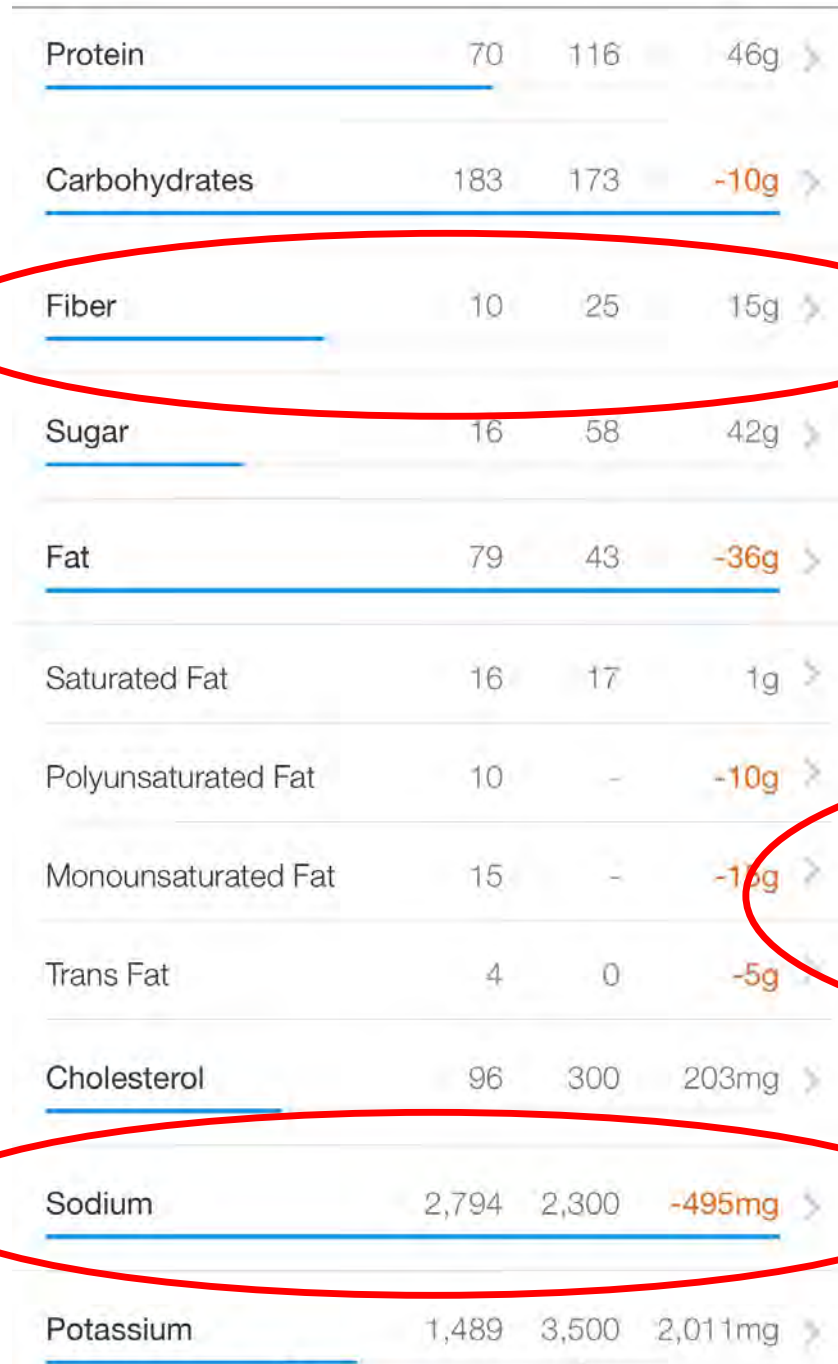
GHT: Borderline

VFI: 98%  
 MD24-2: -2.30 dB P < 5%  
 PSD24-2: 1.70 dB P < 10%

•• P < 5%  
 • P < 2%  
 • P < 1%  
 ■ P < 0.5%

# 24 Hour Food Recall

- “I don’t need a dietician”
- 8:00 AM: salted peanuts (1.75 oz.) and water
- 12:30 PM: banana bread (2 slices) and water
- 4:00 PM: crackers from vending machine
- 8:30 PM: salt fish (cod) with ‘jerk’ seasoning and dumplings





# Idiopathic Intracranial Hypertension (IIH)

- Elevated intracranial pressure of unknown cause occurring predominantly in young women of childbearing age.
- Daily headache, pulse synchronous tinnitus, transient visual obscurations and papilledema with associated visual loss.
- Idiopathic Intracranial Hypertension Treatment Trial (IIHTT), multicenter, double-blind, randomized, placebo-controlled study
  - **Weight-reduction and low sodium diet plus acetazolamide VS. diet plus placebo in subjects with mild visual loss.**
  - Statistically significant improvements in visual field function, quality of life measures, papilledema grade and CSF pressure in the low sodium - acetazolamide group.

# IIIH

- Clinical improvement reported with about 6% weight loss.
- Acetazolamide-plus-diet patients lost twice as much weight as placebo-plus-diet patients but the acetazolamide effect on PMD was independent of the weight loss.
- Treatment failure was much less common in the acetazolamide-plus-diet group compared to the placebo-plus-diet group and risk factors for treatment failure were presence of high grade papilledema and lower ETDRS visual acuity measures at baseline.

Wall M. Update on idiopathic intracranial hypertension. *Neurologic clinics*. 2017;35(1):45-57. doi:10.1016/j.ncl.2016.08.004.

# Foods Beneficial for IIH

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Fruits with contain fiber and vitamins

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Lean meat – poultry and fish have low fat content and can help to keep the calorie count low while supplying body with proteins.

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Low fat dairy products

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Olive oil, canola oil and other sources of monounsaturated fats will help keep cholesterol levels under control.

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Oats

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Whole grain bread

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Healthy lifestyle and exercise regularly

# Foods to Avoid for IIH

- Limit intake of **salt**
- Limit intake of fats: avoid red meat, processed meats (pork, bacon and beef)
- Limit foods high in **vitamin A and tyramine**
- Tyramine is a compound formed during the breakdown of tyrosine and can cause blood vessels dilation.
  - Preserved, dried or aged foods such as pickles, pickled foods, salami, pepperoni, sauerkraut, olives, fermented soy products, nuts, aged cheese, beer and wine.
- Foods with high levels of vitamin A should also be avoided.
  - Liver, carrots, tomatoes, sweet potatoes and green leafy vegetables.
- Alcohol –avoid dehydration
- Coffee – rebound dilation of vessels



# Case 3

- 75 year old white female
- CC: Decreased distance and near vision in both eyes for several years.
- PMX: Hypertension, high cholesterol, arthritis, anemia
- **Medications: aspirin 81mg, atorvastatin 20 mg QD (Lipitor), Lisinopril 20 mg QD**
- Social: **Past smoker 1 pack a day** (quit 5 years ago), alcohol approx. 3 drinks/week.
- BP: 110/70
- Height: 5'3" (161.5 cm) Weight: 85 lb.(38.5 kg) **BMI: 15**
- Other: **poor appetite, paucity of vegetable intake**

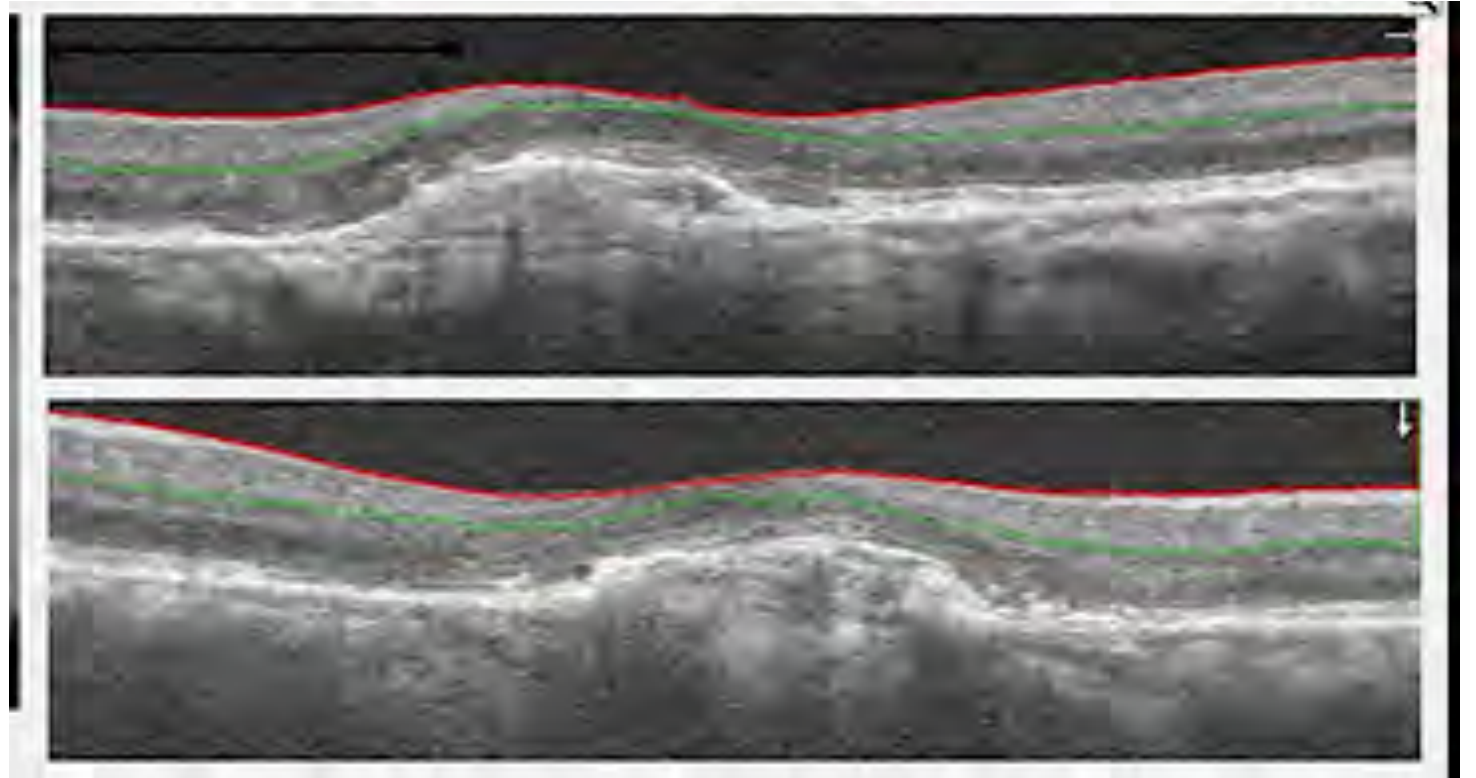


Fundus: Hard macular drusen OD with RPE changes, soft drusen OS with RPE changes and fluid, vessel attenuation OU.

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## Case 3

- BCVA
  - 20/50 OD (6/15)
  - 20/100 OS (6/30)
- IOP:
  - 12 mm Hg OD
  - 14 mm Hg OS
- OCT OS



# Diagnoses

Intermediate dry macular degeneration OD

Advanced wet macular degeneration OS

Iron deficiency anemia, unspecified

Essential (primary) hypertension

Hyperlipidemia, unspecified

Underweight

**What is the ocular management for this patient?**

**What medication considerations should be addressed?**

**What are the dietary recommendations for this patient?**



# Ocular Considerations

OCT

Photo-document

Referral to retina

Anti-VEGF injections

Elderly white female that is frail and underweight with a poor appetite, need to consider **giant cell arteritis**.

CRP and ESR

- ESR can be affected by **Lipitor** and produce a false negative.
- CRP would be the more sensitive test in this patient.

# Medication Considerations

## Atorvastatin

- Statins work by lowering LDL
- LDL's responsible for transport of carotenoids
- Increase intake of carotenoids

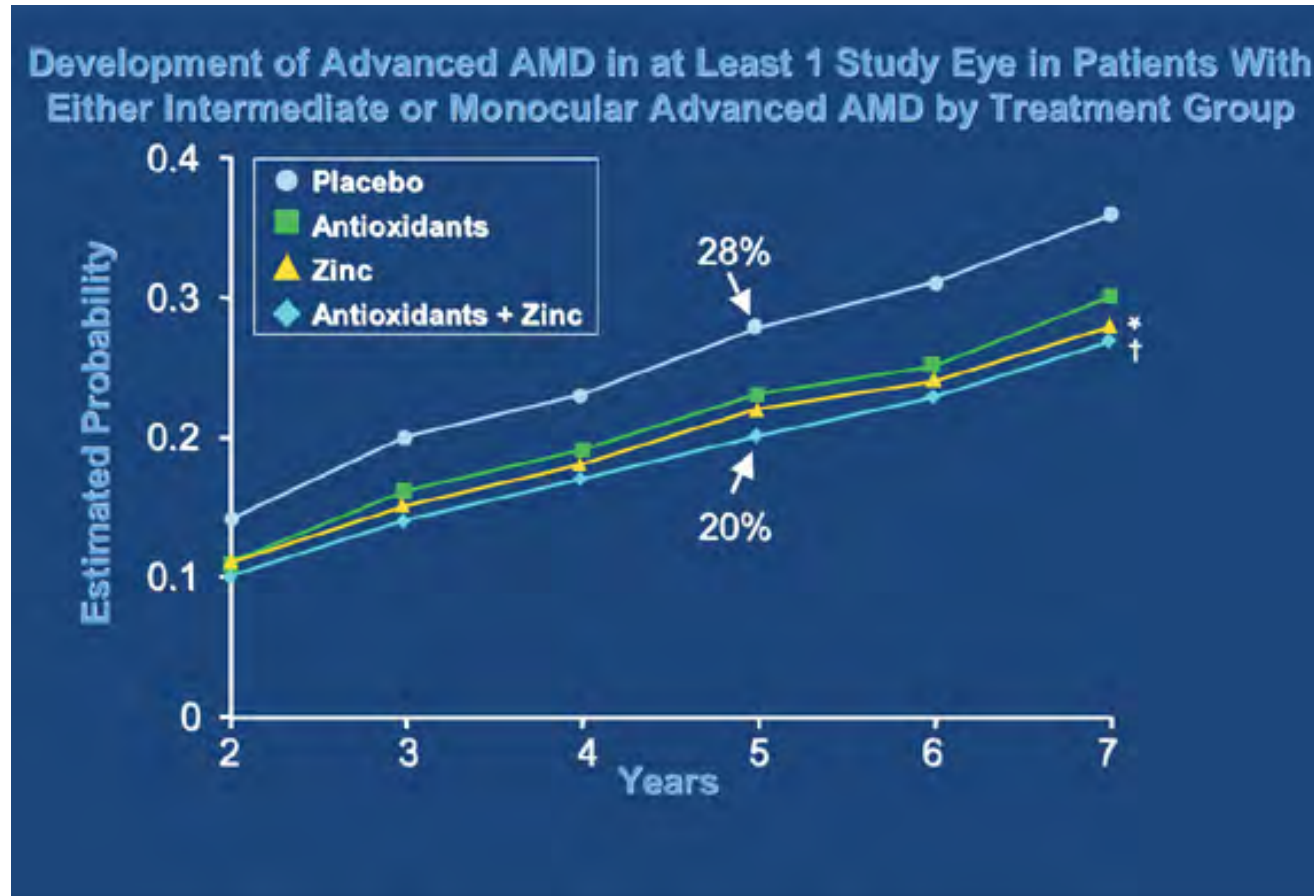
## Lisinopril

- Depletion of zinc levels

# Nutritional Considerations

- Past history of smoking - **supplementation should not include beta carotene.**
- Since patient is also on lisinopril, which can deplete zinc, she may need **AREDS 2** supplement.
- Consider genetic testing for AMD risk alleles since high risk CFH may do worse with zinc.
- Further assessment of anemia
  - B-complex deficiency (B-12 anemia) may cause failure to thrive, frailty, anorexia/poor appetite, and low weight. \*
- Poor appetite may need nutritional meal replacements of high quality.
- Evidence that those who eat a higher proportion of carbohydrates with a low GI compared to high GI have a lower risk of AMD.

# AREDS: Results



- **AREDS formula**

- 500 mg vitamin C
- 400 IU vitamin E
- 15 mg vitamin A (25,000 IU beta carotene)
- 80 mg zinc
- 2 mg copper
- 25% decreased risk of progression from stage 3 to 4 AMD
- Due to low progression to advanced ARMD in categories 1 and 2, even without intervention, no benefit was seen with AREDS

Beta carotene, vitamin C, vitamin E and zinc are all ESSENTIAL nutrients - cannot manufacture them. The doses studied were much higher than USRDI.

The background of the slide features three fresh carrots with their green leafy tops, arranged diagonally from the top left towards the bottom right. The carrots are a vibrant orange color. The entire image is overlaid with a semi-transparent dark grey filter to ensure the text is legible.

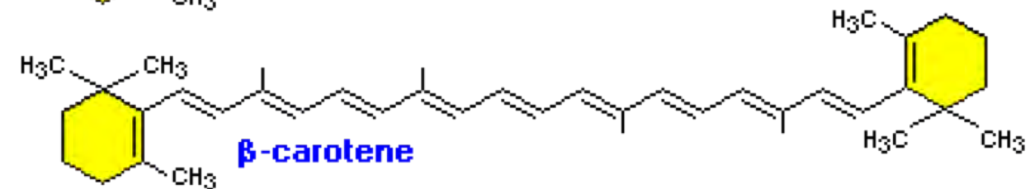
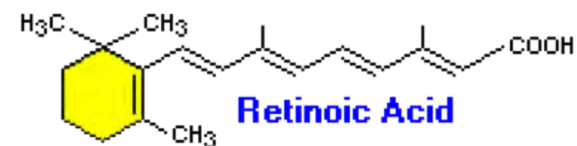
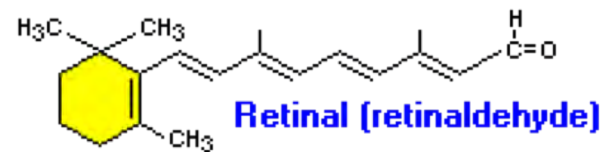
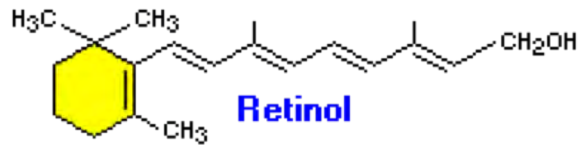
# Beta Carotene

- **Provitamin A carotenoids**
  - $\alpha$ -carotene,  $\beta$ -carotene, and  $\beta$ -cryptoxanthin
  - Can be converted by the body to retinol (vitamin A).
- No vitamin A activity from lutein, zeaxanthin, and lycopene.
- **Carotenoids in food need fat to be absorbed**
  - At least 3-5 grams in a meal
  - They have to be released from food and made into mixed micelles
- **Carotenoids in supplements do NOT need to be released from food matrix.**

**One reason beta carotene in supplements can cause toxicity but not beta carotene from food.**



# Vitamin A



Because the body converts dietary sources of vitamin A into retinol, 1 mcg of physiologically available retinol is equivalent to the following amounts

From dietary sources: 1 mcg of retinol, 12 mcg of beta-carotene, and 24 mcg of alpha-carotene or beta-cryptoxanthin.

From supplements: body converts 2 mcg of beta-carotene to 1 mcg of retinol.

# Zinc and the Eye

- Influences vitamin A metabolism
  - Absorption, transport, and utilization.
- Regulatory role of zinc in vitamin A transport is mediated through protein synthesis.
- The oxidative **conversion of retinol to retinal requires the action of a zinc-dependent retinol dehydrogenase enzyme.**
- Zinc is a component of retinol-binding protein
- Zinc deficiency reduces release of vitamin A from liver
- Bioavailability relatively higher in meat, eggs, and seafood; less from whole grains and legumes due to inhibitory effects of phytic acid on absorption
- **Long term consumption of zinc >40 mg per day can result in copper deficiency**



# AREDS 2: Set Up

## Primary Study:

- Assessed effect on cataracts, AMD and moderate vision loss
- 10 mg lutein + 2mg zeaxanthin and/or
- 650mg EPA + 350 mg DHA

## Second Randomization:

- Original AREDS
- AREDS minus beta carotene
- AREDS with low dose zinc (25mg)
- AREDS with no beta carotene and low dose zinc

Addition of omega 3 fatty acid not harmful nor beneficial

Addition of lutein and zeaxanthin added beneficial effect of 10% beyond original AREDS formula in reducing risk of progressing to advanced AMD

When beta carotene removed incremental benefit increased to 18%

No evidence to support omega 3 fatty acids to the formula; though other studies have shown benefits of eating fish 2-3 times week



# AREDS 2 Results



# AREDS 2 Results

Comparison low dose zinc (25mg) to original dose (80mg) showed no statistical difference

Cataract: dietary supplement with lutein and zeaxanthin no statistically significant difference overall.

Lutein and zeaxanthin **SIGNIFICANTLY MORE BENEFICIAL** than beta carotene in preventing intermediate to advanced AMD progression as a part of a supplement containing zinc + vitamins C and E.

# AREDS 2

- **Beta-carotene ...**
  - Did not contribute to efficacy
  - Increased the risk of lung cancer, especially in people who smoke or previously smoked
  - Led to a reduced absorption of lutein/zeaxanthin
- More patients taking supplement containing beta-carotene died of lung cancer during the study than those not taking beta carotene.
  - Most that died were **former smokers**
- Lowering zinc from 80 mg to 25 mg had no significant effect on the risk of advanced AMD.

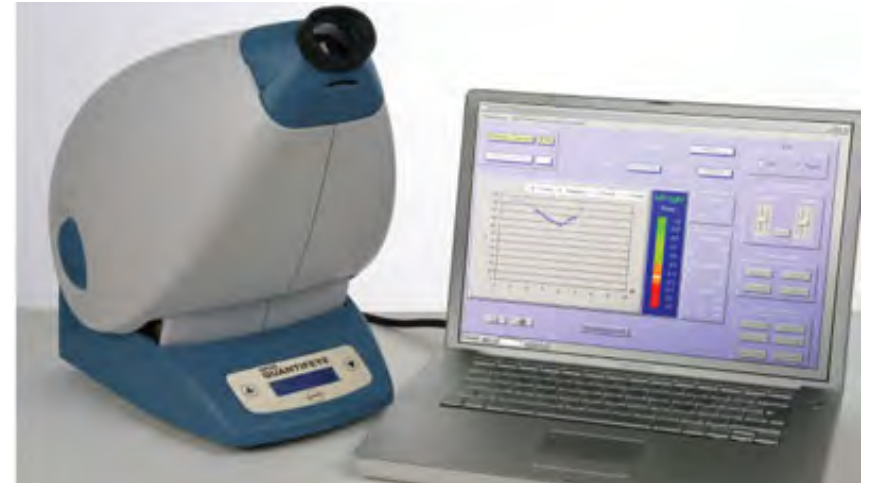
# Carotenoids

- Red, orange, and yellow pigments synthesized by plants, algae, and some bacteria
  - **Lutein**
  - Lycopene
  - **Beta-carotene**
  - Beta-cryptoxanthin
  - Alpha-carotene
  - **Zeaxanthin**
- Antioxidant activity
- Best absorbed with fat in a meal
- Chopping, pureeing, cooking in oil increases the bioavailability

Nutrient	Daily Intake <sup>1</sup>	Examples of food sources	Contains <sup>1</sup>	Examples of food sources	Contains <sup>1</sup>
Lutein and zeaxanthin	6mg <sup>2</sup>	1/2 cup (65g) kale	11.9mg	1/2 cup (120g) pumpkin	1.2mg
		1/2 cup (90g) spinach	10.2mg	1/2 cup (125g) brussel sprouts	1.2mg
		1 cup (30g) raw spinach	3.7mg	1/2 cup (80g) broccoli	0.8mg
		1/2 cup (80g) peas	1.9mg	1/2 cup (80g) corn	0.6mg
		1 cup (55g) cos lettuce	1.3mg	2 eggs	0.5mg
Omega-3	0.9-1.6g	100g salmon	1.8g	100g tuna	0.2g
		100g sardines	0.9g	100g prawns	0.2g
Vitamin C	45 mg	1 medium orange	69mg	1/4 cup capsicum	47mg
Vitamin E	7-10mg	20 almonds (30g)	7.8mg	1 Tbsp wheat germ	2.2mg
Zinc	8-14mg	7 oysters (100g)	59mg	1/2 cup rice bran	3.5mg
Selenium	60-70mcg <sup>3</sup>	2 Brazil nuts (8g)	80mcg	24 cashew nuts (30g)	5.6mcg

# How much should your patient take?

- Try to be patient-specific
- What is the current dietary intake of foods abundant in lutein and zeaxanthin?
- Measure antioxidant capability
- Measure MPOD





# Nutrigenomics and AMD: Where Are We Today?

- Pharmacogenomics is the study of the interaction between drugs and the genome.
- **Nutrigenomics** is the study of the interaction of nutrition and genes, especially with regard to the prevention or treatment of disease.
- More than 30 genes that affect the risk for AMD progression.
- Complement factor H (CFH) and age related maculopathy 2 (ARMS2) risk alleles are most common.



# Vavvas et al 2018

- Evaluated effect of AO and zinc in AREDS formulation on progression to **NV AMD only** as a function of CFH and ARMS2 genotypes.
- Reduction in AREDS was due to slowed progression of wet AMD not dry AMD (GA).
- High CFH and no ARMS2 risk alleles and taking AREDS formulation had increased progression to NV compared to placebo.
- Low CFH and high ARMS2 genotype had decreased progression risk to NV AMD.

Vavvas DG, et al. *CFH* and *ARMS2* genetic risk determines progression to neovascular age-related macular degeneration after antioxidant and zinc supplementation. *Proc Natl Acad Sci USA*. 2018 Jan 23;115(4):E696-E704.

# Vavvas et al 2018

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**Conclusion:** AREDS formulation modifies risk of progression to NV based on individual genetics and use **should be based on patient-specific genotype.**

**Approximately 18% individuals could do WORSE with zinc.**