

Sustainable Paths Family Health Care LLC

www.sustainablepathsNP.com

Presented By:



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Family Nurse Practitioner ANCC Board Certified IFM-Certified Practitioner Natural Family Planning Instructor

Many Slides by:



An Expanded Approach to Dyslipidemia

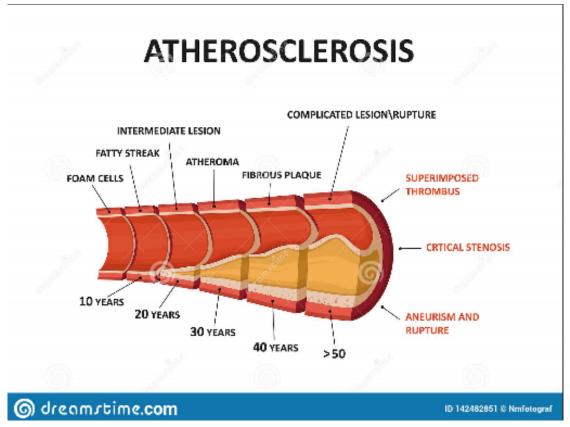


YOUSEF ELYAMAN, MD

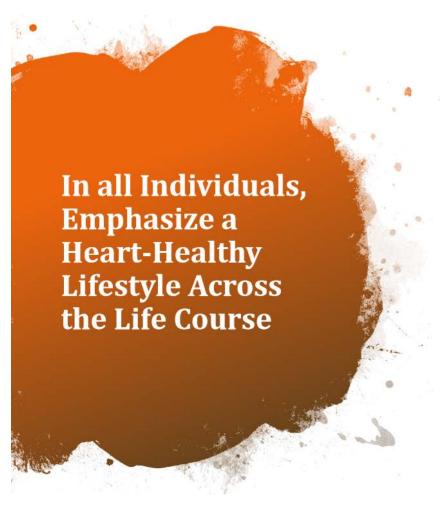
Cardiometabolic Advanced Practice Module Atlanta, GA February 2019

Functional Medicine Series

The Skinny on Fats



2018 Guidelines: Normal Risk



- Start young
- Focus on decreasing components of metabolic syndrome
- Healthy 7:
 - Manage BP
 - Control cholesterol
 - Reduce blood sugar
 - Get active
 - Eat better
 - Lose weight
 - Stop smoking

2018 Guidelines: High Risk

Clinical ASCVD

- Acute Coronary Syndrome
- History of MI
- History of angina (stable or unstable)
- History of arterial revascularization
- History of stroke, TIA or PAD
- Aortic aneurysm
 (atherosclerotic in origin)

 Goal is to lower LDL by 50% or more

- High Intensity Statin:
 - Atorvastatin (40-80 mg)
 - Rosuvastatin (20-40 mg)

2018 Guidelines: Very High Risk

Major ASCVD Event

- ACS within past 12 months
- History of MI
- History of ischemic stroke
- Symptomatic peripheral arterial disease
- History of claudication with ABI < 0.85
- Previous revascularization or amputation



2 From This list

or

High-Risk Conditions

- Age ≥65 y/o
- Heterozygous familial hypercholesterolemia
- History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
- Diabetes mellitus
- Hypertension
- CKD (eGFR 15-59 mL/min/1.73 m2)
- Current smoking
- History of congestive HF

1 + 2

2018 Guidelines: Very High Risk Treatment



Severe Primary Hypercholesterolemia (LDL≥190)

- · Age 20-75?
- · Start high intensity statin
- LDL-C level remains ≥100 mg/dL consider adding ezetimibe
- LDL-C level remains ≥100 mg/dL and has multiple risk factors, consider adding a PCSK9 inhibitor

High-Intensity

Lowers LDL =/> 50%

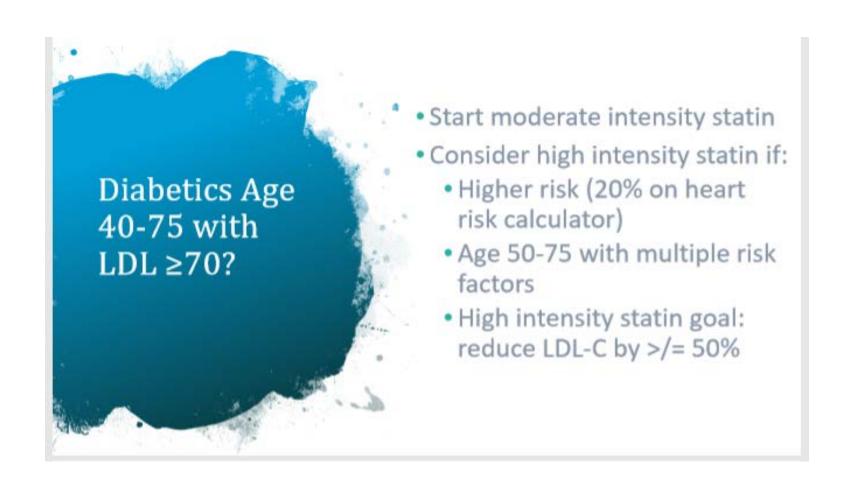
Atorvastatin (40)-80 mg Rosuvastatin 20 (40) mg Goal: LDL-C of 70 mg/dL

PCSK9 Inhibitors

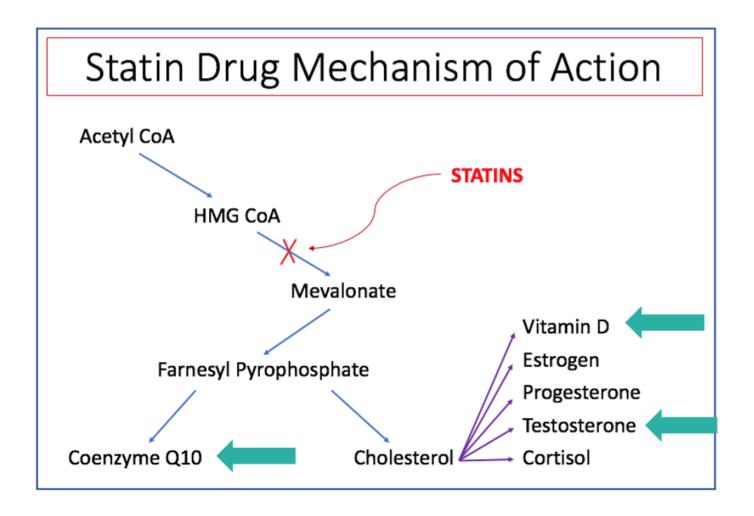
- Alirocumab (Praluent)
 - SubQ: Initial: 75 mg every
 2 weeks or 300 mg every
 4 weeks
- Evolocumab (Repatha)
 - SubQ: 140 mg every 2 weeks or 420 mg once monthly

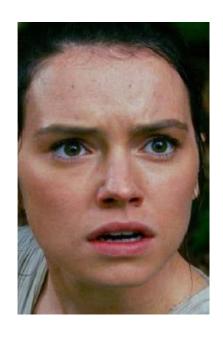
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2018 Guidelines: Diabetic



Why Statins are Risky





Potential Statin Risks

- Statins may be causative in coronary artery calcification and can function as mitochondrial toxins that impair muscle function in the heart and blood vessels
- Thus, the epidemic of heart failure and atherosclerosis that plagues the modern world may paradoxically be aggravated by the pervasive use of statin drugs.

Okuyama H, Langsjoen PH, Hamazaki T, Ogushi Y, Hama R, Kobayashi T, Uchino H. Statins stimulate atherosclerosis and heart failure: pharmacological mechanisms. Expert Rev Clin Pharmacol. 2015 MarsiR01:189-99. doi: 10.1586/17512438.2015.1011125. Frantum in: Expert Rev Clin Pharmacol. 2015:8/16/1503-5.

- 1 in 50 develop Type II Diabetes
- 1 in 10 develop myalgia/muscle atrophy
- Suspected link to MCI/Alzheimer's, neuropathy
- Depression, increased suicide (more in women)
- Atrial fibrillation
- Possible preterm delivery and microcephaly

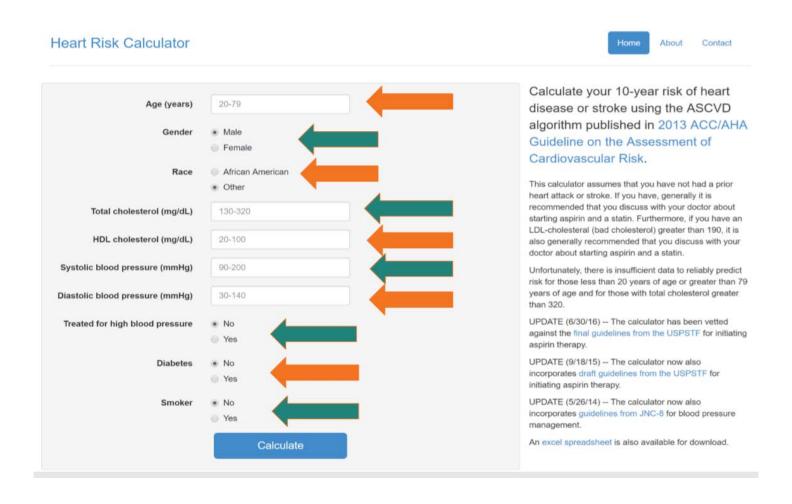
Options: Summary

SUMMARY IFM DYSLIPIDEMIA TREATMENT RECOMMENDATIONS BASED ON REPORTED ACTION

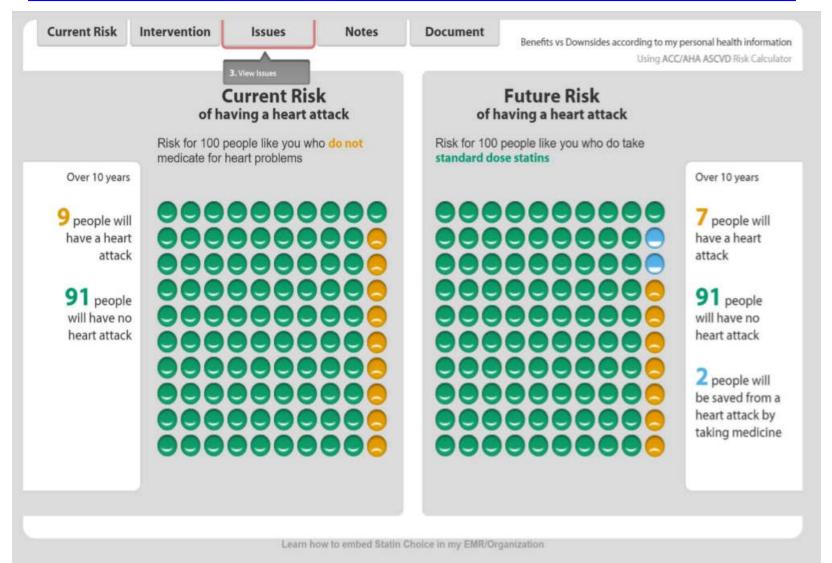
Agent	Dose	Reported Action	↓ LDL	↑ HDL	↓ TG	Pattern B	Mod LDL
Trans Resveratrol	250 mg QD	Reduces TC, TG, and LDL; blocks uptake of modified LDL by CD36SR (1)	*		•		
N-Acetyl- Cysteine	1000 mg BID	Blocks uptake of modified LDL by CD36SR (1)					Y
Aged Garlic Extract	600-900 mg BID	Reduces CAC and plaque progression and lowers HS-CRP (2,3)					
Bergamot	500-1,000mg QD	Reduces TC, LDL, TG, glucose. Increases HDL. Some vasodilatory effect.	٧				
Niacin (B3) Nicotinic Ac.	500 to 4000 mg QD as tolerated	Reduces TC, LDL, APO-B, TG, and shifts LDL from small type B to large type A (4)	٧		٧	*	
Red Yeast Rice	2400-4800 mg QD	Statin like effects (5)			٧		
Curcumin	500 mg BID	Inhibits atherosclerosis, increases HDL, anti-inflammatory (6, 7)		٧	*		
Green Tea/EGCG	500-1000 mf QD or 60oz tea	Inhibits HMG-CoA, reduces oxLDL and APO-B, increases PON-1 and LDL receptor; decreases inflammation decreases body fat. (8, 9)	٧		٧	*	٧
Plant Sterols	2-3 g QD	Reduces TC and LDL, anti-inflammatory (10, 11)	٧		٧		٧
Pomegranate	8 oz. juice or 1-2 c. seeds QD	Anti-inflammatory, improves function of HDL, inhibits platelets, reduces IMT (12, 13, 14)		٧	*		Y
Pantethine	300 mg TID or 450 mg BID	Reduces TC, LDL, APO-B, and TG; increases HDL and APO-A1 (15, 16)	٧	٧	*	Y	
Probiotics	60-100b organisms QD	Reduce TC, LDL, and TG (17)	*		*	*	
Berberine HCL	500 mg QD	Reduces TC, LDL, and TG (19); lowers glucose; anti-inflammatory properties.	٧		٧	Y	
Omega-3 Fatty Acids	1-5g QD mixed EPA DHA	Reduces TG (18), COX-2 inhibition by DHA, (21), IL-1b inhibition by EPA (22), Increases HDL/HDL2 (23), EPA reduces pattern-B, sdLDL & CRP (24)		©2017 The In	w stitute for Fu	w nctional Medici	♥

ACC/AHA ASCVD Risk Calculator

(http://www.cvriskcalculator.com)



StatinDecisionAd.Mayoclinic.org



It's not JUST LDL

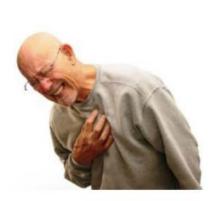
Atherogenic Determinants of LDL

- LDL particle number
- LDL particle size (e.g. nm, Angstroms)
- sdLDL has a 1.7X
 increase in endothelial penetration
- sdLDL has a greater chance of oxidation



... Or even cholesterol

50% of heart attacks leading to sudden death happen in patients with normal cholesterol!







Sachdeva A, Cannon CP, Deedwania PC, et al; for the Get With The Guidelines Steering Committee and Hospitals. Lipid levels in patients hospitalized with coronary artery disease: an analysis of 136,905 hospitalizations in Get With The Guidelines. Am Heart J. 2009;157(1):111–117.e2.

Factors Affecting Cardiometabolic Health

CARDIOMETABOLIC MATRIX (The Usual Suspects)

Retelling the Patient's Story

Antecedents

Age, Smoking, Gender Familial hypercholesterolemia APOE status Family Hx of CVD

Triggering Events

Stress/Injury Infection/Dysbiosis Toxic exposures

Mediators/Perpetuators

Chronic stress

Hyperinsulinemia Visceral Adipose Tissue (VAT) Oxidative stress/Inflammation

Physiology and Function: Organizing the Patient's Clinical Imbalances Assimilation Defense & Repair Hypochlorhydria/ Acid blockers Chronic infections (e.g. dental) Adverse Food Reactions Autoimmune diseases ↑ hs-CRP, MPO Dysbiosis **↑** TMAO ♠ Oxidized LDL Mental Emotional Structural Integrity Stress Grief Energy FBS, HgbA1c, fructosamine ↑ BMI, WHR, VAT **V**GSH, **↑** Oxidative Stress ◆ Sense of ↑ Lp-PLA2, Fibrinogen Connection Mitochodropathies ↑ CAC, CIMT Spiritual Cardiomyopathies Elevated Fe/ferritin Statin use (♥ CoQ10) Microalbuminuria Communication Biotransformation & Elimination Fasting Insulin, ITT Constipation Hyperinsulinemia/DMII POPs/H. metal exp. Transport Dysglycemia Thyroid Dysfunction Hypertension Homocysteine Dyslipidemia Angiotensin II/Renin Angina MTHER SNPs Menopause, PCOS Endothelial Dysf. Dyslipidemia SNPs Hyperuricemia Abn. PWV/A Edema/CHF NAFLD

Modifiable Personal Lifestyle Factors

Sleep apnea Shallow breathing Decreased HRV

Name:

Exercise deficit
Orthopedic pain
Low motivation

Nutrition

Date:

↑/ Cortisol

↑ Glycemic impact
 ↑ Processed foods
 ↑ Na⁺, trans fats
 ↓ Nutrient diversity, Ω3

Stress

Hx of abuse/neglect Poor coping skills Anxiety/Depression Financial stress Drug/Alcohol overuse Tobacco use

Relationships

Isolation Grief No Pets

Renal Disease

Caregiver burden

Non-dipping (BP) Low motivation

↓ Bs, K, D, K⁺ & Mg⁺⁺

Low knowledge Caffeine + slow Cyp1A2

CC:

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RISK FACTOR DISCUSSION



- Family history of premature ASCVD (males <55, females <65)
- Persistently elevated LDL-C levels ≥160 mg/dl
- Metabolic syndrome
- Chronic kidney disease (eGFR 15–59 mL/min/1.73 m2)
- History of preeclampsia or premature menopause (age <40 years)
- Chronic inflammatory disorders (rheumatoid arthritis, psoriasis, lupus, or chronic HIV)
- Hs-CRP ≥2.0 mg/L
- high-risk ethnic groups (e.g., South Asian)
- Persistent elevations of triglycerides ≥175 mg/dl
- Apolipoprotein B ≥130 mg/dl (if measured) (consider if triglyceride ≥200 mg/dL)
- Lipoprotein (a) ≥50 mg/dl (in women, only if they also have high cholesterol)
- ABI < 0.9
- Radiation tx: left main, left anterior descending, and proximal right coronary artery is in the field (left breast cancer)

Coronary Artery Calcium Score

- If 0, treatment with statin therapy may be deferred for 5-10 years
- If 0 but smoker, diabetic, or strong family history of premature
 ASCVD (<55 males & ,65 females) → statin
- A CAC score of 1-99 favors statin
- For any patient, if the CAC score is ≥100 Agatston units or ≥75th percentile: statin therapy is indicated (unless otherwise deferred by the outcome of clinician)

Radiation Dose

- CAC scanning delivered 0.74 to 1.26 mSv* of radiation (similar to mammogram dose)
- There can be up to a 10 fold variance!
- · Radiation increases cancer risk

Test	Radiation Dose
Chest X-ray	0.1 mSv
Coronary Artery Calcium Score	0.99 mSv
Chest CT	7 mSv

*mSV=Millisievert

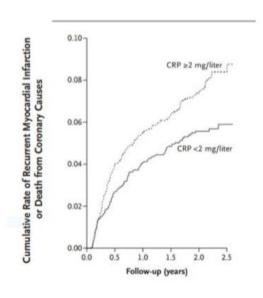
Inflammation

hs-CRP

CONCLUSIONS

Patients who have low CRP levels after statin therapy have better clinical outcomes than those with higher CRP levels, regardless of the resultant level of LDL cholesterol.

Strategies to lower cardiovascular risk with statins should include monitoring CRP as well as cholesterol.



PROVE IT- TIMI = Pravastatin or Atorvastatin Evaluation and Infection Therapy—Thrombolysis in Myocardial Infarction 22 (PROVE IT-TIMI 22) trial, published in 2004, randomized 4,162 patients with recent ACS to high-dose atorvastatin 80mg daily or moderate-dose pravastatin 40mg daily.

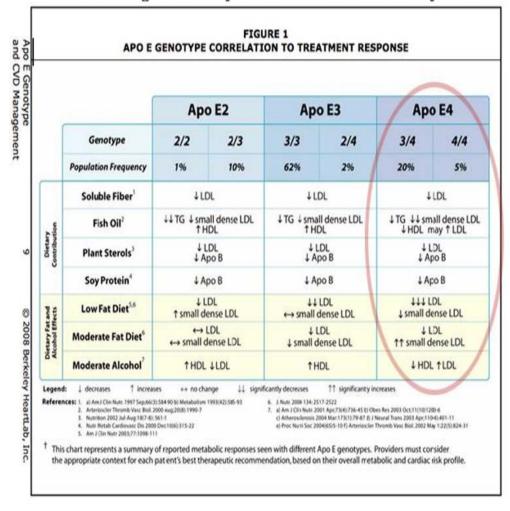
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Genetics

APOE-Genetic Variants

- ApoE2 is associated with lower cholesterol; increased triglycerides; Hyperproteinemia Type III
- ApoE3 & 4 are associated with higher serum cholesterol
- E3/E3, E3/E4 and E4/E4 genotypes were found to be associated with an increase in CA-IMT
- IDIR
- PCSK9
- LDL>190 and 1st degree relative with LDL>190 or premature CVD
- MTHFR, MTR, MTRR
- COMT
 - VA/VAL (upregulated, ADD)
 - NO Vit E, ASA
 - MET/MET: YES Vit E, ASA

Dietary Responses and Apo E



Apo B

Apo B & ApoB:ApoA1 Ratio

permat dispress grown beauty

HOW DO APOLIPOPROTEINS ApoB AND ApoA1 PERFORM IN PATIENTS WITH ACUTE CORONARY SYNDROMES

The superiority of ApoB, and especially the apoB:apoA-I ratio in patients with the highest cardiometabolic risk (known CVD or diabetes) and two additional major risk factors (e.g. smoking, hypertension, or family history of premature CAD), for assessing risk of future events and in the secondary prevention in ACS patients seems to be indisputable

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Lp (a)

Helps assess overall risk of at atherosclerotic process

Most likely involved in coagulation

Dr. Weiss:

When elevated, consider a quality fish oil and additional anticoagulation to mitigate potential risk

Lab Summary: Lipids

Lab	TARGET/OPTIMAL (varies by lab)	Explanation		
LDL-P	< 1000 nmol/L	LDL-Particle count is strong, independent predictor of CHD. When combined with LDL-C, may be used to asset Insulin Resistance risk.		
LDL-Pattern	Pattern B: "Bad" <25.5 nm or <218.2 Angstrom Pattern A: "Good" <25.5 nm or >222.5 Angstrom	Pattern B "Bad" are smaller, and more numerous, i.e. higher LDL-P count Pattern A "Good" are larger, more buoyant and less numerous		
HDL2/3		HDL2 is large, buoyant and most protective HDL; Low HDL2 + normal LDL \rightarrow increased CHD risk HDL3 is smaller, not as protective		
VLDL3	>30 mg/dL is considered elevated; usually calculated as percentage of TG	Densest VLDL → Higher risk than VLDL1 and VLDL 2 The best way to lower VLDL is to lower triglycerides		
ApoE Genotype		Diagnostic value for individuals suspected of type III hyperlipoproteinemia. ApoE2 is associated with lower cholesterol; increased triglycerides; Hyperproteinemia Type III. ApoE3 & 4 are associated with higher serum cholesterol E3/E3, E3/E4 and E4/E4 genotypes were found to be associated with an increase in CA-IMT		
ApoA1	>20 yo female: >130mg/dL is low risk; <115 mg/dL is high risk >20 yo male: >120 mg/dL is low risk; <121 mg/dL is high risk	Protein core of HDL (Good)		
АроВ	>20 yo: <100 mg/dL is low risk; >120 mg/dL is high risk	Protein core of LDL/VLDL (Bad)		
ApoB:ApoA1	Ratio of <0.80			
Ox-LDL	<60 U/L low risk; 60-69 U/L moderate risk; >70 U/L high risk	Oxidized LDL is a risk factor for CHD, independent of TC/LDL Lp(a) and Ox-LDL are correlated		
Lp(a)	<30 mg/dL	Lipoprotein-a is inherited levels of small, low density cholesterol protein; correlated with Ox-LDL		
LpPLA2	<75 nmol/min/mL is low risk >75 nmol/min/mL is high risk	Lipoprotein-associated Phospholipase A-2 is an inflammatory protein produced in the vascular intima; upregulated in atherosclerotic plaques, correlated with progression of atherosclerosis and plaque rupture vulnerability; correlated with Ox-LDL		

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Other Risks: Heavy Metals

Heavy Metals and Dyslipidemia

Mercury and other heavy metals will

- Increase LDL and TG, decrease
 HDL, and induce dysfunctional HDL
- Increase CVD, hypertension, atherosclerosis
- Reduce total antioxidant capacity
- Act as mitochondrial toxins



Skoczyńska A, Poreba R, Steinmentz-Beck A, Martynowicz H et al. The dependence between urinary mercury concentration and carotid arterial intima-media thickness in workers occupationally exposed to mercury vapour. Int J Occup Med Environ Health. 2009;22(2):135-42.

^{2.} Kim DS, Lee EH, Yu SD, Cha JH, Ahn SC. [Heavy metal as risk factor of cardiovascular disease—an analysis of blood lead and urinary mercury]. J Prev Med Public Health. 2005 Nov;38(4):401-7.

Solenkova NV, Newman JD, Berger JS, Thurston G, Hochman JS, Lamas GA. Metal pollutants and cardiovascular disease: mechanisms and consequences of exposure. Am Heart J. 2014 Dec;168(6):812-22.

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Other Risks: Infection

Infectious Agents Associated with Dyslipidemia & Cardiovascular Disease

- Brucella spp.
- Chlamydia pneumonia
- Helicobacter pylori
- Porphyromonas gingivalis
- Hepatitis C (chronic)

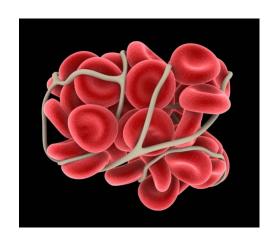


Other Risks: Inflammation

- Proton Pump Inhibitors
- Poor Methylation
- Increased oxidation
- Poor Dietary Choices
- Lack of Exercise
- Visceral Fat
- Chronic infections and dysbiosis
- Toxins (organic pollutants)
- Poor Sleep
- Stress / Sympathetic Dominance



Other Risks: Fibrinogen



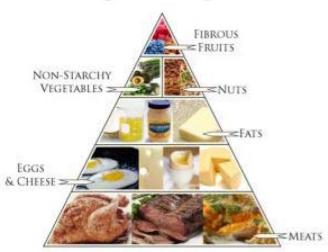
- Independent risk factor for CVD
- Increased in response to:
 - Inflammation
 - Tissue Injury
 - FBG gene

"Lifestyle" can reverse or prevent CVD

- Get off wheat (if it affects you) and all high glycemic foods/sugars
- Choose a diet high in natural protein, fiber, antioxidants, omega fats
 - (Dark chocolate 45-77% lower ASCVD, Nuts 23% decrease cardiovascular mortality)
- Exercise 30 minutes/day
 - (30-40% decrease cardiac events)
- Optimize hormones, remove toxins (Lead etc)
- Alkalize? (High green vegetable)
- Measure and supplement endothelial dysfunction
 - (arginine, folate, Vit C, taurine, Mg, NAC etc)
- Supplement proper inflammatory inhibition
- Own a cat (30% decreased risk of CV death and stroke)

Ketogenic Pyramid

Ketogenic Pyramid





- reduces inflammation (NFkB)
- enhances mitochondrial biogenesis
- enhances ATP production
- reduces ROS production
- reduces apoptosis
- Increases:
 - atherosclerosis/CVD risk
 - Liver fibrosis
 - Sympathetic tone
 - Adrenal "fatigue"
- Very hard for women
- Difficult to maintain long term

Mediterranean Diet

- A diet in the Mediterranean?
- Abundant vegetables, legumes, fruit
- Small amounts of fish/meat/cheese
- Cheese and yogurt
- Olive oil in moderation
- Wine in moderation
- Variety of antioxidants
- Little sugar/refined white flour

EFA: Dosing

- Elevated triglycerides
 - 2–4 g/day g omega-3 fatty acids daily
- 1.5-2.4 gm EPA/1-1.6 g DHA
- Hypertension
 - Average dose 3.6 g/day
- History MI
 - as little as 1g/day omega-3 from fish oil; cons/3g/day
- Arrhythmia
 - 1-4.3 gm/day omega-3 fatty acids from fish oil
- High Cardiovascular disease risk
 - 1-3 gm/day total omega-3 fatty acids from fish oil



Heart

- Reduces triglycerides by 25%-30%
- Improves endothelial function
- Reduces inflammatory markers (CRP)
- Reduces risk of stroke
- Improves blood pressure
- Improves survival after a heart attack
- Lowers risk of heart disease
- Enhances longevity and vitality

Clinical Applications for Essential Fatty Acids

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MCT (Medium Chain Triglycerides

(caprylic and capric acids)

- Absorbed intact across gut wall; transported into mitochondria independent of the carnitine shuttle.*
- MCTs are anti-inflammatory: blunts linoleic acid-induced increases in TNF-alpha production by 45%. (in vitro)
- MCTs prevent <u>endotoxemia-induced</u> liver damage (mice)

MCT foods: coconut oil 66%

*Calabrese C et al. *Altern Med Rev* 1999;4(1):23-28 Kono H et al. *Ann Surg* 2003;237(2):246-55

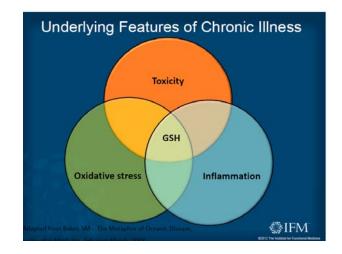


Glutathione

Glutathione: Atherogenesis

• Depletion of the protective glutathione precedes lipid oxidation and atherogenesis in vivo.

Biswas SK et al. Depressed glutathione synthesis precedes oxidative stress and atherogenesis in Apo-E(-/-) mice. *Biochem Biophys Res Comm* 2005; 338: 1368-73.





CASE 1

GEGEGEER			4.0	-2.0	(w) was
CHOLESTEROL		249 H	140 -	199	(MG/DL)
HDL CHOLESTEROL	42		35 -	80	(MG/DL)
LDL (CALCULATED)		164 H	0 -	129	(MG/DL)
CHOL/HDL CHOL RATIO		5.9 H	<	5.0	
LDL/HDL RATIO	3.92		0.9 -	5.3	
VLDL, CALCULATED		42 H	<	41	(MG/DL)
TRIGLYCERIDES		211 H	0 -	150	(MG/DL)

- No medication, no cardiac history
- EKG 8/19 shows I mm T wave inversions V4, minor T inversions V5, V6 (ischemia?)
- Fam hx: Father age 68 heart failure after falling 30' onto concrete

Case 2: 54 yo female

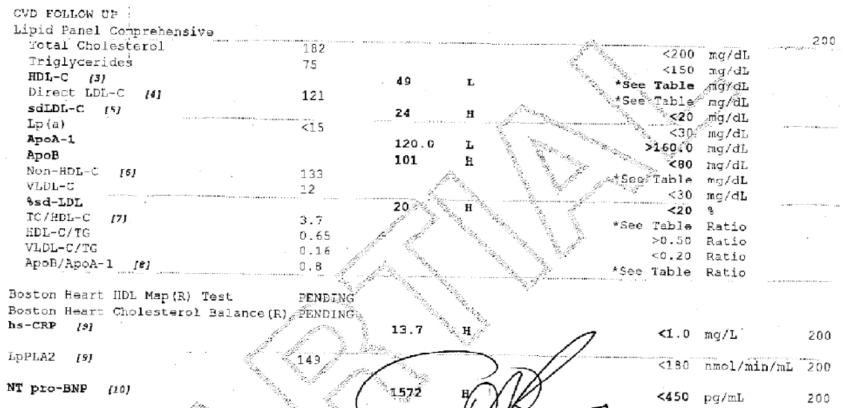
CARDIAC RISK		
CHOLESTEROL	229	100-240 mg/dL
HIGH DENSITY LIPOPROTEIN (HDL)	73.0	25.0-75.0 mg/dL
TRIGLYCERIDES	94	10-200 mg/dL
CHOLESTEROL/HDL RATIO	3.13	1.50-5.00

I have reviewed done his latest results of her cholesterol panel. Her total cholesterol was 298. Her HDL was 102. Her LDL was 179, and her triglycerides were 83. With these numbers her 10-year cardiovascular risk is only at 1.4%. This is well below the 7.5% recommended for statin use. The question is whether she has any evidence of coronary disease given these high numbers. She did have a calcium score several years ago, and the score was 0. I am going to order another calcium score to reassess. If her calcium score is essentially anything except for 0, then she will be instructed to start a statin. I did inform her since she is postmenopausal that her cholesterol panel will continue to slowly worsen.

IMPRESSION

1. Coronary calcium score of zero. No identifiable calcified coronary

Case 3: 79 yo male



- 2012 Calcium score 1027- no observed CAD
- 5/19 echo: Mild aortic stenosis, mild left ventricular diastolic dysfunction (confirms BNP), mild dilated left atrium.

Case 4: 34 yo male smoker

CARDIAC RISK			
CHOLESTEROL	158		140-275 mg/dL
HIGH DENSITY LIPOPROTEIN (HDL)	22.9	LOW	25.0-75.0 mg/dL
LOW DENSITY LIPOPROTEIN (LDL)	67	LOW	80-200 mg/dL
VERYLOW DENSITY LIPO. (VLDL)	68	HIGH	5-40 mg/dL
TRIGLYCERIDES	340	HIGH	10-200 mg/dL
CHOLESTEROL/HDL RATIO	6.89	HIGH	1.50-5.00
LDL/HDL RATIO	2.92		0.00-3.60

- Build 6'0" 220 (BMI 29.8)
- No APS / no admitted history