A Message from your Heart; Answers for Cardiovascular Disease
International College of Integrative Medicine
March 6-10, 2019 Philadelphia.
Coronary Artery Disease

Number One Cause of Death
Atherosclerotic Disease
Atherosclerotic Plaque

- Carotid Bifurcation
- Abdominal Aorta
CXR Coronary Artery Calcification

- Calcified LAD on Lateral Chest X Ray
- Difficult to See Finding
- Coronary Artery Calcification X-Ray Marker for CAD.
CXR Coronary Artery Calcification
CAT Scan
Coronary Artery Calcification

CAT SCAN Showing Calcified LAD - Left Anterior Descending Artery
CAT Allows Quantify Amount of Calcium - Calcium Score

First Person in Human History Diagnosed w/ Coronary Artery Disease.

Egyptian Princess Ahmose-Meryet-Amon, 1550 BC.

Wheat Based Diet.

The Big Picture - Summary Slide

1) Cholesterol Theory Falsified by Modern Imaging Techniques.
2) 16s Ribosome: Atherosclerotic Plaque is Infected Bio-Film.
3) Arterial Damage at Sites of Shear Stress, associated with underlying Vitamin C Deficiency.
5) Soft Tissue Calcification is Inflammatory Response to Infection
6) Calcium Score Predicts Future Risk of CAD EVENT
7) Annual Progression of Calcium Score Highly Predictive of MI and Failure of Treatment.
8) Halting or Slowing Progression of Calcium Score Indicates Good Prognosis and Response to Treatment.
9) Statin drugs Benefits Are Due to Pleiotrophic Effects, (anti-inflammatory and antibacterial). Not Cholesterol Lowering.
## Interventions for Calcium Score?

- Statin Drugs
- Estrogen
- Testosterone
- Thyroid
- Vitamin C
- Vitamin K2
- Tocotrienol Vit E (Ramanathan, 2018)
- Magnesium
- Leaky Gut Protocol
- Blood Sugar Protocol
- Wheat- Gluten Free
Interventions for Calcium Score?
Botanicals

- Aged Garlic (Hom, Budoff 2015)
- Berberine (Zhang, 2016)
- Chinese Skullcap baicalin (Dinda, 2017)
- Curcumin (Olszanecki, 2005)
- Resveratrol/Pterostilbene (Li 2018)


Cholesterol Theory Falsified

1) Calcium Score - No Correlation between Cholesterol level and Calcium Score. (Harvey Hecht, 2001)

2) Autopsy Studies show No Correlation between Cholesterol level and Amount of Atherosclerotic Plaque.

3) 2004 Raggi Study 495 pts on statins- 41 Heart Attacks Over 6 Years – They had Same Cholesterol and LDL as Heart Attack Free Patients. (Raggi, Paolo, 2004)

4) CETP Inhibitor Evacetrapib - Lowers LDL - Fails Clinical Trials

5) Elderly Patients w/ Familial HyperCholesterolemia- Zero CAC-No CAD-Simon Broome Registry (Neil Andrew, 2008)

Reverse Epidemiology for Dialysis, CHF, RA, COPD, and in elderly High Cholesterol Improves Survival. (Horwich, 2007)


Cholesterol Theory Falsified

LDL - Cholesterol Does Not Cause Coronary Artery Disease

CAC for 930 Asymptomatic Pts, NOT ON STATINS

No Significant Differences in the Calcium Scores throughout the entire range of all lipid parameters.

Calcium Percentiles Were Virtually Identical within Lipid Value Subgroups.

TC, LDL-C, HDL-C, TC/HDL-C, and triglyceride levels DO Not Correlate with either the extent or prematurity of calcified plaque burden.

Autopsy Studies – No Correlation Between Cholesterol and Atherosclerosis Severity

"No relationship was present in any age group. It is concluded that the incidence and severity of atherosclerosis in man is not directly correlated with the blood serum cholesterol content." (Lande, 1936)

"No correlation could be observed between the serum cholesterol level and the amount and severity of atherosclerosis in the arteries." (Mathur, 1961)

Non-Statin Lipid Lowering Drug Fails
Evacetrapib - CETP

- Cholesteryl Ester Transfer Protein Inhibitor
- Multicenter, randomized, double-blind, placebo-controlled phase 3 trial,
- 12,092 patients w/CAD. Over 26 months.
- Reduced LDL 31%, Increased HDL 131%
- Evacetrapib Did Not Result in a Lower Rate of Cardiovascular Events than Placebo among Patients with High-Risk Vascular Disease.
- Statin Benefits are Due to Pleotrophic effects, NOT Cholesterol Lowering.

Falsifying the Cholesterol Theory
Zero CAC – Lifelong Cholesterol 580

72 year old male with untreated familial hypercholesterolemia with cholesterol level 580 and LDL-C 480 mg/dl.

Calcium Score of Zero

Atherosclerotic Plaque

Soft Tissue Calcification

“Vascular calcification is a clinical marker for atherosclerosis and may represent a special example of the general phenomenon of soft tissue calcification surrounding chronic inflammatory foci.” (Abedin, 2004)

Inflammatory Foci = Infection

Atherosclerotic Plaque as Poly-Microbial Biofilm

Plaque is Infected Biofilm

- Atherosclerotic Plaque Samples
- 16s Ribosome Technique
- Atherosclerotic Plaque is Infected Biofilm Colonized by Bacterial, Fungal and Protozoal Organisms.

LPS From Gut Drives Atherosclerosis

Atherosclerotic Plaque as Poly-Microbial Biofilm

Atherosclerotic Plaque as Polymicrobial Infected Biofilm

63 Studies and 23 Bacteria in Human Atherosclerotic Plaque Samples.

### Atherosclerotic Plaque as Polymicrobial Infected Biofilm

- Lanter BB, et al. Bacteria present in carotid arterial plaques are found as biofilm deposits which may contribute to enhanced risk of plaque rupture. MBio. 2014;5(3):
Infected Biofilms

- Organisms Secrete Matrix
- Cell to Cell communication
- Quorum Sensing
- Resistant to antibiotics
Intestinal Origin of Bacteria in CAD

Detection of Intestinal Bacterial by 16S rRNA in both the Blood sample and Atherosclerotic plaques. (Li, 2016)

Intestinal Bacteria in Plaques may Originate from Intestine.

“Endotoxin-treated Rabbits exhibited significantly Accelerated Atherosclerosis compared with Control Animals” (Lehr et al. 2001).

White Cliffs of Dover
Microbial Calcification
Calcium Score Highly Predictive of Future Event

Calcium Score Predicts Survival

Calcium Score NOT Perfect

- Calcium Score Best Use: Asymptomatic Pts.
- If Symptomatic Patient w/ Angina, then Proceed to CTA or SPECT Perfusion Scan Regardless of Zero or Low Calcium Score

Calcium Score – CT Angio Add-On

Left Main CAD with Zero CAC (+)SPECT Perfusion Scan

- 61 y/o female ER 18-mo. hx of Angina, AODM, HTN, hypothyroidism. 20-pack year smoker.
- CAC score of ZERO.
- SPECT: Extensive Myocardial Ischemia Anteriorly, Septally, Laterally and Apically.
- Cardiac Cath: 95% Stenosis of Ostiam Left Main
- Symptom Free 12 months since 2 vessel CABG.

CAC Progression Paradigm Shift - 2004

- 495 Asymptomatic Pts - ALL on Statins.
- No History of Coronary Artery Disease, stent or CABG.
- 42 MI’s over 6 years.
- Mean LDL Did Not Differ !!!
- 118 vs. 122 mg/dL, (MI versus NON-MI)

CAC Progression Paradigm Shift - 2004

Annual Calcium Score $>15\%$

CAC progression of $<15\%$ per year is associated with a benign prognosis
Harvey S. Hecht  JACC: Cardiovascular Imaging Volume 8, Issue 5, May 2015
Non-Progressors

Progressors

4,609 asymptomatic referred by primary for CAC.

All cause mortality data.

Fig 2 Budoff, Matthew “Progression of coronary artery calcium predicts all-cause mortality” JACC: Cardiovascular Imaging 2010
Statin Drugs

- Beneficial in Males w/ Known CAD
- Not Useful for Primary Prevention, Women, Hemodialysis, COPD, Elderly (reverse epidemiology)
- Beneficial in Diabetics - 20-30% Reduction Mortality
- Not Useful for Calcium Score - May Increase Calcification

- All Benefits Due to Pleotrophic Effects – Not Due to Cholesterol Lowering
- Anti-Inflammatory - Inhibits Activation of Nuclear Factor Kappa Beta
- Anti-Bacterial Effects
“As of 2010 there had been five randomized controlled studies showing that statin drug treatment does not reduce coronary calcium score.

Worse, the statin treatment showed progression of coronary calcium score indistinguishable from the non-treated placebo group.”

New Studies: Statins Increase Arterial Calcification

Depletion of Vitamin K2

Quote Edward A. Gill, MD
Statins Pleiotrophic Effects  
Clinical Observations

Statins While Undergoing CABG: 50-70% reduction in Mortality. (Curtis 2017) (Barakat 2016)

Statins Improve Survival in Sepsis and Pneumonia. (Hennessy, 2016)

Statins Pleotrophic Effects
Anti-Inflammatory Mechanisms

- Suppresses LPS Signaling in Monocytes (Patel, 2004)
- Blocks LPS-release of IL-6 and TNF-alpha. Decreases Nuclear factor-kappaB - direct anti-inflammatory effect. (Devaraj, 2006)
- Prevents TNF-alpha-induced NF-kappaB activation and gene transcription in cultured EC. (Hölschermann, 2006)

Diabetics Accelerated CAD
Elevated Blood Sugar is a “A Driver of Intestinal Barrier Dysfunction”.

“Glucose as an Orchestrator of Intestinal Barrier Function.”

Diabetics Have Leaky Gut and Low Level Endotoxemia

Patients with elevated fasting blood sugar had significantly higher levels of LPS, zonulin and oxLDL compared to control subjects.

Diabetics had significantly higher serum LPS, and higher inflammatory cytokines IL-6 and TNF-alpha.


Diabetics Have Accelerated Coronary Artery Disease
Elevated Glucose Induces Leaky Gut
Statins Reduce Mortality by 20-30% in early Diabetic
Statins Ineffective for End Stage Diabetics on Hemodialysis.
Statin Benefits NOT DUE to Cholesterol Lowering
All of Statin Benefits Due to Pleotrophic Effects (anti-inflammatory, antibacterial)

Calcium Score in Diabetics

Progression of Calcium Score in Diabetics

296 asymptomatic DM, 300 controls, 59 +/- 6 years, 29% women
Scan interval 1-2 yrs; f/u 5 6 +/- 11 mos

Event-free survivals with and without DM and with and without CAC progression

Estrogen Prevents Coronary Artery Disease – Calcium Score
Estrogen Prevents Heart Disease

- Martha is Asymptomatic 56 year old Nurse
  CAC = 101 (94th Percentile)
- Rx: Bioidentical Hormone Program
- Rx: Aged Garlic, Vit C, Toco Vit E, Vit K2 (MK-7), Gluten Free Diet
- One Year Later CAC =109, 9% annual increase
- (22% increase expected, Budoff 2005 Manson 2007)

Estrogen Slows Calcium Progression

7.4 Year Follow Up of WHI (50-60 yrs) Premarin-Alone

32% Less Calcium in the Estrogen Treated Arm of the Women’s Health Initiative.

Estrogen Prevents Heart Disease

11 Year Follow Up of WHI

“Younger” age group (age 50-60 yrs),
HRT with Premarin-Alone
41% Reduction in Coronary Artery Disease.
46% Reduction in Myocardial Infarctions.
27% Reduction in All Cause Mortality.
20-30% Reduction in Invasive Breast Cancer.

JAMA. 2011;305(13):1305-1314. Health Outcomes After Stopping Conjugated Equine Estrogens Among Postmenopausal Women With Prior Hysterectomy A Randomized Controlled Trial –Andrea Z. LaCroix, PhD; Rowan T. Chlebowski, MD, PhD; JoAnn E. Manson, MD, DrPH; for the WHI Investigators
What Works for Calcium Score?

- Estrogen HRT
- Aged Garlic
- Vit C, Lysine (Linus Pauling)
- Tocotrienol Vit E
- MK7- Vit K2
- Gluten Free Diet
- ? MTHFR – Methyl-folate
- ? Homocysteine – B6, B12, Methylfolate

References:


Testosterone for Males
Testosterone Improves Survival in AODM

- JIM, 46 y/o Stockbroker with Chronic Fatigue, AODM.
- Testosterone 290
- FBS =120  HgbA1c =6.2
- LH,FSH Low Normal
- Rx: Testosterone Cyp Injections 100 mg weekly, Metformin, Gluten Free Low Carb Diet.
- One Year Later: More Energy, Lost 20 LBS Weight.
- Testosterone = 650
- FBS = 98
- HgbA1c = 5.8

Testosterone Improves Survival in AODM

Testosterone for Males w/ CVD

- Testosterone RX for 77 males w/ CVD Over 8 Yrs.
- Improved Glycemic Control, FBS, HgbA1c
- Decrease Weight
- Decrease in Waist Circumference
- Decrease in BMI.
- Improved BP
- No Calcium Score Data? Would be Nice.

Testosterone for Males w/ CVD

- “No Patient Suffered Major Adverse Cardiovascular Event “
- “Sustained Improvements in All Cardiometabolic Risk Factors “
- “May be Effective in Secondary Prevention CV Events in Hypogonadal Men with CVD.”

**Final Word from the Mayo Clinic**

• “Testosterone levels may directly cause (or prevent) CAD and CVD events, or testosterone levels may simply be a **MARKER** of overall quality of health and have no direct effect on CAD and CVD events at all”. Quote: Dr Andrew Elagizi  Mayo Clinic 2018

• **Leaky Gut ? Low FSH, Low LH**

• **Low Level Endotoxemia LPS Causes CAD**

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Thyroid and the Heart
HUNT Study

TSH in 17,000 women, no thyroid or heart disease.
All patients had “normal TSH” 0.5 to 3.5
Lower TSH, Intermediate and Upper TSH levels
Mortality from heart disease over an 8 years.

<table>
<thead>
<tr>
<th>Group</th>
<th>TSH</th>
<th>Death from Heart Disease</th>
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<tbody>
<tr>
<td>1</td>
<td>0.50-1.4</td>
<td>baseline risk</td>
</tr>
<tr>
<td>2</td>
<td>1.5-2.4</td>
<td>40% higher than baseline</td>
</tr>
<tr>
<td>3</td>
<td>2.5-3.5</td>
<td>70% higher than baseline</td>
</tr>
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Sub-Clinical Hypothyroidism

- Elevated Serum TSH 5 - 10 mIU/L
- Normal Thyroid Hormone Levels (Free T3, Free T4)

Sub-Clinical Hypothyroidism

3040 pts, 40-70 yrs. Randomized to Levo 75 or Placebo, Followed 8 yrs.
Levo Treated: Fewer Ischemic Heart Disease Events, Reduced All-Cause Mortality

Levothyroxine treatment of subclinical hypothyroidism, fatal and nonfatal cardiovascular events, and mortality

Thyroid Enhances Immune System

Mouse Model of Endotoxemia
IP INJ LPS.

- 70% survival in T3 -Treated Mice.
- 10 % Survival in Hypothyroid Mice.
- T3 Significantly Protected Mice Against LPS Endotoxemia.

Hypothyroidism and CAC

Low FT3 Level is Important Risk Factor of High Calcification Scores and MACE (Major Adverse Cardiac Event).”


<table>
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<th>Linus Pauling Protocol</th>
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<td>High Dose Vitamin C Slows Progression of CAC</td>
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- 55 patients treated with High Dose Vitamin C, (and other nutrients)
- Subset of 21 patients with CAC <100
- Serial EBT (Electron Beam CAT Calcium Score)
- Treated Patients had significant slowing of progression of CAC
- Untreated pts 34% annual progression
- Treated pts 6% annual progression. (Fig 3b. Niedzwiecki, 1996)

Aged Garlic for Calcium Score

- Reduces Progression of Calcium Score by 60-70% compared to controls.


Aged Garlic
Mechanism for Prevention
in Apo-E Mouse

Daily Garlic (Allicin) Reduced Plaque Area 70% in ApoE-Deficient Mice, and 60% in LDL receptor knockout mice.

Garlic (Allicin) : NO Effect on Lipid Levels.

Allicin Reduces Plaque in Apo-E Mice
Pseudomonas infected biofilm

- Pseudomonas in 6 of 15 atherosclerotic plaques. (Bernard Lanter, 2014)
- Pseudomonas (Chryseomonas) in all (100%) plaque specimens (Omry Koren 2011)

Lanter BB, Sauer K, Davies DG. Bacteria present in carotid arterial plaques are found as biofilm deposits which may contribute to enhanced risk of plaque rupture. MBio. 2014;5(3):e01206-14.
Garlic (Allicin) Effective For Pseudomonas Biofilm

- Garlic is Anti-Microbial.
- Garlic Effective Against Pseudomonas Biofilm.
- Inhibits Quorum Sensing and Virulence. (66-67)

Leaky Gut, Gluten Sensitivity, Early Auto-Immune Disease

Lab Pattern- Low B12, Low Fe, Low Se, Low Triglycerides, Hair Loss, Muscle Cramping.
Elevated Anti-Gliadin Antibodies (blood or stool)
Chronic Low Grade Endotoxemia – Coronary Artery Calcium Score
Food Sensitivity Testing
Gluten Free Diet- Wheat, Dairy, Egg, Soy etc.
Hypochlorhydria? – Betaine HCL
Leaky Gut and Coronary Artery Disease

- Leaky Gut Causes Metabolic Endotoxemia
- Elevated Cytokines (IL-6, CRP)
- Activation of Nuclear Factor Kappa Beta (NFKB)
- Linked to Metabolic Syndrome, AODM, Obesity, Atherosclerosis, Parkinson’s


## Treatment For Leaky Gut

### Eliminate
- NSAIDS
- PPI’s
- Alcohol
- Wheat Gluten
- Reactive Foods
- Glyphosate
- GMO Food
- Pesticides

### Give
- Berberine
- Probiotics
- Digestive Enzymes
- Fiber
- Glutamine
- Colostrum
- Zinc (Resnick, 2010)
Summary/Conclusion

Low Level Endotoxemia/ Leaky Gut

Depression
Chronic Fatigue

Hypothalamic Dysfunction

Coronary Artery Disease

- Endocrinopathy
- Central Hypothyroid
- HypoGonadism
- Hypertension

- Garlic (Allicin)
- Berberine
Calcium Score Progression Indicates Treatment Failure

“If someone is on a statin or not and they are progressing (meaning the calcium score is progressing), They Are Failing their current therapy.” (Matthew Budoff, 2017)

“It’s time that we should let traditional risk scores and risk factor-based management rest in peace.... . They have served their “purpose” for the last 50 years and now in 2017, we have the ability to look at the actual disease with calcium testing.....CAC (Calcium Score) testing provides the most precise insight of what your actual risk is so you can tailor the treatment. (Nasir 2017)
Calcium Score
My Treatment Protocol

- Vitamin C
- Vitamin K2
- Tocotrienol Vitamin E
- Berberine
- Fibrinolytic Enzymes
- Diet Lifestyle - Eliminate Wheat, Sugar, Low Carb Diet, Weight Loss
- Control Diabetes
Thank You – Any Questions?

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