At the Heart of the Matter: Using Functional Medicine to Heal Vessels on Fire

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Objectives

• Understand root causes of vascular disease, such as inflammation, oxidative stress and auto-immunity

• Learn about integrating genetic, environmental, nutritional, behavior and exercise strategies into continuum of cardiovascular care

• Understand clinical applications of functional cardiovascular medicine
Functional Cardiovascular Medicine

Healing the Vessels on Fire
Objectives

Understand root causes of vascular disease, such as inflammation, oxidative stress and auto-immunity
**Disease-Centric Model**

- **Screen**
  - Patient and family history
  - BMI, waist circumference, BP
  - Fasting glucose, chemistries, HgA1C, lipids, urinalysis

- **Diagnose**
  - Early Disease and end-organ damage (CAC, ABI, CIMT)
  - Assess function, define extent of obstructive CAD (echo, SPECT, CTA, angiogram)

- **Treat**
  - Medical therapy
  - Revascularization
Vulnerable Plaque

Source: Cleveland Heart Lab
Mechanisms of myocardial ischaemia

Epicardial coronary arteries

- Atherosclerotic disease
  - Stable plaque
  - Reduction in CFR
  - Demand ischaemia ± angina
  - Acute coronary syndromes/infarction

- Vulnerable plaque
  - Plaque rupture
  - Thrombosis

Coronary microcirculation

- Vasospastic disease
  - Focal/transient vasospasm
  - Prinzmetal angina
  - Acute coronary syndromes/infarction

- Persistent vasospasm
  - Myocardial infarction

- Microvascular dysfunction
  - Impairs coronary physiology and myocardial blood flow in subjects with risk factors
    - Contributes to myocardial ischaemia in CAD and CMP
    - Induces severe acute ischaemia ‘Takotsubo’

These three mechanisms can overlap

Age-adjusted death rates for heart disease, stroke, combined heart disease/stroke, and cancer
United States
Selected years 1990-2009 with projected rates in 2015 and 2020

1 in 3 deaths in the United States is due to cardiovascular disease

Source: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6337a6.htm
Source: http://millionhearts.hhs.gov/learn-prevent/risks.html
Cardiac Merry-Go-Around
Prevalence of Cardiovascular Disease in the United States

Go AS et al. Circulation 2003;127:e6-e245
U.S. Heart Disease Prevalence Is Projected to Double in the Next Half Century

Cost of Cardiovascular Disease in the United States

CHD=Coronary heart disease, CHF=Congestive heart failure, CVD=Cardiovascular disease, HBP=High blood pressure

Go AS et al. Circulation 2003;127:e6-e245
The High Cost of Chronic Diseases

- $128 Billion¹ for Arthritis and Related Conditions
- $147 Billion² for Obesity
- $157 Billion³ for Cancer
- $315.4 Billion³ for Heart Disease and Stroke

Chronic Conditions - Percent with 0, 1, 2 or more

Source: https://www.bcbs.com/issues-indepth/why-does-healthcare-cost-so-much:
Prevalence of CHD associated with 3 projections of adult obesity

Extrapolation from current data suggests that overweight adolescents will increase rates of CHD among future young and middle-aged adults

Bibbins-Domingo K et al. NEJM 2007;357:2371-2379

CHD=Coronary heart disease
Obesity

Opioid

Depression

Source: http://www.cdc.gov/dhdsp/maps/atlas/help.htm
Stroke Death Rates, 2011-2013
Adults, Ages 35+, by County

Changing Geographic Patterns of Heart Disease Mortality in the US
1973-2010

Source: http://www.cdc.gov/dhdsp/maps/atlas/help.htm
Diabetes Mellitus: Prevalence in U.S. Adults

Percentage and absolute numbers of diabetics in the United States

Source: Centers for Disease Control and Prevention, Division of Diabetes Translation National Diabetes Surveillance System. Available at http://www.cdc.gov/diabetes/statistic
From 1997 to 2011, the number of people aged 35 years or older with diabetes and with self-reported heart disease or stroke increased from 4.2 million to 7.6 million. In 2011, among people with diabetes aged 35 years and older and with self-reported heart disease or stroke, 5.0 million reported having coronary heart disease, 3.7 million reported having other heart disease or condition, and 2.1 million reported having stroke.

Source: Centers for Disease Control and Prevention, Division of Diabetes Translation National Diabetes Surveillance System. Available at http://www.cdc.gov/diabetes/statistic
Years from diagnosis
-10 -5 0 5 10 15

Onset Diagnosis

Insulin resistance
Insulin secretion

Postprandial glucose
Fasting glucose

Microvascular complications
Macrovascular complications

Pre-diabetes Type II diabetes

Nathan DM et al. NEJM 2002;347:1342-1349
Prevalence of Glycemic Abnormalities

U.S. Population: 309 Million in 2010

- Type 1 DM: 0.9 Million
- Type 2 DM: 17.8 Million
- Prediabetes: 79 Million
- Undiagnosed DM: 7 Million

Total: 104.7 Million

Sources:
http://www.diabetes.org/diabetes-basics/type-1/
Metabolic Syndrome

- Consists of a constellation of major risk factors, life-habit risk factors, and emerging risk factors
- Over-represented among populations with CVD
- Often occurs in individuals with a distinctive body-type including an increased abdominal circumference

Source: Centers for Disease Control and Prevention, Division of Diabetes Translation National Diabetes Surveillance System. Available at http://www.cdc.gov/diabetes/statistic
### Definition of Metabolic Syndrome

Defined by the presence of ≥3 risk factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Defining Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist circumference (abdominal obesity)</td>
<td>&gt;40 in (&gt;102 cm) in men</td>
</tr>
<tr>
<td></td>
<td>&gt;35 in (&gt;88 cm) in women</td>
</tr>
<tr>
<td>Triglyceride level</td>
<td>&gt;150 mg/dl</td>
</tr>
<tr>
<td>HDL-C level</td>
<td>&lt;40 mg/dl in men</td>
</tr>
<tr>
<td></td>
<td>&lt;50 mg/dl in women</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>&gt;130/&gt;85 mmHg</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>&gt;110 mg/dl</td>
</tr>
</tbody>
</table>

HDL-C=High-density lipoprotein cholesterol

## Diagnostic Criteria for Pre-diabetic Conditions

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Defining Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired fasting glucose</td>
<td>5.6-6.9 mmol/L or 100-125 mg/dL</td>
</tr>
<tr>
<td>Impaired glucose tolerance</td>
<td>2 hour glucose concentration of 7.8-11.0 mmol/L or 140-199 mg/dL following a 75 gram OGTT</td>
</tr>
</tbody>
</table>

OGTT = Oral glucose tolerance test

Source: Genuth S et al. *Diabetes Care* 2003;26:3160-3167
Diabetes Mellitus: Risk of Cardiovascular Events and Death

U.S. adults aged 30-74 years

* p < .05 compared to none, ** p < .01 compared to none, *** p < .0001 compared to none

CHD = Coronary heart disease, CVD = Cardiovascular disease, MetS = Metabolic syndrome

Attributable Risk Factors for a First Myocardial Infarction

INTERHEART Study

n=15,152 patients and 14,820 controls in 52 countries

MI=Myocardial infarction, PAR=Population attributable risk (adjusted for all risk factors)

Vulnerable Patient

Clinical Phase
Usually middle age to elderly

- Mural thrombosis
- Embolization
- Wall weakening

ANEURYSM AND RUPTURE

- Plaque rupture
- Plaque erosion
- Plaque hemorrhage
- Mural thrombosis
- Embolization

OCCLUSION BY THROMBUS

- Progressive plaque growth

CRITICAL STENOSIS

Fig. 10–12. The natural history, morphologic features, main pathogenic events, and clinical complications of atherosclerosis.
Personalize Risk

- Anthropometric measurements (BIA)
- Biomarkers (hsCRP, BNP, hsTnT, Lp-PLA2, Gal-3, IL1, 6, 8), lipoproteins fractions
- SNPs (PPARG, ApoE, 9p21, MTHFR)

Find Root Causes of Patient Vulnerability

- Vascular and neuro-mediated responses (ischemia, HRR, ANS blunted response)
- Endothelial dysfunction, vulnerable plaque (carotid IMT, NO-mediated dilation, Lp-PLA2)

Guide Prevention and Treatment

- Population-based interventions
- Personalized Lifestyle and Precision Medicine (N=1)
"It is more important to know what sort of person has a disease than to know what sort of disease a person has."

~HIPPOCRATES
(460–377 B.C.)
"It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has."

Sir William Osler
the founder of modern medicine

The First Patient-Centric Physician!
Inflammation
On the
Molecular
Level...

Source: European Heart Journal (2013), 34, 3035-3087
ESC Guideline on diabetes, pre-diabetes and cardiovascular
Disease in collaboration with EASD
Mechanisms by which Diabetes Mellitus Leads to Coronary Heart Disease

Inflammation
- ↑ IL-6
- ↑ CRP
- ↑ SAA
- ↓ Defense mechanisms
- ↑ Pathogen burden

Hyperglycemia
- ↑ AGE
- ↑ Oxidative stress

Insulin Resistance
- HTN Endothelial dysfunction

Dyslipidemia
- ↑ LDL
- ↑ TG
- ↓ HDL

Thrombosis
- ↑ PAI-1
- ↑ TF
- ↓ tPA

Infection
- ↓ Defense mechanisms
- ↑ Pathogen burden

Subclinical Atherosclerosis
- Disease Progression
- Atherosclerotic Clinical Events

Source: Biondi-Zoccai GGL et al. JACC 2003;41:1071-1077
Role of Lipoproteins in Atherogenesis

- HDL
  - LDL + VLDL
    - LCAT
    - APO-A1
      - Liver
        - Cholesterol excreted
      - Oxidative modification of LDL (induced by infection)
        - Macrophages
          - Foam cells
            - Fatty streak
          - LDL infiltration into intima (small dense LDL)
  - High plasma LDL (infection, immune dysfunction, oxidative stress, reduced NO)
  - Endothelial injury (metabolic and infectious endotoxemia)
    - Adherence of platelets
      - Release of PDGF
        - Other growth factors
          - Advanced fibrocalcific lesion

APO-A1=Apolipoprotein A1, HDL=High density lipoprotein, LCAT=Lecithin cholesterol acyltransferase, LDL=Low density lipoprotein, PDGF=Platelet-derived growth factor, VLDL=Very low density lipoprotein
Cardiovascular disease in patients with chronic inflammation: mechanisms underlying premature cardiovascular events in rheumatologic conditions.
Cardiovascular disease in patients with chronic inflammation: mechanisms underlying premature cardiovascular events in rheumatologic conditions.
Advanced Systolic Heart Failure

Cardiac cachexia and abnormal systemic metabolism:
- Weight loss, poor nutritional intake, sarcopenia
- Inflammatory activation, adiponectin resistance
- Insulin resistance, hyperglycemia
- Low lipid levels, hypoalbuminemia
- Hepatic congestion, decreased synthetic activity
- Myocardial lipotoxicity

Associated with
Increased Mortality Risk

LVAD implantation

Myocardial recovery:
Proposed improvements in nutritional intake, inflammation, adiponectin resistance, insulin resistance, hepatic congestion, myocardial lipotoxicity

Increased total cholesterol levels

? relationship

Associated with
Decreased Mortality Risk

Source: Circulation Heart Failure 2016, 9:e002881 Sep 2016
Objectives

Learn about integrating genetic, environmental, nutritional, behavior and exercise strategies into continuum of cardiovascular care
Matters of Your Heart

RISKS
- 56% of adults have been told by a healthcare professional to improve their health
- 60% of adults don’t know their blood pressure and cholesterol numbers
- 44% monitor their blood pressure outside of the doctor’s office
- 83% believe that heart attacks and stroke can be prevented, but aren’t motivated to do anything
- 99% of Americans need to improve their heart health
- 72% don’t consider themselves at risk for heart disease
- 58% put no effort into improving their heart health

Heart disease is the #1 leading cause of death in the United States

Every 25 seconds, an American will have a coronary event
Every 39 seconds, someone dies from heart disease and stroke

Lowering your blood pressure may decrease your risk of stroke and heart disease by about 50%

More than 62,000 visits per day on heart.org and strokeassociation.org

Join our Facebook communities every day
Join our conversation every day at facebook.com/AmericanHeart

1 of every 3 deaths in the United States is caused by heart disease and stroke

Each year, an estimated 785,000 Americans will have their first heart attack
Each year, an estimated 470,000 Americans will have another heart attack
Although the collective health of the nation has improved dramatically in the past 30 years, surveys reveal declining satisfaction with personal health during the same period. Increasingly, respondents report greater numbers of disturbing somatic symptoms, more disability, and more feelings of general illness. Four factors contribute to the discrepancy between the objective and subjective states of health. First, advances in medical care have lowered the mortality rate of acute infectious diseases, resulting in a comparatively increased prevalence of chronic and degenerative disorders. Second, society’s heightened consciousness of health has led to greater self-scrutiny and an amplified awareness of bodily symptoms and feelings of illness. Third, the widespread commercialization of health and the increasing focus on health issues in the media have created a climate of apprehension, insecurity, and alarm about disease. Finally, the progressive medicalization of daily life has brought unrealistic expectations of cure that make untreatable infirmities and unavoidable ailments seem even worse. Physicians should become more aware of these paradoxical consequences of medical progress so that they do not inadvertently contribute to a rising public dissatisfaction with medicine and medical care.


The Paradox of Health
Holistic or Integrative Cardiology is Based on Functional Medicine

Disease-Oriented Medical Model
- Disease Model dominates medical thinking
- Defines health as a disease-free state
- Traditional Medicine

Patient-Focused Medical Model
- Emphasizes prevention and lifestyle intervention
- Defines health as a state of optimal wellness
- Functional Medicine
Disease-Free State of Optimal Wellness

- Physical Ability
- Energy
- Resilience
- Mental Focus and Clarity
- Vitality
- Emotional Stability
- Meaningful Relationships

Integrative Medicine View of Health
- Chronic conditions are on the rise
- Obesity is sky rocketing
- Expenses are mounting
- High deductible insurance plans turned patients into consumers
- Business are looking to save by implementing wellness programs

Patients Search for Well, Physicians Focus on Not Sick
Antecedents, Triggers, and Mediators

- Nutrition
- Sedentary Lifestyle
- Chronic Stress
- Poverty/Uninsured
- Environmental Toxicity
- Fragmented families and communities
- Indoor Living
- Aging Population

Chronic Disease
One Condition: Many Imbalances

- Inflammation
- Hormones
- Genetics and Epigenetics
- Diet and Exercise
- Mood Disorders

Obesity

One Imbalance: Many Conditions

- Inflammation

Heart Disease
- Depression
- Arthritis
- Cancer
- Diabetes
Two Simple Questions:

Causes and Function

• Does this person need to be rid of something (toxic, allergic, infectious, poor diet, stress)?

• Does this person have some unmet individual need required for optimal function?
Fit in Your GENES™

Genome
Environment
Nutrition
Exercise
Supplements

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Fit in Your GENES
Integrative Heart Health Solution

- Environment
- Diet
- Body Composition
- Lifestyle

Genes
Body Chemistry
Toxins
Nutrients

Exercise
Stress Reduction
Weight Loss
Hormonal Balance
Exposure Control
Detoxification

Nutraceuticals
Supplements
Essential Oils

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A Patient-Centered Approach

- Evaluate events sequentially (ATMs)
- Determine imbalances
- Focus on the matrix
- Reverse root causes (inflammation, oxidation)
- Treat with nutritional, lifestyle, and supplement approaches
3 Phases of FIYG Program

I
- Genetic, biometric, metabolic, nutritional and environmental assessments
- Vascular and cardiac testing
- 1-7 days

II
- Detoxification, nutritional program
- Foundational nutraceutical regime
- Exercise program
- 30 days

III
- Condition-specific supplements
- Bioidentical hormones (only if needed)
- Advance exercise and nutrition program
- Re-assessment in 3 months
Role of Lipoproteins in Atherogenesis

HDL

LDL + VLDL

Liver

Cholesterol excreted (fiber, plant sterols)

High plasma LDL (statins, RYR, niacin, omega-3)

LDL infiltration into intima

Oxidative modification of LDL (soy, almonds, fiber, berberine)

+ Macrophages

Foam cells

Fatty streak

Endothelial injury (curcumin, resveratrol, EGCG, nitrates)

Adherence of platelets

Release of PDGF

Other growth factors

Advanced fibrocalcific lesion

APO-A1=Apolipoprotein A1, HDL=High density lipoprotein, LCAT=Lecithin cholesterol acyltransferase, LDL=Low density lipoprotein, PDGF=Platelet-derived growth factor, VLDL=Very low density lipoprotein
Practice Models Building Blocks

- Genome
  - MD Lead
  - Geneticist
  - Health Coach

- Environment
  - Detoxification Lead
  - Stress Reduction specialist

- Nutrition
  - Nutritionist Lead
  - Chef
  - Demo Kitchen/Cafe

- Exercise
  - Fitness Lead
  - Yoga
  - Gym/Studio
  - Spa/Massage
  - Chiropractic

- Supplements
  - Compounding Lead
  - Botanicals
  - Naturopath

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Clinical Benefit of EDTA Chelation Therapy in Patients with Diabetes in the Trial to Assess Chelation Therapy (TACT)

Esteban Escolar, Gervasio A. Lamas, Daniel Mark, Pamela Ouyang, Allan Magaziner, Robin Boineau, Ralph Miranda, Christine Goertz, Yves Rosenberg, Richard Nahin, Richard Nahas, Eldrin Lewis, Lauren Lindblad, Kerry L Lee

For the TACT Investigators

No disclosures to report

The National Center for Complementary and Alternative Medicine (U01AT001156) and the National Heart, Lung and Blood Institute (U01HL092607) provided sole support for this study.
• Disodium ethylene diamine tetra acetic acid (EDTA) binds metal cations and permits renal excretion

• Since 1956, EDTA chelation has been used to treat atherosclerotic disease without evidence of benefit.

• In 2001, NCCAM and NHLBI released an RFA for a definitive trial of EDTA chelation
Background

- TACT showed a statistically significant reduction of a combined cardiovascular endpoint (HR 0.82 [95% CI, 0.69-0.99]; \( p = 0.035 \)) with an EDTA-based infusion regimen in patients with prior MI

- There was an interaction between chelation infusion and self-reported diabetes

- The present analyses provide greater detail on the effect of chelation therapy in patients with diabetes

## Design Overview

<table>
<thead>
<tr>
<th>Chelation + high-dose vitamins</th>
<th>Placebo chelation + high-dose vitamins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chelation + placebo vitamins</td>
<td>Placebo chelation + placebo vitamins</td>
</tr>
</tbody>
</table>

40 infusions at least 3 hours each; 30 weekly infusions followed by 10 maintenance infusions 2-8 weeks apart.

Infusion components

Chelation Infusion

- disodium EDTA, 3 grams (adjusted by GFR)
- ascorbic acid, 7 grams
- magnesium chloride, 2 grams
- potassium chloride, 2 mEq
- sodium bicarbonate, 840 mg
- pantothenic acid, thiamine, pyridoxine
- procaine, 100 mg
- unfractionated heparin, 2500 U
- sterile water to 500 mL

Placebo Infusion

- Normal Saline
- 1.2% dextrose, 500 mL

Inclusion Criteria

- Age 50 or older
- MI > 6 months prior
- Creatinine $\leq$ 2.0 mg/dL
- No coronary or carotid revascularization within 6 months
- No active heart failure or heart failure hospitalization within 6 months
- Able to tolerate 500cc infusions weekly
- No cigarette smoking within 3 months
- Signed informed consent
End points

Primary endpoint:
Time to first occurrence of either
- death from any cause,
- reinfarction,
- stroke,
- coronary revascularization, or
- hospitalization for angina

Secondary endpoint:
Time to first occurrence of either
- cardiovascular death,
- reinfarction, or
- stroke
**Primary Endpoint by infusion arm**

**Diabetes**

EDTA Chelation vs. Placebo

HR (95% CI): 0.59 (0.44, 0.79); P = 0.0002

Bonferroni Adjusted: (0.39, 0.88); P = 0.002

RR = 41%

NNT = 6.5 over 5 years  CI (4.4, 12.7)

<table>
<thead>
<tr>
<th>Months since randomization</th>
<th>Placebo Infusions</th>
<th>EDTA Chelation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>322</td>
<td>311</td>
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<tr>
<td>6</td>
<td>286</td>
<td>270</td>
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<td>12</td>
<td>262</td>
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<tr>
<td>60</td>
<td>74</td>
<td>63</td>
</tr>
</tbody>
</table>
Primary Endpoint by infusion arm

**Diabetes**

- EDTA Chelation vs. Placebo
  - HR (95% CI): 0.59 (0.44, 0.79);
  - P = 0.0002
  - Adjusted: (0.39, 0.88);
  - P = 0.002

**No Diabetes**

- EDTA Chelation vs. Placebo
  - HR (95% CI): 1.02 (0.81, 1.28);
  - P = 0.8768
  - Adjusted: (0.39, 0.88);
  - P = 0.002

---

**Number at Risk:**

<table>
<thead>
<tr>
<th>Infusion Arm</th>
<th>0</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
<th>30</th>
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<tr>
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<td>474</td>
<td>441</td>
<td>407</td>
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<tr>
<td>Placebo</td>
<td>558</td>
<td>506</td>
<td>466</td>
<td>424</td>
<td>379</td>
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<td>320</td>
<td>295</td>
<td>268</td>
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<td>142</td>
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</table>
Secondary Endpoint by infusion arm
Diabetes

EDTA Chelation vs. Placebo
HR (95% CI): 0.60 (0.39, 0.91); P = 0.0170
Bonferroni Adjusted: (0.32, 1.09); P = 0.153

Number at Risk:
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<td>149</td>
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<td>90</td>
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</tbody>
</table>
Death by infusion arm - Diabetes

EDTA Chelation vs. Placebo

HR (95% CI): 0.57 (0.36, 0.88); P = 0.0111

Bonferroni Adjusted: (0.30, 1.06); P = 0.099

Number at Risk:

<table>
<thead>
<tr>
<th></th>
<th>EDTA Chelation</th>
<th>Placebo</th>
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<td>128</td>
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<tr>
<td></td>
<td>101</td>
<td>83</td>
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</table>
Conclusions

- Post-MI diabetic patients age 50 or older on evidence-based medications demonstrated a marked reduction in cardiovascular events with EDTA-based chelation therapy.

- These findings support the initiation of clinical trials in patients with diabetes and vascular disease to replicate these findings, and define the mechanisms of benefit.

- They do not, as yet, constitute sufficient evidence to indicate routine use of chelation therapy for post-MI diabetic patients.
Objectives

Understand clinical applications of functional cardiovascular medicine
Risk Stratification:
Framingham Risk Score On Line Calculator

Risk Assessment Tool for Estimating Your 10-year Risk of Having a Heart Attack
The risk assessment tool below uses information from the Framingham Heart Study to predict a person’s chance of having a heart attack in the next 10 years. This tool is designed for adults aged 20 and older who do not have heart disease or diabetes. To find your risk score, enter your information in the calculator below.

Age: ___________ years
Gender:  
  ○ Female  ○ Male
Total Cholesterol: ___________ mg/dL
HDL Cholesterol: ___________ mg/dL
Smoker:  
  ○ No  ○ Yes
Systolic Blood Pressure: ___________ mm/Hg
Are you currently on any medication to treat high blood pressure.  
  ○ No  ○ Yes

Calculate Your 10-Year Risk

In addition to information collected as part of the Framingham Risk Score, the Reynolds Risk Score includes a hs-CRP level and a family history of premature CV disease in predicting one’s risk of adverse CV events.
# ATP III LDL-C Goals and Cut-points for Drug Therapy

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>LDL-C Goal</th>
<th>Initiate TLC</th>
<th>Consider Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High risk:</strong> CHD or CHD risk equivalents (10-year risk &gt;20%)</td>
<td>&lt;100 mg/dL (optional goal: &lt;70)</td>
<td>≥100 mg/dL</td>
<td>&gt;100 mg/dL (&lt;100 mg/dL: consider drug options)</td>
</tr>
<tr>
<td><strong>Moderately high risk:</strong> 2+ risk factors* (10-year risk 10% to 20%)</td>
<td>&lt;130 mg/dL (optional goal: &lt;100)</td>
<td>≥130 mg/dL</td>
<td>&gt;130 mg/dL (100-129 mg/dL: consider drug options)</td>
</tr>
<tr>
<td><strong>Moderate risk:</strong> 2+ risk factors* (10 year risk &lt;10%)</td>
<td>&lt;130 mg/dL</td>
<td>≥130 mg/dL</td>
<td>&gt;160 mg/dL</td>
</tr>
<tr>
<td><strong>Lower risk:</strong> 0-1 risk factor*</td>
<td>&lt;160 mg/dL</td>
<td>≥160 mg/dL</td>
<td>&gt;190 mg/dL (160-189 mg/dL: LDL-C lowering drug optional)</td>
</tr>
</tbody>
</table>

*Risk factors for CHD include: cigarette smoking, hypertension (blood pressure ≥140/90 mmHg or on antihypertensive medication, HDL-C <40 mg/dl (≥60 mg/dl is a negative risk factor), family history of premature CHD, age ≥45 years in men or ≥55 years in women

ATP=Adult Treatment Panel, CHD=Coronary heart disease, LDL-C=Low density lipoprotein cholesterol, TLC=Therapeutic lifestyle changes

### ATP III Classification of Other Lipoprotein Levels 2011

<table>
<thead>
<tr>
<th>Total Cholesterol Level (mg/dl)</th>
<th>Classification</th>
<th>HDL-Cholesterol Level (mg/dl)</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200</td>
<td>Desirable</td>
<td>&gt;40</td>
<td>Minimum goal*</td>
</tr>
<tr>
<td>200-239</td>
<td>Borderline High</td>
<td>40</td>
<td>Desired goal*</td>
</tr>
<tr>
<td>&gt;240</td>
<td>High</td>
<td></td>
<td>High</td>
</tr>
</tbody>
</table>

**Triglyceride Level (mg/dl) Classification**

| <150                            | Normal         |
| 150-199                         | Borderline High|
| 200-499                         | High           |
| >500                             | Very High      |

*These goals apply to men. For women, the minimum goal is >50 mg/dL.

HDL=High density lipoprotein

Overview of the Expert Panel's Guideline
RCTs indicates randomized controlled trials.


C-reactive protein; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; and RCT, randomized controlled trial.

Figure Legend:
Heart-healthy lifestyle habits are the foundation of ASCVD prevention (See 2013 AHA/ACC Lifestyle Management Guideline)

- **Age ≥21 y and a candidate for statin therapy**

  - **Clinical ASCVD**
    - **Yes**
      - Age ≤75 y
        - **High-intensity statin** (Moderate-intensity statin if not candidate for high-intensity statin)
    - **No**
      - Age >75 y OR if not candidate for high-intensity statin
        - **Moderate-intensity statin**

  - **LDL-C ≥190 mg/dL**
    - **Yes**
      - **High-intensity statin** (Moderate-intensity statin if not candidate for high-intensity statin)
    - **No**
      - **Diabetes**
        - LDL-C 70-189 mg/dL
          - Age 40-75 y
            - **Yes**
              - **Moderate-intensity statin**
            - **No**
        - Age ≥75 y
          - **Yes**
            - Estimation 10-y ASCVD risk ≥7.5%†
              - **High-intensity statin**
          - **No**

  - **Estimation 10-y ASCVD risk every 4-6 y using Pooled Cohort Equations†**

  - **DM age <40 or >75 y or LDL-C <70 mg/dL**

Definitions of High- and Moderate-Intensity Statin Therapy* (See Table 5)
- **High**
  - Daily dose lowers LDL-C by approx. ≥50%
- **Moderate**
  - Daily dose lowers LDL-C by approx. 30% to <50%

Regularly monitor adherence to lifestyle and drug therapy with lipid and safety assessments (See Fig 5)
Primary prevention
(No diabetes, LDL-C 70 to 189 mg/dL, and not receiving statin therapy)

Estimate 10-y ASCVD risk every 4-6 y using Pooled Cohort Equations†

- <5% 10-y ASCVD risk‡
- Age <40 or >75 y and LDL-C <190 mg/dL‡
- ≥7.5% 10-y ASCVD risk (Moderate- or high-intensity statin)
- 5% to <7.5% 10-y ASCVD risk (Moderate-intensity statin)

In selected individuals, additional factors may be considered to inform treatment decision making§

Clinician-Patient Discussion
Prior to initiating statin therapy, discuss:
1. Potential for ASCVD risk-reduction benefits ||
2. Potential for adverse effects and drug–drug interactions††
3. Heart-healthy lifestyle
4. Management of other risk factors
5. Patient preferences
6. If decision is unclear, consider primary LDL-C ≥160 mg/dL, family history of premature ASCVD, lifetime ASCVD risk, abnormal CAC score or ABI, or hs-CRP ≥2 mg/L§

Emphasize adherence to lifestyle
Manage other risk factors
Monitor adherence

No to statin
Yes to statin

Encourage adherence to lifestyle
Initiate statin at appropriate intensity
Manage other risk factors
Monitor adherence* (See Fig 5)
Change in Total Cholesterol Levels in the United States Over Time

National Health and Nutrition Examination Survey (NHANES)

# HMG-CoA Reductase Inhibitor Evidence: Degree of Benefit In Prevention Types

Meta-analysis of randomized controlled trials comparing risk reductions between primary and secondary prevention patients

<table>
<thead>
<tr>
<th></th>
<th>Relative Risk Reduction</th>
<th>Absolute Risk Reduction</th>
<th>Number Needed To Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Primary</td>
<td>Secondary</td>
<td>Primary</td>
</tr>
<tr>
<td>Major CHD events</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>29.2</td>
<td>20.8</td>
<td>1.66</td>
</tr>
<tr>
<td>Major CV events</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>14.4</td>
<td>17.8</td>
<td>0.37</td>
</tr>
<tr>
<td>Nonfatal MI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>31.7</td>
<td>NA</td>
<td>1.65</td>
</tr>
<tr>
<td>PCI or CABG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>33.8</td>
<td>20.3</td>
<td>1.08</td>
</tr>
</tbody>
</table>

CABG=Coronary artery bypass graft surgery, CHD=Coronary heart disease, CV=Cardiovascular, MI=Myocardial infarction, PCI=Percutaneous coronary intervention

77 y/o man with known CAD, has 2 stents

HTN, Hyperlipidemia

Lopressor, ASA, Plavix, Zocor

No acute complaints
Active, works out, independent

“My doctor tells me “do what you want” when I ask about supplements”
Cost of supplements: $700/month
77 y/o man with known CAD, has 2 stents

HTN, Hyperlipidemia

Lopressor, ASA, Plavix, Zocor

No acute complaints
Active, works out, independent

What about his lifestyle?
He is eating out
He has a girlfriend
He wants his doctor to look inside the BAG!
I was diagnosed with elevated cholesterol 2 and ½ years ago (total cholesterol 280, LDL 171). I took Crestor but started getting strange neurological symptoms, and became borderline diabetic. Internist wants me to take Lipitor but I will not. There simply has to be a better way.”

54 y/o woman seeks second opinion
Early menopause
Hyperlipidemia
Osteoarthritis, allergies, osteoporosis
Weight gain
Dizziness and neurological symptoms
Not very Active
Healthy diet “on” and “off”
56 y/o woman with exertional dyspnea for several years

Overweight, hypertension, dyslipidemia, chronic chest pain, depression, arthritis, fatty liver (abnl LFTs, sono), metabolic syndrome, elevated hsCRP and pro-insulin

Multiple cardiac and pulmonary tests over several years, no structural or ischemic heart disease, no pulmonary diagnosis ($$$)

Several ER visits ($$$)

Poor exercise tolerance and poor diet

Good medication compliance (Metoprolol, Diovan HCT, Celexa, Alprazolam, Seroquel, NSAIDS)
### Baseline and On FIYH Program

<table>
<thead>
<tr>
<th>BIOMETRICS</th>
<th>JANUARY 2015</th>
<th>MARCH 10th</th>
<th>MARCH 25th</th>
<th>MAY 2015</th>
<th>Percent Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>WEIGHT (lbs)</td>
<td>257</td>
<td>260</td>
<td>248</td>
<td>242</td>
<td>-5.6%</td>
</tr>
<tr>
<td>BMI</td>
<td>45.5</td>
<td>46.1</td>
<td>43.9</td>
<td>42.9</td>
<td>-5.7%</td>
</tr>
<tr>
<td>HEIGHT (in)</td>
<td>63</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LAB MARKERS (fasting)</th>
<th>JANUARY 2015</th>
<th>MARCH 2015</th>
<th>MAY 2015</th>
<th>Percent Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLUCOSE (mg/dL)</td>
<td>131 H</td>
<td>129 H</td>
<td>123 H</td>
<td>-6.1%</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>55</td>
<td>57</td>
<td>61</td>
<td>+1.8%</td>
</tr>
<tr>
<td>CHOLESTEROL (mg/dL)</td>
<td>226 H</td>
<td>213 H</td>
<td></td>
<td>-5.7%</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>141 H</td>
<td>105</td>
<td>102 H</td>
<td>-27.6%</td>
</tr>
<tr>
<td>HBA1C (%)</td>
<td>7.1 H</td>
<td>NA</td>
<td>6.3 H</td>
<td>-0.8%</td>
</tr>
<tr>
<td>TRIGLYCERIDES (mg/dL)</td>
<td>100</td>
<td>70</td>
<td>78</td>
<td>-22%</td>
</tr>
</tbody>
</table>
Case Discussion

Symptom Improvement:
• Dyspnea resolved
• Chest pain resolved
• Exercise tolerance improved to 1 mile per day

Weight Loss:
• Modest, comparable to pharmacological weight loss drugs
• Unlike drugs, no side-effects, part of sustainable lifestyle modification

Reversal of Diabetes and Dyslipidemia:
• Metabolic remodeling (inflammation and oxidative stress reduction) produced significant decreases in fasting glucose, HgA1C, and drastically improved cholesterol profile AND THID IS JUST A BEGINNING!
ASCVD Risk Modification

10 year ASCVD risk:
Baseline 6.6%-moderate intensity statin recommended
FLYG program at 4 months 3.0%-ASCVD risk <5%, not in statin-benefit group

http://tools.cardiosource.org/ASCVD-Risk-Estimator/: SBP 130 mmHg, non-smoker, white, woman
Metabolic Remodeling Case Conclusion

FIYG Program resulted in sustained lifestyle modification through application of genomic, environmental, nutritional, exercise and supplements approaches. As a result, patient experienced weight loss, and reversal of metabolic cardiac disease risk factors, such as diabetes and dyslipidemia. Her ASCVD short-term risk was decreased in half in 4 months on the program. She experienced dramatic improvement in symptoms, and regained wellness and vitality.

How Many Patients Like HER Do You See in Your Practice?
Destination: HEALTH

- Decline in generational health
- Epidemic of chronic diseases
- Cost per year $3 trillion
- 80% disease prevention
- Food as Medicine
Destination: **HEALTH**

Decline in generational health

Cost per year: $3 trillion

Epidemic of chronic diseases

Food as Medicine

80% disease prevention

The Future

NEXT EXIT
Questions? Comments?

• md@iccli.com
• Iccli.com
• 516-746-1103
References


References


Back Up Slides
Pre-Diabetic Conditions: Benefit of Lifestyle Modification

458 Japanese men with impaired glucose tolerance randomized to standard lifestyle intervention (goal BMI <24 kg/m²) or intensive lifestyle intervention (goal BMI <22 kg/m²).

More intensive lifestyle modification reduces the risk of DM.

BMI=Body mass index, DM=Diabetes mellitus

531 Asian Indians with impaired glucose tolerance randomized to placebo, metformin, lifestyle modification, or lifestyle modification plus metformin for 30 months

Lifestyle modification and metformin reduce the incidence of DM with no additional benefit from their combination

## Dietary Adjuncts Evidence: Efficacy at Reducing LDL-C

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose (g/day)</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary soluble fiber</td>
<td>5-10 (psyllium)</td>
<td>↓ LDL-C 10-15%</td>
</tr>
<tr>
<td>Soy protein</td>
<td>20-30</td>
<td>↓ LDL-C 5-7%</td>
</tr>
<tr>
<td>Stanol esters</td>
<td>1.5-2</td>
<td>↓ LDL-C 15-20%</td>
</tr>
</tbody>
</table>

LDL-C=Low density lipoprotein cholesterol

Sources:
- Kwiterovich Jr PO. *Pediatrics* 1995;96:1005-1009
Metabolic Syndrome: Risk of Coronary Heart Disease*

National Health and Nutrition Examination Survey (NHANES)

CHD Prevalence

<table>
<thead>
<tr>
<th>Condition</th>
<th>% of Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>No MS/No DM</td>
<td>54%</td>
</tr>
<tr>
<td>MS/No DM</td>
<td>29%</td>
</tr>
<tr>
<td>DM/No MS</td>
<td>2%</td>
</tr>
<tr>
<td>DM/MS</td>
<td>15%</td>
</tr>
</tbody>
</table>

*Among individual ≥50 years

CHD=Coronary heart disease, DM=Diabetes mellitus, MS=Metabolic syndrome

Source: Alexander CM et al. Diabetes 2003;52:1210-1214