Primary Causes of Heart Disease

Insulin Resistance Vs “Bad Cholesterol”

Ivor Cummins, BE(Chem) CEng MIEI

...with thanks to
Gabor Erdosi MSc Molecular Biology / Molecular Genetics
Disclosure

1. My work is supported by David Bobbett and the Irish Heart Disease Awareness (http://www.ihda.ie/)
2. David Bobbett and the IHDA are funding myself and Dr. Gerber’s new book which includes the content in this presentation
3. No financial ties to the heart imaging industry (!)
Doctor told an Engineer to walk on Grass

Engineer found the Solution
Myself:

- BE Chemical Engineering (Biochemical)
- 6 years Medical Device Engineering
- 20 years High-Volume Engineering
  - Structured Problem Solving Focus
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2013, Personal health issue arises:

- Abnormal blood test readings
- Apparently a medical mystery
- Apply engineering problem-solving skill
- Mystery resolved – and then some…
Why you should be interested in this chat...

A. In this room, over a third of you
   ...will have a heart attack by your early 70’s.

From the graph “Annual number of adults per 1000 having diagnosed heart attack or fatal coronary heart disease (CHD) by age and sex” Atherosclerosis Risk in Communities Surveillance: 2005–2011 and Cardiovascular Health Study.
Mozaffarian D et al. Circulation. 2015;131:e29-e322
Why you should be interested in this chat…

A. In this room, over a third of you
   …will have a heart attack by your early 70’s.

B. You could do some pretty simple measurements
   - and mostly know who’ll be going down…

From the graph “Annual number of adults per 1000 having diagnosed heart attack or fatal coronary heart disease (CHD) by age and sex”
Mozaffarian D et al. Circulation. 2015;131:e29-e322
Content

1. The Cholesterol Conundrum High Level
2. Beyond Cholesterol - to CVD Primary Causes
3. The Ultimate Test for CVD Presence - CAC
4. A Critique of “Cholesterol as Cause”
PART I

The ‘Cholesterol Conundrum’
(the quick version!)
From VLDL to LDL..... to **Damaged LDL**
From VLDL to LDL..... to Damaged LDL
From VLDL to LDL..... to Damaged LDL

YER LIVER!
From VLDL to LDL….. to Damaged LDL
From VLDL to LDL….. to Damaged LDL
From VLDL to LDL..... to Damaged LDL
From VLDL to LDL..... to Damaged LDL
From VLDL to LDL….. to Damaged LDL
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YER LIVER!
From VLDL to LDL..... to Damaged LDL
From VLDL to LDL..... to Damaged LDL

Atherosclerosis (and MORE...)

Blood Sugar ↑
Blood Triglycerides ↑
Blood Pressure ↑
Middle Obesity ↑
Blood Clotting ↑
Insulin ↑
HDL ↓

OX LDL

Root Causes

VLDL

HDL

Ch
Tg
Tg
Tg
Tg

Ch
Tg
Tg
Tg

B100

E

CII

E

Middle Obesity

Blood Sugar

Blood Pressure

Blood Clotting

Insulin

HDL

OX LDL

Ch
Tg
Tg
Tg

Ch
Ch
Ch

LDL Particle Count / ApoB

YER LIVER!

Body Fat
From VLDL to LDL..... to Damaged LDL

Atherosclerosis (and MORE...)

Fix Root Causes!!!
PART 2

Beyond ‘Cholesterol’

To The Primary Drivers of Heart Disease
What do Leading-Edge Experts Say?

➢ ‘Cholesterol and Disease’ Experts are called ‘Lipidologists’

➢ One of the USA’s foremost is Thomas Dayspring, MD, FACP, FNLA, NCMP
  ▪ Clinical Assistant Professor of Medicine, Director of Cardiovascular Education
What do Leading-Edge Experts Say?

- ‘Cholesterol and Disease’ Experts are called ‘Lipidologists’
- One of the USA’s foremost is Thomas Dayspring, MD, FACP, FNLA, NCMP
  - Clinical Assistant Professor of Medicine, Director of Cardiovascular Education

In reply to Ivor Cummins

Thomas Dayspring @Drlipid · 11 Nov 2014
@FatEmperor Current NHANES data: majority of MI are explained by IR. But real message is unless >200 mg/dL - LDLc is terrible biomarker
What do Leading-Edge Experts Say?

- ‘Cholesterol and Disease’ Experts are called ‘Lipidologists’
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My translation:

1) In reality, the majority of Heart Attacks are due to INSULIN RESISTANCE
What do Leading-Edge Experts Say?

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- One of the USA’s foremost is Thomas Dayspring, MD, FACP, FNLA, NCMP
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My translation:

1) In reality, the majority of Heart Attacks are due to INSULIN RESISTANCE

2) LDL is a near-worthless predictor for cardiovascular issues*

*(people with LDLc above 200mg/dL, or 5.3mmol/L are rare…)*
So what’s this ‘**Insulin Resistance**’ thing then?
So what’s this ‘**Insulin Resistance**’ thing then?

Well, if this is ‘**LDL**’ as a causal driver of Coronary Vascular Disease...
So what’s this ‘Insulin Resistance’ thing then?

...then this is INSULIN RESISTANCE!

Well, if this is ‘LDL’ as a causal driver of Coronary Vascular Disease...
"The Adipose Tissue falls first..."
AdipoShield® - Bodyfat as universal Energy Buffer System

**SAFE FAT**

- Bad Food
- Excessive Food

**MHNW** (Metabolically Healthy Normal Weight)

**INSULIN SENSITIVE. Risk Level**
AdipoShield© - Bodyfat as universal Energy Buffer System

**MHNW** (Metabolically Healthy Normal Weight)

**MONW** (Metabolically Obese Normal Weight)

**INSULIN SENSITIVE. Risk Level**

**INSULIN RESISTANT. Risk Level**
AdipoShield® - Bodyfat as universal Energy Buffer System

MHNW (Metabolically Healthy Normal Weight)
INSULIN SENSITIVE. Risk Level

MONW (Metabolically Obese Normal Weight)
INSULIN RESISTANT. Risk Level

MUO (Metabolically Unhealthy Obese)
INSULIN RESISTANT. Risk Level 😞
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INSULIN RESISTANT. Risk Level

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INSULIN SENSITIVE. Risk Level

**MUO** (Metabolically Unhealthy Obese)
INSULIN RESISTANT. Risk Level
And what can IS vs IR Obesity Phenotypes Tell Us?

<table>
<thead>
<tr>
<th>~45 y.o. BMI: 45</th>
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<th>IR Obese</th>
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<tr>
<td>GIR</td>
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Insulin-sensitive obesity  
Insulin resistant

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**Insulin-sensitive** vs **Insulin resistant**

Insulin-sensitive obesity  
And what can IS vs IR Obesity Phenotypes Tell Us?

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Glucose Infusion Rate (µmol/kg/min)

- Insulin resistant obese
- Insulin sensitive obese
- Background population
- Non-obese reference population

"Low macrophage infiltration into omental fat and higher circulating adiponectin almost entirely predict the IS obese Phenotype $r^2=0.98$, $P < 0.0001$"
The Insulin Resistance Journey
The Insulin Resistance Journey
The Insulin Resistance Journey

Adipose Tissue

GLUT4

DNL

Insulin

Pancreas

Liver

Insulin...
The Insulin Resistance Journey

CARBOHYDRATES
(i.e. Glucose)

Pancreas

Glucagon

Insulin

Adipose Tissue

GLUT4

DNL

Liver

“Lipokines”

GLUT4
The Insulin Resistance Journey

CARBOHYDRATES (i.e. Glucose)

“Too Much”

Pancreas

Insulin...

Insulin

Liver

Adipose Tissue

↑ GLUT4

↑ DNL

“Lipakines”
CARBOHYDRATES (i.e. Glucose) “Too Much” → Pancreas → Insulin → Adipose Tissue → GLUT4, DNL → "Lipokines" → Liver → Insulin → "The Insulin Resistance Journey"
The Insulin Resistance Journey

CARBOHYDRATES (i.e. Glucose)
“Too Much”

Pancreas

Insulin

Liver

Adipose Tissue

GLUT4

DNL

“Lipokines”
The Insulin Resistance Journey

CARBOHYDRATES (i.e. Glucose)

Too Much

Insulin...

Insulin

Adipose Tissue

GLUT4

DNL

Liver

Pancreas

"Lipokines"
The Insulin Resistance Journey

CARBOHYDRATES (i.e. Glucose)
“Too Much”

Pancreas

Insulin...

Liver

Adipose Tissue

GLUT4

DNL

“Lipokines”

Asprosin

FRUCTOSE
CARBOHYDRATES (i.e. Glucose) → "Too Much"

Pancreas → Insulin

Liver → Insulin... → "Too Much"

Adipose Tissue → ↓GLUT4, ↓DNL, "Lipokines", "Asprosin"

"The Insulin Resistance Journey"
The Insulin Resistance Journey

CARBOHYDRATES (i.e. Glucose) → Pancreas

Too Much → Insulin

Pancreas → Insulin

Liver → Insulin

Insulin Resistance Journey

Adipose Tissue → GLUT4

DNL

“Lipokines” → Asparosin

FRUCTOSE → ‘Too Much’
The Insulin Resistance Journey

CARBOHYDRATES (i.e. Glucose) → “Too Much”

Insulin…

Adipose Tissue

Liver

Smoking
Low Sleep / Exercise
Stress
Low Sun / Vitamin D
Genetic Tendency
Omega 6 Seed Oils
Low Omega 3
Sedentary Behaviour

Too Much

Too Much

FRUCTOSE
CARBOHYDRATES (i.e. Glucose)

"Too Much"

Pancreas

Insulin...

Insulin

Liver

Adipose Tissue

Smoking

Genetic Tendency

Low Sleep/

Exercise

Sedentary Behaviour

Omega 6

Seed Oils

Low Sun/

Vitamin D

Low Omega 3

Stress

The Insulin Resistance Journey
The Insulin Resistance Journey

CARBOHYDRATES (i.e. Glucose)

“Too Much”

Pancreas

Insulin…

Insulin

Liver

Adipose Tissue

Smoking
Genetic Tendency
Low Sleep / Exercise
Sedentary Behaviour

Omega 6 Seed Oils
Low Sun / Vitamin D
Low Omega 3
Stress
The Insulin Resistance Journey

CARBOHYDRATES (i.e. Glucose)

"Too Much"

Pancreas

Liver

Adipose Tissue

Too Much

Too Much

Too Much

Too Much

Too Much

Too Much

Too Much

Too Much
The Insulin Resistance Journey

CARBOHYDRATES (i.e. Glucose) "Too Much"

Pancreas

Insulin

Adipose Tissue
Adipose Macrophage (Inflammation)

Liver

Insulin Resistance

FRUCTOSE ‘Too Much’
But Blood Glucose is still under control...

...so how do you get into Endgame?
The Insulin Resistance Journey

CARBOHYDRATES
(i.e. Glucose)

"Too Much"

Insulin... Insulin

Adipose Tissue

Adipose Macrophage
(Inflammation)

Liver

FRUCTOSE
'Too Much'

Too Much

Inflammation

Insulin Resistance

Insulin
The Insulin Resistance Journey

CARBOHYDRATES (i.e. Glucose)

Too Much

Pancreas

Insulin... Brake Failure

Insulin

Free Fatty Acids
Glycerol

Adipose Tissue

Liver

Fructose

Too Much
The Insulin Resistance Journey

CARBOHYDRATES (i.e. Glucose)

"Too Much"

Pancreas

Insulin…

Adipose Tissue

Free Fatty Acids

Glycerol

‘Too Much’

Insert Insulin to Continue
Measuring it - part 1

Metabolic Mayhem
Measuring Metabolic Mayhem…

Defined in 1988 by Gerald M Reaven, MD
Professor emeritus in medicine at the Stanford University School of Medicine
Measuring Metabolic Mayhem…

1. Low HDL “Good Cholesterol”
2. High Blood Triglycerides
3. Large Waist Measurement
4. Elevated Blood Pressure
5. High Blood Sugar
The Metabolic Syndrome

1. Low HDL “Good Cholesterol”
2. High Blood Triglycerides
3. Large Waist Measurement
4. Elevated Blood Pressure
5. High Blood Sugar

Measuring Metabolic Mayhem…

- Atherosclerosis
- Coronary Heart Disease
Measuring Metabolic Mayhem...

1. Low HDL “Good Cholesterol”
2. High Blood Triglycerides
3. Large Waist Measurement
4. Elevated Blood Pressure
5. High Blood Sugar

- Atherosclerosis
- (*Obesity)
- Gout
- Cancer
- Stroke
- Atherosclerosis
- Coronary Heart Disease
- Type 2 Diabetes
- Alzheimer's
- Fatty Liver Disease
- Asthma
- Arthritis
- Etc. etc. …
Measuring Metabolic Mayhem…

1. Low HDL “Good Cholesterol”
2. High Blood Triglycerides
3. Large Waist Measurement
4. Elevated Blood Pressure
5. High Blood Sugar

But…didn’t I say earlier that Insulin Resistance was the big player…?
Measuring Metabolic Mayhem…

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2. High Blood Triglycerides
3. Large Waist Measurement
4. Elevated Blood Pressure
5. High Blood Sugar

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- Etc. etc. …

Master Measure…

HIGH INSULIN SECRETION !!!

INSULIN RESISTANCE SYNDROME
1. Low HDL “Good Cholesterol”
2. High Blood Triglycerides
3. Large Waist Measurement
4. Elevated Blood Pressure
5. High Blood Sugar

INSULIN RESISTANCE SYNDROME

- Atherosclerosis
- Coronary Heart Disease
- (*Obesity)
- Fatty Liver Disease
- Gout
- Stroke
- Cancer
- Type 2 Diabetes
- Alzheimer's
- Arthritis
- Fatty Liver Disease
- Asthma
- Etc. etc. ...

“If you don’t measure it, it don’t get fixed.”
Dr. Joseph R. Kraft, MD, MS, FCAP
Chairman, Department of Clinical Pathology and Nuclear Medicine, St. Joseph’s Hospital 1962-1990 (appointed Chairman Emeritus on retirement)
The Kraft “Diabetes In Situ” Test
The Kraft “Diabetes In Situ” Test

1. Drink 75g Glucose…
The Kraft “Diabetes In Situ” Test

1. Drink 75g Glucose…

2. Measure the Insulin Response over time…
The Kraft “Diabetes In Situ” Test

Kraft Patterns - The Earliest Diagnosis of Diabetes

1. Drink 75g Glucose...

2. Measure the **Insulin** Response over time…
The Kraft “Diabetes In Situ” Test

1. Drink 75g Glucose…

2. Measure the Insulin Response over time…
Kraft Pattern 1 - Euinsulinemia (Non-Diabetic)

Pattern 1 = Healthy
Kraft Pattern 2, 3, 4 - Hyperinsulinemia (Diabetes in Situ)
Kraft Pattern 2, 3, 4 - Hyperinsulinemia (Diabetes in Situ)

“The Earliest Laboratory Diagnosis for Diabetes” - Dr. Joseph R. Kraft
Patterns of Insulin Concentration During the OGTT Predict the Risk of Type 2 Diabetes in Japanese Americans

DIABETES CARE, VOLUME 36, MAY 2013
Kraft predicts Full-blown T2D...2013 Study

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DIABETES CARE, VOLUME 36, MAY 2013

Kraft predicts Full-blown T2D...2013 Study

DIABETES INCIDENCE 11 Years Later

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**DIAGRAM:**

- **Pattern 1:** 3%
- **Pattern 2:** 10%
- **Pattern 3:** 15%
- **Pattern 4:** 48%
- **Pattern 5:** 38%

**Graph A:**

- **Pattern 1** shows a rapid increase followed by a decrease.
- **Pattern 2** shows a steady increase.
- **Pattern 3** shows a peak at 60 minutes.
- **Pattern 4** shows a gradual increase.
- **Pattern 5** shows a rapid increase and then a plateau.

*Source: Kraft predicts Full-blown T2D...2013 Study*
And did you know...
And did you know...

That 49%-52% in the US are now...

pre-Diabetic or Diabetic.

Pre-Diabetic ≈ Diabetic ≈ Insulin Resistant ≈ Hyperinsulinemic

And did you know…

That 49%-52% in the US are now…

pre-Diabetic or Diabetic.

Pre-Diabetic ≈ Diabetic ≈ Insulin Resistant ≈ Hyperinsulinemic

Using Kraft’s test, probably >65% would have

Hyperinsulinemia / Diabetes In Situ
And did you know...

“Those with cardiovascular disease not identified with diabetes... are simply undiagnosed” - Dr. Joseph R. Kraft

Screening for dysglycaemia in patients with coronary artery disease as reflected by fasting glucose, oral glucose tolerance test, and HbA1c: a report from EUROASPIRE IV—a survey from the European Society of Cardiology

European Heart Journal, 02/12/2015  Evidence Based Medicine  Clinical Article

- In EUROASPIRE IV, a cross-sectional survey of patients aged 18–80 years with coronary artery disease in 24 European countries, 4004 patients with no reported history of diabetes had FPG, 2hPG, and HbA1c measured.
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- In EUROASPIRE IV, a cross-sectional survey of patients aged 18–80 years with coronary artery disease in 24 European countries, 4004 patients with no reported history of diabetes had FPG, 2hPG, and HbA1c measured.

- Using all screening tests together, 1158 (29%) had undetected diabetes.
I’d be surprised if many of the remaining 34% would pass a Kraft Test…
So now let’s see the Root Cause Diagram for CVD...and how you avoid the mess.
Draft Root Cause Diagram for Cardiovascular Disease

- Insulin Resistance
- Hyperinsulinemia
- IR Fatty Liver...
Draft Root Cause Diagram for Cardiovascular Disease

- Insulin Resistance
- Hyperinsulinemia
- IR Fatty Liver...

- ↑ Blood Insulin
- ↑ Blood Glucose
- ↑ Blood Pressure
Draft Root Cause Diagram for Cardiovascular Disease

- Insulin Resistance
- Hyperinsulinemia
- IR Fatty Liver
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- ↑ Blood Pressure
Draft Root Cause Diagram for Cardiovascular Disease

ATHEROGENIC DYSLIPIDEMIA

↑ VLDL
↑ TRIGLICERIDES
↑ OXIDISED LDL
↑ LDL COUNT
↓ HDL
↑ Tot/HDL Ratio

IR FATTY LIVER...

INSULIN RESISTANCE
HYPERINSULINEMIA

↑ BLOOD INSULIN
↑ BLOOD GLUCOSE
↑ BLOOD PRESSURE
Atherogenic Dyslipidemia

- ↑ VLDL
- ↑ Triglycerides
- ↑ Oxidised LDL
- ↓ HDL
- ↑ LDL Count
- ↑ Total/HDL Ratio

Insulin Resistance

Hyperinsulinemia

IR Fatty Liver...

Heart Disease

Blood Insulin

Blood Glucose

Blood Pressure
And what about the ACTIONABLE Root Causes of this Mess?
ATHEROGENIC DYSLIPIDEMIA

- Excess Fructose
- Excess Carb

INSULIN RESISTANCE
HYPERINSULINEMIA
IR FATTY LIVER...

ATHEROGENIC DYSLIPIDEMIA

- ↑ VLDL
- ↑ TRIGLecerides
- ↑ OXIDISED LDL
- ↓ HDL
- ↑ LDL COUNT
- ↑ Tot/HDL Ratio

HEART DISEASE

- ↑ BLOOD INSULIN
- ↑ BLOOD GLUCOSE
- ↑ BLOOD PRESSURE

Visceral Fat
atherogenic dyslipidemia

↑ VLDL

↑ TRIGLCEIDES

↑ LDL

↑ LDL COUNT

↓ HDL

→ INSULIN RESISTANCE

HYPERINSULINEMIA

IR FATTY LIVER...

ATHEROGENIC DYSLIPIDEMIA

↑ BLOOD INSULIN

↑ BLOOD GLUCOSE

↑ BLOOD PRESSURE

HEART DISEASE

Excess Fructose

Excess Carb

Sub-Opt Omega 3

Excess Omega 6

AND

AND

Visceral Fat

Draft Root Cause Diagram for Cardiovascular Disease
Atherogenic dyslipidemia

↑ VLDL
↑ Triglycerides
↑ Oxidised LDL
↑ LDL count
↓ HDL

Insulin resistance
Hyperinsulinemia
IR Fatty liver...

Heart disease

↑ Blood insulin
↑ Blood glucose
↑ Blood pressure

Sub-Opt Sun / Vit D
Sub-Opt K2, C, Mg
Genetic Tendency
Excess Fructose
Excess Carb
Sub-Opt Omega 3
Excess Omega 6

AND

AND
Importance of Diet for Cardiovascular Disease

- Excess fructose and carb intake
- Omega 3 deficiency
- Omega 6 excess
- Lack of K2, C, Mg
- Sun / Vitamin D deficiency
- Genetic tendency

Pathways:
- Insulin resistance
- Hyperinsulinemia
- Fatty liver
- Atherogenic dyslipidemia
- Elevated blood pressure
- Elevated blood glucose
- Elevated blood insulin

Factors:
- Smoking
- Pollutants
- Lack of sleep / exercise
- Genetic tendency
- Insulin resistance
- Hyperinsulinemia
- Fatty liver

Disease:
- Heart disease
Draft Root Cause Diagram for Cardiovascular Disease

- Atherogenic Dyslipidemia
  - ↑ VLDL
  - ↑ Triglycerides
  - ↑ Oxidised LDL
  - ↓ HDL
  - ↑ LDL Count

- Insulin Resistance
- Hyperinsulinemia
- IR Fatty Liver...

- Heart Disease

- Lack of Sleep / Exercise
- Smoking
- Pollutants

- Genetic Tendency
- Excess Fructose
- Excess Carb
- Sub-Opt Omega 3
- Sub-Opt Omega 6
- Excess K2, C, Mg
- Sub-Opt Sun / Vit D

- Visceral Fat

- ↑ Blood Insulin
- ↑ Blood Glucose
- ↑ Blood Pressure

- Other
Draft Root Cause Diagram for Cardiovascular Disease

- **Atherogenic Dyslipidemia**
  - ↑ VLDL
  - ↑ LDL
  - Count
- Excess Fructose
- Excess Carb
- Sub-Opt Omega 3
- Excess Omega 6

- **Excess Blood Insulin**
- ↓ HDL
- ↑ Blood Glucose
- ↑ Blood Pressure

- **Insulin Resistance**
- Hyperinsulinemia
- Fatty Liver

- Metabolic Mayhem

- Visceral Fat
- Sub-Opt Sun / Vit D
- Sub-Opt K2, C, Mg
- Genetic Tendency
- Excess Fructose
- Excess Carb
- Sub-Opt Omega 3
- Excess Omega 6
- Lack of Sleep / Exercise
- Smoking
- Pollutants

- Multiple Non-IR Mech

- Oxidative Stress Inflammation Ages / Nages
PART 3
The Power of the CAC Score
The Ultimate Test for CVD Presence
“We Stand on the Shoulder’s of Giants…”

Bruce Brundage
Cardiologist
Former Professor David Geffan
School of Medicine UCLA

Doug Boyd
Physicist, Inventor of CAC Technology
Former Professor of Radiology (Physics)
UCSF

Harvey S. Hecht
Cardiologist
Professor Mount Sinai Medical Centre New York

John A. Rumberger
Cardiologist
Princeton Longevity Centre

Arthur Agatston
Cardiologist
Associate Professor of Medicine
University of Miami

Matthew J. Budoff
Cardiologist
Professor of Medicine UCLA
“We Stand on the Shoulder’s of Giants…”

Bruce Brundage
Cardiologist
Former Professor David Geffan
School of Medicine UCLA

Doug Boyd
Physicist, Inventor of CAC Technology
Former Professor of Radiology (Physics)
UCSF

Harvey S. Hecht
Cardiologist
Professor Mount Sinai Medical Centre
New York

John A. Rumberger
Cardiologist
Princeton Longevity Centre

Matthew J. Budoff
Cardiologist
Professor of Medicine UCLA

Arthur Agatston
Cardiologist
Associate Professor of Medicine
University of Miami

On iTunes
Or Amazon Prime
watch this film... it could save your life
THE WIDOWMAKER

www.widowmakerthemovie.com
The CT Scan – and the CAC Score
The CT Scan – and the CAC Score
What about Studies on CAC?
Framingham Versus Calcium Scoring & CAC

<table>
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| 10% | ? | ? | ? | ? | ? |

???
## Framingham Versus Calcium Scoring & CAC

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- 10%: 2.4%, 5.4%, ?, ?, ?
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    - 0: 2.4%
    - 1-80: 5.4%
    - 81-400: 16%
    - 401-600: 25%
    - >600: 36%

- **1-80**
  - Framingham Risk Score: 10%
  - AND WITH YOUR CAC SCORE?
    - 0: 2.4%
    - 1-80: 5.4%
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- **81-400**
  - Framingham Risk Score: 10%
  - AND WITH YOUR CAC SCORE?
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- **>600**
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**Muddy Framingham Takes a Guess...**
Framingham Versus Calcium Scoring & CAC

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MUDDY FRAMINGHAM TAKES A GUESS...

THE CALCIUM SCAN SEES THE DISEASE.
Always the best test, across all the studies....

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100’s of thousands of people tracked in these and other CAC studies.
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Coronary Calcium is not a ‘Risk Factor’

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Coronary Calcium is not a ‘Risk Factor’

CALCIUM SEES THE DISEASE PROCESS ITSELF

100’s of thousands of people tracked in these and other CAC studies.
CAC Score

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<tr>
<th>Calcium Score</th>
<th>Risk Equivalent</th>
<th>10-Year Event Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Very low</td>
<td>1.1-1.7</td>
</tr>
<tr>
<td>1-100</td>
<td>Low</td>
<td>2.3-5.9</td>
</tr>
<tr>
<td>101-400</td>
<td>Intermediate</td>
<td>12.8-16.4</td>
</tr>
<tr>
<td>&gt;400</td>
<td>High</td>
<td>22.5-28.6</td>
</tr>
<tr>
<td>&gt;1000</td>
<td>Very high</td>
<td>37</td>
</tr>
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J Am Coll Cardiol Img. 2015;8(5):579-596
CAC Score Obliterates the “Risk Factors”…!

Mortality rate (per 1000 person-years) with increasing coronary artery calcium (CAC) scores according to burden of risk factors (RFs).

<table>
<thead>
<tr>
<th></th>
<th>0 RF</th>
<th>1 RF</th>
<th>2 RF</th>
<th>≥3RF</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAC=0</td>
<td>9,805</td>
<td>4,558</td>
<td>3,322</td>
<td>2,123</td>
<td>19,898</td>
</tr>
<tr>
<td>CAC 1-100</td>
<td>5,994</td>
<td>3,250</td>
<td>2,913</td>
<td>2,204</td>
<td>14,181</td>
</tr>
<tr>
<td>CAC 101-400</td>
<td>1,883</td>
<td>1,301</td>
<td>1,371</td>
<td>1,184</td>
<td>5,739</td>
</tr>
<tr>
<td>CAC&gt;400</td>
<td>1,047</td>
<td>984</td>
<td>1,148</td>
<td>1,055</td>
<td>4,234</td>
</tr>
<tr>
<td>Total</td>
<td>18,819</td>
<td>10,093</td>
<td>8,754</td>
<td>6,386</td>
<td>44,052</td>
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And what about CAC Score progression ??
And what about CAC Score progression??

Yearly CAC Score Increase High (more than 15%)

Starting Score 100-1000

3.5 Years Pass by…
And what about CAC Score progression??

Yearly CAC Score Increase High (more than 15%)

Starting Score 100-1000

3.5 Years Pass by…

“Progression of Coronary Artery Calcium and Risk of First Myocardial Infarction in Patients Receiving Cholesterol-Lowering Therapy”
And what about CAC Score progression??

Yearly CAC Score Increase High (more than 15%)

Starting Score 100-1000
3.5 Years Pass by...

And what about CAC Score progression??

Yearly CAC Score Increase Low (less than 15%)

Starting Score 100-1000
6 Years Pass by...

“Progression of Coronary Artery Calcium and Risk of First Myocardial Infarction in Patients Receiving Cholesterol-Lowering Therapy”
DOI: 10.1161/01.ATV.0000127024.40516.ef
And what about CAC Score progression??

Yearly CAC Score Increase High (more than 15%)

Starting Score 100-1000
3.5 Years Pass by...

Yearly CAC Score Increase Low (less than 15%)

Starting Score 100-1000
6 Years Pass by...
CAC Score is now obligatory for all US presidents and all Astronauts
PART 4
“Cholesterol Capers”

Hyperinsulinemia as Prime Driver
.....versus Cholesterol as Cause.
LDLc

“The Bad Cholesterol”
Insulin Versus ‘Bad Cholesterol’


Helsinki: One of the few studies to properly use a Kraft-type test…

INSULIN

Helsinki: One of the few studies to properly use a Kraft-type test...

Insulin Versus ‘Bad Cholesterol’

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Insulin Versus ‘Bad Cholesterol’

Helsinki: One of the few studies to properly use a Kraft-type test…


INSULIN

Low Insulin

High Insulin

Hyperinsulinemia / Insulin Resistance

Helsinki: One of the few studies to properly use a Kraft-type test…

“Bad Cholesterol”

Insulin Versus ‘Bad Cholesterol’
# Insulin Vs ‘Bad Cholesterol’ in head-to-head Studies

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<th>Insulin /Glucose</th>
<th>‘Bad Cholesterol’</th>
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<td>“Lipid levels in patients hospitalized with coronary artery disease:…” (2009)</td>
<td>Not available</td>
<td>Inverse 🎁</td>
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<tr>
<td>“Interrelation between angiographic severity of coronary artery disease and…” (1993)</td>
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Prospective Predictions Based on IR Level

- Apparently healthy, non-obese (body mass index < 30 kg/m²) individuals
- Split into tertiles of Insulin Resistance by SSPG via Insulin Suppression Test
- What happened ~6.5 years later?
Prospective Predictions Based on IR Level

- Apparently healthy, non-obese (body mass index < 30 kg/m²) individuals
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Well, here’s what transpired:

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Insulin Resistance as a Predictor of Age-Related Diseases The Journal of Clinical Endocrinology & Metabolism 86(8):3574–3578
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Insulin Resistance as a Predictor of Age-Related Diseases The Journal of Clinical Endocrinology & Metabolism 86(8):3574–3578
AND...If CAC Score Obliterates the “Risk Factors”...

...which it does
The mainstream hypothesis that LDL cholesterol drives atherosclerosis may have been falsified by non-invasive imaging of coronary artery plaque burden and progression.

**Then WHY doesn’t LDLc correlate with it?**

- Why do autopsy studies of the correlation between the extent of coronary atherosclerosis and serum cholesterol yield null results? The answer that the blood samples, mostly from accident victims, didn’t correlate with outcomes.

- Why did Hecht et al. [7] fail to find no correlation between LDL and the coronary calcium percentile (correlation coefficient 0.06 with a scatter plot showing no visible correlation) for 304 asymptomatic individuals judged free of CHD (Spearman’s coefficient = 0.07 and 0.08, respectively). Even the correlation coefficient was very low.

- Why in a study of 177 asymptomatic patients of intermediate risk of CHD did Ramadan et al. [14] find a null result (OR = 1.022, p = 0.361) for the odds of positive coronary calcium outcome and LDL in a multivariate model? The group studied had a wide range of both LDL levels and calcium scores.

- Why did Kronmal et al. [12] find among approximately 2900 individuals that the relative risk of incident coronary calcium associated with LDL was only 1.03 per 10 mg/dL and barely reached statistical significance (lower CI 1.01) whereas both HDL and triglycerides exhibited much stronger associations?

- Why were Takamiya et al. [15] unable to find any association in a meta-analysis of 30,500 and 19,000 individuals diagnosed with and without CHD respectively? The correlation coefficient was very low as well.

- Why did Arad et al. [10] in the St. Francis Heart Study find no correlation (r = 0.03, p = 0.15) between LDL levels and coronary calcium scores in 4903 asymptomatic individuals?
LDLp (ApoB)

“The New Bad Cholesterol”
What about LDLp/ApoB Independence...?

- Increased VLDL
- Increased LDL
- Excess Fructose
- Excess Carb
- Sub-Opt Omega 3
- Excess Omega 6
- Excess Natural Fats...
- Lack of Sleep / Exercise
- Smoking

**INSULIN RESISTANCE**

**HYPERINSULINEMIA**

**ATHEROGENIC DYSLIPIDEMIA**

- Increased LDL
- Oxidised LDL
- Increased VLDL
- Increased TRIG
- Decreased HDL
- Decreased Tot/HDL

**BLOOD PRESSURE**

**BLOOD GLUCOSE**

**MIDDLE OBESITY**

**FATTY LIVER**

**IR LIVER...**

**Heart Disease**
What about LDLp/ApoB Independence...?

“ApoB/ApoA1 ratio in regression model had an OR of 17.95 for Insulin Resistance”

“ApoB/ApoA1 ratio in regression model had an OR of 17.95 for Insulin Resistance”

What about LDLp/ApoB Independence…?

- Sub-Opt Sun/Vit D
- Sub-Opt K2, C, Mg
- Genetic Tendency
- Excess Fructose
- Excess Carb
- Sub-Opt Omega 3
- Excess Omega 6
- Lack of Sleep/Exercise
- Smoking

INSULIN RESISTANCE

“ApoB/ApoA1 ratio in regression model had an OR of 17.95 for Insulin Resistance”


- ↑ Blood Glucose
- ↑ Blood Pressure
- ↑ VLDL
- ↑ Triglycerides
- ↓ HDL
- ↑ LDL Count
- Oxidised LDL
- ↓ Tot/HDL
- ↑ ApoB/ApoA1 Ratio

Other (Stress etc.)

Heart Disease
Lp(a)

“The Sexy Bad Cholesterol”
Ask WHY?

Figure 2. Relationship between OxPL-apoB (A) and Lp(a) (S) tertile groups and CVD risk according to tertiles of Lp-PLA2 activity ($P=0.018$ and $P=0.008$ for interaction of OxPL-apoB and Lp(a), respectively).
Ask WHY?


Figure 2. Relationship between OxPL/apoB (A) and Lp(a) (S) tertile groups and CVD risk according to tertiles of Lp-PLA2 activity (P=0.018 and P=0.008 for interaction of OxPL/apoB and Lp(a), respectively).

Fig. 2. Risk of angina according to Lp(a) concentration (A).
Why is high Lp(a) only significant for people with existing inflammatory issues?
WRAPUP

“Striking at the Root”

What would I personally prioritise?
“There are a thousand hacking at the branches of evil, - to one who is striking at the root (causes).”
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Cancers
Obesity/
Hypertension
Diabetes &
Alzheimers
General Chronic
Disease / early
death
Cardiovascular
Disease

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3 children.
Concerned.

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* Cousin died of Heart Attack at 50
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