Primary Causes of Heart Disease

Framingham and the Muddy Waters

Jeffry N. Gerber, MD
Denver’s Diet Doctor
“Those with cardiovascular disease not identified with diabetes… are simply undiagnosed” - Dr. Joseph R. Kraft
Dr. Joseph R. Kraft - diabetes-epidemic.com
Standard Methods Inferior

- FBG > 100 mg/dl (5.5 mmol/l) screening
- 2hr OGTT > 140 mg/dl (7.8 mmol/l)
- HbA1c
Dr. Kraft 5hr Insulin Assay

- Gold standard based on RIA insulin (uIU/ml)
- 14,384 subjects, 5hr glucose plus insulin
- Defined 5 distinct patterns
- 3 patterns of hyperinsulinemia – Diabetes In-Situ
- Redefining diabetes at its earliest stage
Pattern 1 - Euinsulinemia

Kraft Patterns - The Earliest Diagnosis of Diabetes

Pattern 1 = Normal Euinsulinemia

These people are Not Diabetic
Patterns 2,3,4 - Hyperinsulinemia

Insulin Response Patterns 2 to 4 are: Hyperinsulinemia/Diabetes In Situ

These people are Diabetic. Period.

Image courtesy Ivor Cummins BE(Chem) CEng MIEI
Patterns 2, 3, 4 - Hyperinsulinemia

Kraft Patterns - The Earliest Diagnosis of Diabetes

Insulin Response Patterns 2 to 4 are:
Hyperinsulinemia/Diabetes In Situ
These people are Diabetic. Period.

Image courtesy Ivor Cummins BE(Chem) CEng MIEI
Patterns 5 - Insulinopenic

Kraft Patterns - The Earliest Diagnosis of Diabetes

Patterns 5 = Low Insulin

*These people are Insulinopenic*

Image courtesy Ivor Cummins BE(Chem) CEng MIEI
**Glucose vs. Insulin**

<table>
<thead>
<tr>
<th>Hyperglycemia Test</th>
<th>Hyperinsulinemia</th>
<th></th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Disease</td>
<td>No Disease</td>
</tr>
<tr>
<td>Positive</td>
<td>True Positives</td>
<td>False Positives</td>
</tr>
<tr>
<td></td>
<td>6180</td>
<td>186</td>
</tr>
<tr>
<td>Negative</td>
<td>False Negatives</td>
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</tr>
<tr>
<td></td>
<td>5764</td>
<td>2254</td>
</tr>
<tr>
<td>Totals</td>
<td>11944</td>
<td>2440</td>
</tr>
</tbody>
</table>

**Sensitivity** 52%

**Specificity** 92%

Data recompiled from Kraft J. R. Diabetes Epidemic & You. 2011
Euglycemia

NFG & NGT
Negative Predictive Value

- 28% Normal - Kraft Pass
  True Negatives
- 72% 'Normal' - Kraft Fail
  False Negatives
Hyperglycemia

IFG or IGT or DMGT

Sensitivity

- 52% Abnormal - Kraft Fail True Positives
- 48% 'Normal' - Kraft Fail False Negatives
Predicting population risk
Predicting population risk

That 49%-52% in the US are now…

pre-Diabetic or Diabetic.

*Pre-Diabetic ≈ Diabetic ≈ Insulin Resistant ≈ Hyperinsulinemic*
Predicting population risk

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

Diabetes Paradox?

• Despite more diabetes & obesity there’s less heart disease
• Morbidity & mortality not to be confused with incidence and prevalence
Dr. Kraft on CV risk

• Atherosclerosis is a metabolic disease
• Missing pre-diabetes and diabetes also misses cardiovascular disease
The Metabolic Syndrome

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

INSULIN RESISTANCE SYNDROME
- Atherosclerosis
- Coronary Heart Disease
The Metabolic Syndrome

1. Glucose Intolerance
2. Hyperinsulinemia
3. Low HDL/ High TRGs
4. Elevated Blood Pressure
5. Abdominal obesity

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

- Cholesterol, Smoking, HTN, Diabetes
- Guidelines, tools, risk calculators
- Central theme to lower cholesterol
- Diabetes risk buried
The Framingham Risk Score

‘Bad’ Cholesterol?
Do You Smoke?
Are you male?
High Blood Pressure?
Diabetes?
The Framingham Risk Score

‘Bad’ Cholesterol?

Do You Smoke?

Are you male?

High Blood Pressure?

Diabetes?

THIS IS STATISTICAL GUESSWORK
The Framingham Risk Score

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HEAVILY CHOLESTEROL WEIGHTED
The Framingham Risk Score

‘Bad’ Cholesterol?

Do You Smoke?

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This is statistical guesswork

Heavily cholesterol weighted

These are the muddy waters.
Lipid Lowering Therapy
Lipid Lowering Therapy

- Hyperlipidemia requires remedy
- Is cholesterol innately toxic?
- Mechanisms remain elusive
- Diet-heart hypothesis unproven
- Statins provide small benefit
Debunking the Lipid Hypothesis

- Get with the Guidelines 2009
- Towards a Paradigm Shift in Cholesterol Treatment 2015
Mechanisms for metabolic disease are established...

**Atherogenic Dyslipidemia**
- ↑ VLDL
- ↑ LDL
- ↑ Oxidised LDL
- ↑ Count
- ↑ TG
- ↓ HDL

**Insulin Resistance**

**Hyperinsulinemia**

**IR Fatty Liver**

**Arterial Damage**

- ↑ Blood Insulin
- ↑ Blood Glucose
- ↑ Blood Pressure
- ↑ tot/HDL Ratio

**Mechanisms for metabolic disease are Established...**
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- ↑ VLDL
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**METABOLIC MAYHEM:**

**ARTERIAL DAMAGE!**

**HYPERINSULINEMIA**
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**FATTY LIVER...**

**Insulin Resistance**

Mechanisms for metabolic disease are Established...
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METABOLIC MAYHEM:
  - Inflammation
  - Oxidative Stress
  - Advanced Glycation

ATHEROGENIC DYSLIPIDEMIA
  - ↑ VLDL
  - ↑ LDL COUNT
  - ↑ BLOOD INSULIN
  - ↓ HDL
  - ↑ TRIGL/CERIDES
  - ↑ BLOOD PRESSURE
  - ↑ OXIDISED LDL
  - ↑ Tot/HDL Ratio

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**Insulin Resistance**
- HYPERINSULINEMIA

**Metabolic Mayhem:**
- Inflammation
- Oxidative Stress
- Advanced Glycation

**Arterial Damage!**

- 'BAD CHOLESTEROL' ???
Studies supporting these mechanisms

- Diabetes and heart disease
- Proper measurement of glucose and Insulin
- Insulin vs. cholesterol
INSULIN Versus ‘CHOLESTEROL’

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

INSULIN Versus ‘CHOLESTEROL’

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

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<th>Insulin /Glucose</th>
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<td>“Lipid levels in patients hospitalized with coronary artery disease:…” (2009)</td>
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Doi:10.1111/j.1365-2796.2004.01371.x

Circ J 2004; 68: 47 –52

http://dx.doi.org/10.1016/j.ahj.2008.08.010

Am J Cardiol. 1993 Aug 15;72(5):397-401

Dioid:10.1161/01.ATV.0000127024.40516.ef

doi:10.1093/eurheartj/ehp221


Future research...

• Insulin vs. ‘bad cholesterol’
• Interventional food trials - low carb vs low fat
• Tracking subclinical disease using calcium scans
• Cardiovascular outcomes
It’s the Insulin Stupid!

- Atherosclerosis is a symptom of diabetes
- Focus on metabolic disease and hormonal dysregulation
- Many at risk are missed
- Diet and lifestyle, not medicine
Diet and Lifestyle

✓ Low carb best
✓ Eliminating processed food
✓ Eating less
✓ Movement & activity
✓ Smoking cessation
✓ Sunlight
✓ Proper sleep & happiness
Clinical assessment

- Early level of suspicion
- FBG & HbA1c - are poor screening tools
- 2 hr OGTT including 1hr glucose <155 mg/dl (8.6 mmol/l)
- Insulin - fasting, 5hr assay, 2hr <30 uIU/ml
- Inflammatory markers, lipid quality, etc…
- Body fat, waist-to-height

doi: http://dx.doi.org/10.1210/jc.2015-2573
Cardiovascular imaging

- Heart catheterization
- CT angiogram
- IVUS
- Cardiac MR
- CIMT
- Coronary artery calcium score
“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
The CT Scan – and the CAC Score
The CT Scan – and the CAC Score
What about Studies on CAC?
## Screening Power of CAC Scoring

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Always the best test, across all the studies....

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Screening for Ischemic Heart Disease with Cardiac CT: Current Recommendations Volume 2012, Article ID 812046, http://dx.doi.org/10.6064/2012/812046

Calcium is not a ‘Risk Factor’

CALCIUM SEES THE DISEASE PROCESS ITSELF
# CAC Score

<table>
<thead>
<tr>
<th>Calcium Score</th>
<th>Risk Equivalent</th>
<th>10-Year Event Rate, %</th>
</tr>
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<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>
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<tr>
<td>&gt;1000</td>
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J Am Coll Cardiol Img. 2015;8(5):579-596
## Framingham Versus Calcium Scoring & CAC

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**Muddy Waters: Framingham Risk Score**

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*Muddy Framingham takes a guess...*
The calcium scan sees the disease.

Muddy Framingham takes a guess... and with your CAC score?

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Muddy Framingham takes a guess... The calcium scan sees the disease.
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…
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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…

“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…

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”
The CAC Score is now in the 2013 guidelines - but hardly anyone knows (!)

Primary care doctors should be using this as an important screening tool to support and encourage people to take action.

The test when used properly does not lead to more unnecessary testing.

Relatively inexpensive and non-invasive

Although soft plaque is not detected it doesn’t matter – it’s mathematics

Screening age 45 and older

Goal is to stabilize calcium. Very few reduce calcium.
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Final Gem:
The CAC is now obligatory for all US Presidents and all Astronauts. Go figure.
Diabetes is a Vascular Disease