Primordial Prevention of CVD: Analysis of the Bogalusa Heart Study

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for the Bogalusa Heart Study group
Atherosclerotic Involvement in Sampling of Human Aortas of Various Ages
Serum Cholesterol and Triglycerides and Lipoprotein Analyses

Advanced by:

1. Gofman and ultracentrifuge Svedberg Units.
2. Frederickson and coworkers – electrophoretic analyses of Type IIa, IIb and III.
TURBIDIMETRIC ASSAY OF CHOLESTEROL FROM SERUM β AND PRE-β LIPOPROTEINS

Serum
Water
CaCl₂ (0.5 M)
Heparin (0.25 %)

0.2 ml 0.2 ml
3.3 ml 3.2 ml
0.5 ml 0.5 ml
——— 0.1 ml

Srinivasan SR et al. Angiologica 1970
Serum Lipoprotein Elevation Relative to Risk Factors in Patients with Angina Pectoris

Normal Angiograms

Abnormal Angiograms

RISK FACTORS

Elevation of lipoproteins associated with various “risk factors.” The clear bars indicate the low lipid patterns (arbitrary values of pre-β- and β-lipoprotein less than 100 mg/100 ml and 250 mg/100 ml, respectively). The hatched bars represent elevated lipid profiles over and above these “normal” limits. The “risk factors” are given on the horizontal axis and percentage of patients having “normal” or high lipid profiles on the vertical axis. It is evident that smoking and diabetes are associated with lipid elevations and are both more prevalent in patients with abnormal angiograms. Studies of much larger numbers of patients are needed to relate significantly all “risk factors” to coronary angiography and lipid studies.

Berenson GS et al. Southern Medical Journal. 1975
The relationship of pre-β- to β-lipoproteins among four groups of patients with angina pectoris. Notice the absence of pre-β-lipoprotein elevation alone in patients with abnormal angiograms and myocardial infarction.

Berenson GS et al. Southern Medical Journal. 1975
Obesity trend in US, 2005
Body Mass Index in Children and Young Adults: The Bogalusa Heart Study
Height in Children and Young Adults

The Bogalusa Heart Study

Height (m)

Year
- 73-74
- 76-77
- 78-79
- 81-82
- 83-84
- 87-91

Age (Years)
Risk factors change by age, race, and gender
RELATIONSHIP OF $\beta$-LP/$\alpha$-LP-CHOLESTEROL RATIO AND MATURATION
BOGALUSA HEART STUDY, 1976-1977

Race and Sex Distribution of Ponderal Index in 5 to 24 Year Olds
The Bogalusa Heart Study

Male
- White (N=1325)
- Black (N=720)

Female
- White (N=1331)
- Black (N=781)

Ponderal Index (kg/m²)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>10</th>
<th>15</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-6</td>
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<tr>
<td>7-8</td>
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<tr>
<td>9-10</td>
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<tr>
<td>11-12</td>
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<td>13-14</td>
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<td>15-16</td>
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<td>17-18</td>
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<tr>
<td>19-20</td>
<td></td>
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<tr>
<td>21-24</td>
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</tbody>
</table>

85th Percentile

Median
Interrelationship of Cardiovascular Risk Factors in Children

“Clustering” (aggregation) of risk factors occurs with an interactive or additive effect on CV risk
Relationship of VLDL-Cholesterol with Wt/Ht$^3$ by Age Group, Race and Sex
The Bogalusa Heart Study

Correlation Coefficient

Age (yrs)

- 5-10
- 11-16
- 17-22
- 23-26

a p<.05
b p<.01
d p<.0001
Relationship of HDL-Cholesterol with Wt/Ht$^3$ by Age Group, Race and Sex

The Bogalusa Heart Study

![Graph showing correlation coefficients by age group, race, and sex.

- Age (yrs):
  - 5-10
  - 11-16
  - 17-22
  - 23-26

- Correlation Coefficient:
  - a p<.05
  - b p<.01
  - c p<.001
  - d p<.0001]
Persistence of Multiple CV Risk Clustering from Childhood to Young Adulthood
The Bogalusa Heart Study

Individuals Remaining at Respective Quintiles of Multiple Risk Index* over 8 year Period

* Rank sum of systolic BP, insulin and TC/HDL-C
Tracking of Multiple Risk Index after 8 Years by Age and Ponderal Index among Children and Young Adults

P = 0.0001

Spearman Correlation

Age at Year 1, y

Ponderal Index Tertile at Year 1

5-8 9-12 13-17

1 2 3
Role of Insulin and CV Disease

• Strong obesity – insulin association
• Insulin - a growth factor
• Renal electrolyte exchange
• Insulin resistance and RAS system
• Blacks > whites – insulin levels
• Blacks < whites - C-peptide levels
  – suggests reduced liver extraction of insulin
Comparison of insulin metabolic parameters in adolescents by obesity status: The Bogalusa Heart Study

<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-Obese (n=1047)</th>
<th>Obese** (n=110)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>C-peptide (ng/ml)</strong></td>
<td>1.74 ± 0.75</td>
<td>2.66 ± 0.9*</td>
</tr>
<tr>
<td><strong>Insulin (µU/ml)</strong></td>
<td>11.7 ± 6.9</td>
<td>23.7 ± 12.3*</td>
</tr>
<tr>
<td><strong>C-peptide/Insulin</strong></td>
<td>0.16 ± 0.06</td>
<td>0.13 ± 0.04*</td>
</tr>
<tr>
<td><strong>Insulin/Glucose</strong></td>
<td>0.15 ± 0.08</td>
<td>0.29 ± 0.15*</td>
</tr>
</tbody>
</table>

* P <0.001 (adjusted for age), ** BMI > 90th percentile
Racial contrasts of Insulin and C-peptide levels in adolescents: The Bogalusa Heart Study

Insulin (µU/ml)

<table>
<thead>
<tr>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whites</td>
<td>P=NS</td>
</tr>
<tr>
<td>Blacks</td>
<td></td>
</tr>
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</table>

C-peptide (ng/ml)

<table>
<thead>
<tr>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whites</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Blacks</td>
<td></td>
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</tbody>
</table>
Which Comes First?

Obesity or Hyperinsulinemia?
Incidence of Clustering of Risk Variables of Syndrome X in Adulthood by Childhood BMI and Insulin Quartiles. The Bogalusa Heart Study

Odds Ratios for Developing Clustering of Risk Variables of Syndrome X in Adulthood Based on Childhood Levels of BMI and Insulin

<table>
<thead>
<tr>
<th>Childhood Quartiles * (Top vs. Bottom)</th>
<th>Odds Ratio (95% Confidence Interval)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>11.7 (3.4-39.7)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Adjusted, insulin</td>
<td>10.0 (2.8-35.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Insulin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>3.6 (1.5-8.7)</td>
<td>0.01</td>
</tr>
<tr>
<td>Adjusted, BMI</td>
<td>1.8 (0.7-4.7)</td>
<td>NS</td>
</tr>
</tbody>
</table>

The earliest childhood and latest adulthood measurements with a mean ± SD follow-up period of 11.6 ± 3.4 years were used.

* Specific for age, race, sex, and survey year (only those without clustering at baseline (n=718) were used.

Why do we need to do primordial prevention?
DISTRIBUTION OF SERUM $\beta$-AND PRE-$\beta$-LIPOPROTEINS IN PATIENTS WITH ANGINA PECTORIS

The relationship of pre-$\beta$- to $\beta$-lipoproteins among four groups of patients with angina pectoris. Notice the absence of pre-$\beta$-lipoprotein elevation alone in patients with abnormal angiograms and myocardial infarction.

Berenson GS et al. Southern Medical Journal. 1975
The Deadly Quartet

• Upper Body Obesity
• Glucose Intolerance
• Hypertriglyceridemia
• Hypertension

Norman M. Kaplan
Atherosclerotic Surface Involvement in Children and Young Adults by Risk Factor Status
The Bogalusa Heart Study

- Fatty Streak
- Fibrous Plaque

P=0.01
P=0.003

Percent (%)
Number of Risk Factors
- 0
- 1
- 2
- 3-4
Influence of Cigarette Smoking on Atherosclerosis in children and Young Adults

Fatty Streak

Prevalence (%)

Surface Involvement (%)

Aorta  Coronary  Aorta  Coronary

Fibrous Plaque

Smoker  Unknown  Nonsmoker

p<0.01  p<0.01  p<0.05

Prevalence (%)

Unknown  Nonsmoker
The Effect of Multiple Risk Factors on Carotid Intima-Media Thickness in Young Adults

Risk factors included were total cholesterol to HDL cholesterol ratio, waist circumference, systolic blood pressure, insulin level (> 75th percentile specific for age, race, and gender), and smoking.

Effect of Framingham Risk Score on IMT in Young Adults

*The Bogalusa Heart Study*

Linear trend for Common and Carotid bulb $P<0.0001$
The Effect of Multiple Risk Factors on Pulse Wave Velocity in Young Adults
The Bogalusa Heart Study

Risk factors included waist circumferences, homeostasis model assessment of insulin resistance, systolic blood pressure, total cholesterol to HDL cholesterol.
Correlates of Left Ventricular Hypertrophy by Vascular Compliance Measures by Multiple Instruments (n=867)

- Omron pAl@75
- C1: large artery elasticity index
- C2: small artery elasticity index
- SVR: systemic vascular resistance
- Ep: Peterson’s elastic modulus
- YEM: Young’s elastic modulus
- afPWV: aorto-femoral pulse wave velocity
- O/R: odds ratio
- CI: confidence interval

*All regression models included: ethnicity, gender, age, BSA, BMI, LDL-C, HDL-C, TG, and Glc.

Fernandez et al. J. Clin Card 2013
Non-traditional CV Risk Factors
Adiponectin levels by risk factors of metabolic syndrome*

**Risk Factors**
- 0
- 1
- 2
- 3 or more

* NCEP ATP III

P for trend <0.0001

**Patel et al. Metabolism 2005. The Bogalusa Heart Study**
Mean C-Reactive Protein levels by risk factors of metabolic syndrome: The Bogalusa Heart Study

Risk Factors of Metabolic Syndrome (NCEP ATP III)

- White Male
- Black Male
- White Female
- Black Female
- Total

C-Reactive Protein (mg/L)

- 0
- 1
- 2
- 3 or more

Patel et al. Metabolism 2006.
Markers of Nonalcoholic Fatty Liver and Metabolic Syndrome in Young Adults

Risk Factors of Metabolic Syndrome (NCEP ATP III)

- Gamma-Glutamyl Transferase (IU/L)
  - P for trend: <0.0001

- Alanine Aminotransferase (IU/L)
  - P for trend: <0.0001
Public Health

What to do?
"I’ve always been a high achiever, always striving for bigger, faster, greater...and now suddenly I’m expected to settle for lower blood pressure and less cholesterol?!"
Practical Concepts for Prevention in Children of Adult Heart Disease
“Heart Smart” Program

*Intervention Methods:*

**Population Strategy**
C-V Health Education for School Children

**High Risk Strategy**
Family Health Promotion
Why Families?

• Child’s primary social system

• CV disease risk factors aggregate in families

• Parent modeling and support
Guidelines for Prevention of Adult Heart Disease in Early Life

A Family at Risk – A Member with

- Myocardial infarction before age 60 years
- Hypertension and/or CVA
- High level of LDL-C (>75th percentile for age, sex)
- Low level of HDL-C (<25th percentile for age, sex)
- Obesity (>85th percentile for age, sex)
- Adult onset diabetes
- Smoking habit
HOW ABOUT AN ANTI-OBESITY PROGRAM FOR KIDS THAT ACTUALLY WORKS?

UM... IT'S CALLED "PARENTING"...
Forced Feeding
In Year 2020

Today’s 60 million school children and young adults will begin dying of heart disease
Poor Health Leads to:

- Poor academic performance
- Societal problems
  - school dropouts
  - unemployment
  - poverty
  - crime

(From Nation’s Health, 10/92)
C-V HEALTH PROMOTION FOR SCHOOL CHILDREN

An Interactive Program

Multiple Targeted Areas
- Nutrition
- Exercise
- Cognitive/Behavior (skills)

Multiple Approaches
- School
- Family
- Community
- Media
Cardiovascular Health Promotion in School-Aged Children

- School Lunch
- Exercise
- Staff Development
- Parents
- Environmental Supports
- Curriculum

Heart Smart
HEART SMART
JEFFERSON PARISH
SCHOOL SYSTEM

NATIONAL RESEARCH
DEMONSTRATION CENTER-
ARTERIOSCLEROSIS

SUPERKIDS
SUPERFIT

LSU MEDICAL CENTER
UNIVERSITY OF NEW ORLEANS
Practical Problems Addressed by Health Education

- Dropouts
- Alcohol
- Drug abuse
- Teenage pregnancies
- Suicides
- Violent behavior
M. POWERMENT LOG

FOR THE NEXT 24 HOURS, YOU ARE TO RECALL ONLY THE POSITIVE THINGS THAT HAPPEN TO YOU. REMEMBER “EMPOWERMENT” FOR YOU IS JUST AS IMPORTANT AS THE SUN IS FOR SOLAR ENERGY

<table>
<thead>
<tr>
<th>NAME:</th>
<th></th>
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<tbody>
<tr>
<td>DATE</td>
<td>SITUATION</td>
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</table>
Now Playing

Starring Role:

Name

List the 10 best things about you

1. 
2. 
3. 
4. 
5. 
6. 
7. 
8. 
9. 
10.
Change in Risk Factors:  
*The Heart Smart Program*  
*The Bogalusa Heart Study*

*P values for treatment x time interaction ≤0.02.*
Prevention Programs as Outgrowth of the Bogalusa Heart Study

• Health Ahead/ Heart Smart (K-6)

Health Education for Elementary School Children

• Family Health Prevention Program

• Washington Parish (County) – wide Health Promotion for Children

www.som.tulane.edu/cardiohealth/bog.html
Relation of ApoE Polymorphism to Clustering of Multiple Cardiovascular Risk Factors in Children
No Simple Answer to the Obesity Epidemic

- Food Industry
- Glycemic index
- TV
- Sugar
- Decreased PE in schools
- Energy density
- Decreasing physical activity
- School feeding
- Poor parenting

- Candy
- Genes
- Soft drinks
- Pouring contracts
- Junk food
- Restaurants
- Fast Food
- Working mothers
- Poverty
- Computers

Decreasing physical activity
Syndrome X, Metabolic Syndrome, Insulin Resistance Syndrome, Cardiometabolic Syndrome, Deadly Quartet, Atherogenic Dyslipidemia, etc.

- **NCEP ATP III** – any 3 risk factors
- **WHO** – diabetes, insulin, microalbuminuria
- **Intl. Diabetes Federation** – 2 hr glucose, diabetes, fasting glucose > 100 mg
- **American Association of Clinical Endocrinology** - 2 hr glucose

**Limitations:**
Since age-, gender-, ethnicity- specific--- risk factor burden is a continuum, cut points/percentiles are arbitrary.
Criteria for Metabolic Syndrome in Children

- RF* > 75th Percentile (<25th Percentile for HDL-C)
- Positive Family History

* Select 3 or more risk factors but include at least 1 measure of obesity, e.g. BMI, Waist.

Available population data: NHANES
BHS
Muscatine Study.
Prevalence of Adverse Risk Factors among Young Adults, ages 19-32 years: The Bogalusa Heart Study

* BMI > 31.1 kg/m² in males and 32.3 kg/m² in females