Cardiovascular Disease: Exploring Disease Progression and Preventative Strategies

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Skidmore College
Approach

Heart Disease

• What is it?  (definition)

• Who has it?  (prevalence/impact)

• What can you do about it?  (prevention/trt)

• How does it relate to my research program?
What is CVD? (definition)

- Heart disease?
- Heart failure?
- Clogged arteries?
- Arrhythmias?
- Heart attack?
- Myocardial infarction?
- High blood pressure?
- High cholesterol?
What is CVD? (definition)

• Cardiovascular disease is any disease of pathology that affects the cardiovascular system---
  – HEART
  – BLOOD VESSELS
  – BLOOD
CVD

- Atherosclerotic heart disease affects all three systems
The Heart

Overview

Coronary Circulation
Cardiovascular Disease

- We will focus on atherosclerotic heart disease, also called
  - ischemic heart disease
  - coronary artery disease

- Atherosclerotic heart disease leads to:
  - sudden cardiac syndromes (heart attacks, MI)
  - chronic heart failure
Progression of Atherosclerotic CVD

• Long-term disease
• Silent, undetected in early stages
• General progression
  – Narrowing of arteries caused by **plaque** buildup (atherosclerosis)
  – If artery is completely blocked by plaque or a clot, then blood supply to organ stops (ischemia)
    • Plaque rupture may trigger blood clot formation
    • If an artery in the heart is blocked ➔ **Heart Attack**
    • If an artery in the brain is blocked ➔ **Stroke**
  – If artery is partially blocked over a period of many years, then blood supply is diminished ➔ **Heart Failure**
A Schematic History of an Atherosclerotic Lesion (plaque)

Libby, P. In: Braunwald, Zipes, & Libby. *Heart Disease: A Textbook of Cardiovascular Medicine*. 6th Ed. Volume 1 Page 996. Figure 30-1
Progression of CVD

Netter, F.
The CIBA Collection of Medical Illustrations. Volume 5
The Heart. 1978
A Model to Describe Atherosclerotic CVD

Sudden – acute coronary events
Chronic – progressive

Disease Progression

Trigger Heart Attack

Progressing Heart Failure

Age (yrs)
Blocked Coronary Artery

Blockage (Occlusion)

Area of tissue death (infarct)
Ruptured Fibrous Cap
Who Has It?
Prevalence/Cost of CVD

CVD is leading cause of death in the U.S.
~ 1,000,000 deaths per year (911,000 in ’03)

Economic cost (direct and indirect) of CVD in the U.S.
~ $403 billion in 2006 (AHA)

CVD is a major cause of death worldwide
- proportion of deaths expected to increase from 28.9% in 1990 to 36.3% in 2020 (Hanson, 1993)
Prevalence of Cardiovascular Diseases in Americans Age 20 and Older by Age and Sex

NHANES: 1999-2002

Source: CDC/NCHS and NHLBI. These data include coronary heart disease, heart failure, stroke and hypertension.
Age-Adjusted Death Rates for Coronary Heart Disease, Stroke, and Lung and Breast Cancer for White and Black Females
United States: 2003*

Source: CDC/NCHS and NHLBI. * Preliminary
Cardiovascular Disease Mortality Trends for Males and Females
United States: 1979-2003

Source: CDC/NCHS. * Preliminary
Deaths From Diseases of the Heart*
United States: 1900–2003*

Note: Total CVD data are not available for much of the period covered by this chart.

Source: CDC/NCHS. *Preliminary.
Percentage Breakdown of Deaths From Cardiovascular Diseases
United States: 2003*

- **Coronary Heart Disease**: 53%
- **Stroke**: 17%
- **Heart Failure**: 13%
- **High Blood Pressure**: 6%
- **Diseases of the Arteries**: 6%
- **Congenital Cardiovascular Defects**: 6%
- **Rheumatic Fever/Rheumatic Heart Disease**: 1%
- **Other**: 0%

Source: CDC/NCHS and NHLBI. *Preliminary
What Can We Do About It?
Decreasing Risk Factors

Atherosclerosis often progresses without any symptoms, so how do we predict who is at risk of a heart attack?

Risk factor – a characteristic that is present early in life and is associated with an increased risk of developing future disease.
# Risk Factors for Developing CVD

<table>
<thead>
<tr>
<th>Non-Modifiable</th>
<th>Modifiable Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Age</td>
<td>• Smoking</td>
</tr>
<tr>
<td>• Sex</td>
<td>• Obesity</td>
</tr>
<tr>
<td>• Race</td>
<td>• High Blood Pressure</td>
</tr>
<tr>
<td>• Family History</td>
<td>• High Cholesterol</td>
</tr>
<tr>
<td></td>
<td>• Type II Diabetes (impaired glucose tolerance)</td>
</tr>
<tr>
<td></td>
<td>• Inactivity</td>
</tr>
</tbody>
</table>
Risk Factors for Developing CVD

Non-Modifiable
• Age
• Sex
• Race
• Family History

Modifiable Risk Factors
• Smoking
• Obesity
• High Blood Pressure
• High Cholesterol
• Type II Diabetes (impaired glucose tolerance)
• Inactivity

Metabolic Syndrome
Smoking Cessation (cont)
Association Between BMI and CVD

BMI = Wt/Ht^2

Example

Wt = 220 lbs or 100 kg
Ht – 5’10” or 177 cm or 1.77 m

BMI = 100/(1.77^2)

= 31.9

Gaziano, Manson & Ridker. In: Braunwald, Zipes, & Libby. Heart Disease: A Textbook of Cardiovascular Medicine. 6th Ed. Volume 1 Page 1045 Figure 32-4
Relative Risk of CVD versus BP and Percent Population at Given BP
Trends in Age-Adjusted Prevalence of Health Conditions, U.S. Adults Ages 20-74
NHANES: 1971-74 to 1999-2000

Trends in Cardiovascular Risk Factors in the U.S. Population Aged 20-74


Risk of CHD - Diabetes

Physical Activity & CV Risk

The graph illustrates the relationship between cardiovascular mortality, relative risk, and level of fitness or activity. Various studies, such as Paffenbarger et al. (1986), Morris et al. (1990), Blair et al. (1992), Leon et al. (1993), Ekelund et al. (1994), and Sandvik et al. (1995), are shown with distinct symbols. The x-axis represents the level of fitness or activity, while the y-axis shows the relative risk. As the level of fitness or activity increases, the relative risk decreases, indicating a lower cardiovascular mortality.
Multiple Risk Factors versus Risk of Sudden Death

Variables: Age, systolic blood pressure
ECG abnormality: LVH, I-V block, non-spec abn
Serum cholesterol
Vital capacity
Cigarettes per day
Relative weight
Heart rate

Men
Women

What Can We Do About Risk Factors…and Disease Progression?

Strategies for Modifying Risk Factors

A. Increased Physical Activity/Exercise
B. Improved Diet/Nutrition
# Strategies for Reducing CV Risk

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Risk Factor Influenced</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exercise Moderately</strong></td>
<td>Decreased Blood Pressure&lt;br&gt;Improved Lipid (Chol) Profile&lt;br&gt;Decreased Body Weight&lt;br&gt;Improved Glucose Tolerance</td>
</tr>
<tr>
<td><strong>Eat a Balanced Diet</strong></td>
<td>Improved Lipid (Chol) Profile&lt;br&gt;Decreased Body Weight&lt;br&gt;Improved Glucose Tolerance&lt;br&gt;May Decrease Blood Pressure</td>
</tr>
<tr>
<td><strong>Don’t Smoke</strong></td>
<td>Smoking</td>
</tr>
</tbody>
</table>
Heat Stress and Cardiovascular Strain
Firefighting Fatalities

• The leading nature of line of duty deaths (LODD) is heart attack (43.9%)
• The leading cause of LODD is overexertion/strain (46.6%)
• 800-1,000 non-fatal heart attacks while on duty
• Number of fatal and non-fatal heart attacks among off duty FF is not known
LODD by Cause

![Graph showing LODD by Cause with lines for Burns and Heart Attack over years 1991 to 1999. The graph indicates fluctuations in LODD due to these causes.]
Simplified Schematic of Possible Causes of Heart Attack in FF

- Perfuse sweating
- Increased Body Temperature
- Activation of SNS
  - Decreased Plasma volume → Circulatory Shock
  - Altered Electrolytes → Arrhythmias
  - Increased viscosity → Clot Formation
  - Changes in HR and BP → Plaque Disruption

Heart Attack
Models of Lessening CV Fatalities in the Fire Service

Disease progression

Trigger
Heart attack

0 20....

Years

0 20....

Years
Models of Lessening CV Fatalities in the Fire Service
Theoretical Background
(need for research)

“Probably the greatest stress ever imposed on the human cardiovascular system is the combination of exercise and hyperthermia. Together these stresses can present life-threatening challenges, especially in highly motivated athletes who drive themselves to extremes in hot environments.”

Changes During FF

- Drills
- Drills
- Drills

Rehab
Rc1
Rc2

~ 8 min
~ 8 min
~ 8 min

= measurement period

Stress of Firefighting
Firefighting Tasks

- Dummy drag
- Carry and discharge extinguisher
- Hose pull
- Wood chopping
Physiological/Psychological Stress

**Stroke Volume Response**

# $p < .05$ vs T1
Physiological/Psychological Stress

Changes in Core Temperature

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Trial 1</th>
<th>Trial 2</th>
<th>Trial 3</th>
<th>10 min rec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trectal</td>
<td>36</td>
<td>36.5</td>
<td>37</td>
<td>37.5</td>
<td>39</td>
</tr>
</tbody>
</table>

Legend:
- Trectal
Changes after 90 min Recovery

Physiological/Psychological Stress

Pre

Post

Post 90min

Rehab

Recovery

drills

drills

drills

~6 min

~6 min

~6 min

90 min

= blood draw
Physiological/Psychological Stress

Effects of Simulated Fire-Fighting Stress on Plasma Volume Shifts

-16 -14 -12 -10 -8 -6 -4 -2 0 2 4
Change in Plasma Volume (%)

Pre                          Post                     Post 90'

\( a \) significantly (\( p < .05 \)) different pre and post 90’
Physiological/Psychological Stress

Effects of Simulated Fire-Fighting Stress on Sodium

```
<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Post</th>
<th>Post 90'</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value (mmol/L)</td>
<td>136</td>
<td>140</td>
<td>138</td>
</tr>
</tbody>
</table>
```

\(^a\) significantly (p < .05) different pre and post90
Effects of Simulated Fire-Fighting Stress on Glucose

Physiological/Psychological Stress

$^a$ significantly ($p < .05$) different pre and post 90
$^c$ significantly ($p < .05$) different pre and post 90’
Physiological/Psychological Stress

Changes in Cortisol

- Pre
- Post
- Recovery
Physiological/Psychological Stress

Effects of Simulated Fire-Fighting Stress on Leukocyte Numbers

<table>
<thead>
<tr>
<th>Variable (x10⁹/L)</th>
<th>Pre</th>
<th>Post</th>
<th>Post 90’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Leukocytes</td>
<td>4.94 ± 0.3</td>
<td>9.15 ± 0.7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8.12 ± 0.6&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>2.74 ± 0.2</td>
<td>4.22 ± 0.3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6.27 ± 0.5&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>1.67 ± 0.2</td>
<td>4.03 ± 0.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.25 ± 0.1&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Monocytes</td>
<td>0.29 ± 0.04</td>
<td>0.68 ± 0.2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.44 ± 0.1&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0.15 ± 0.02</td>
<td>0.16 ± 0.02</td>
<td>0.06 ± 0.01&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Basophils</td>
<td>0.09 ± 0.1</td>
<td>0.07 ± 0.01&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.04 ± 0.01</td>
</tr>
</tbody>
</table>

<sup>a</sup> significantly (p< .05) different from pre,  
<sup>b</sup> significantly (p< .05) different from pre and post  
<sup>c</sup> significantly (p< .05) different from pre and post 90’
**Effect of Firefighting on Coagulation Factors (N=10; Mean ± SD)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelets (x10³/uL)</td>
<td>236.6 (48.2)</td>
<td>290.37 (83.4)*</td>
</tr>
<tr>
<td>Prothrombin Time (s)</td>
<td>10.18 (0.6)</td>
<td>10.13 (0.6)</td>
</tr>
<tr>
<td>Activated Partial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombopastin Time (s)</td>
<td>25.2 (2.3)</td>
<td>25.5 (2.7)</td>
</tr>
<tr>
<td>Fibrinogen (mg/dL)</td>
<td>254.5 (17.2)</td>
<td>243.9 (20.8)†</td>
</tr>
<tr>
<td>Antithrombin III (%)</td>
<td>109.7 (4.9)</td>
<td>116.8 (6.9) *</td>
</tr>
</tbody>
</table>

* p<0.001
† p < 0.05
Physiological/Psychological Stress

Changes during Serial Days of Firefighting

<table>
<thead>
<tr>
<th>Day</th>
<th>Body Weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>200</td>
</tr>
<tr>
<td>Day 2</td>
<td>202</td>
</tr>
<tr>
<td>Day 3</td>
<td>204</td>
</tr>
<tr>
<td>Day 4</td>
<td>202</td>
</tr>
</tbody>
</table>

Body Weight Am vs Body Weight Pm
Physiological/Psychological Stress

Plasma Volume Change (%)

Day 1
Day 2
Day 3
Day 4
Plasma Volume Am
Plasma Volume Pm
Physiological/Psychological Stress

![Graph showing fibrinogen levels over days]

- **Fibrinogen (mg/dL)**
  - **Day 1**
  - **Day 2**
  - **Day 3**
  - **Day 4**

**Fibrinogen Am** and **Fibrinogen Pm** are compared across the days.
Acknowledgements

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• United States Fire Administration


