**CHD – Makers and Markers**

**The Makers – Risk Factors**
- Non Modifiable – The tough six
- Modifiable – The conventional six
- Modifiable – The contributing six

**The Markers – Surrogate tests**
- We rarely care – The simple six
- We barely know – The complex six
- We hardly use – The experimental six

---

**CHD Risk Factors - Makers**

- If non modifiable – why study them ?
- Non Modifiable – The Tough Six
  - Age
  - Gender
  - Ethnicity
  - Family H/o of premature CHD
  - Phenotype B
  - Type A personality (partly modifiable)

---

**CHD Risk Factors - Makers**

- If modifiable – why not control them ?
- Modifiable – The Conventional Six
  - Diabetes Mellitus (and Prediabetes)
  - Metabolic Syndrome (IR+BB)
  - Dyslipidemia (HDL, N-HDL, LDL, TG)
  - Hypertension (Systolic & Diastolic)
  - Smoking / tobacco
  - Sedentary life, Physical Inactivity

---

**CHD Risk Factors - Makers**

- Modifiable – The contributing six
  - hs-CRP
  - Lp(a)
  - sLDL
  - Endothelial dysfunction
  - Apo B / Apo A1 ratio
  - Homocysteine (? Cause ? Effect)

---

**CHD Risk Factors - Markers**

- We rarely care to use or do – The simple six
  - WC – Waist Circumference – Are we tailors?
  - ED – Erectile Dysfunction; ED = ED
  - ABI – Ankle Brachial Index, IC, PP, Pedal pulse
  - TMT – Simple, Available, Highly useful
  - MAU – Micro Albuminuria – Dip stick (ACR)
  - LVH – By Echocardiography, ECG, CXR, Clinical

---

**CHD Risk Factors - Markers**

- We barely know & test – The complex six
  - ABPM – Dippers & Non Dippers
  - FMD – Brachial Flow Mediated Dilatation
  - PCOS – Polycystic Ovarian Syndrome - NAFLD
  - CIMT – Carotid Intima Media Thickness
  - FFAG – Florescence Fundus Angiography
  - STS – Stress Thallium Scan – for perfusion study
**CHD Risk Factors - Markers**

- We hardly test – The experimental six
  - C Peptide – Measure of Insulin Resistance
  - Uric Acid, hs-CRP – Surrogate for Inflammation
  - Fibrinogen – Surrogate for coagulability
  - PAI 1 – Plasminogen Activator Inhibitor 1
  - Inflam. markers – sICAM, ICAM, SAA, IL-6, MMP
  - Sub fractions – of LDL and HDL, IVUS

**How to be wise in HT?**

It is wrong
To consider Hypertension as an isolated disease

The Truth is
Hypertension, DM, Dyslipidemia, Obesity often coexist
They are the 4 pallbearers to the grave of CHD, CVD
For all of them
Primary and secondary prevention by TLC is the answer
Afflicted with one, must be screened for all other thieves

**Lipid Peroxidation**

- LDL, sLDL
  - Not normally taken up by the vessel wall
- ROS – Free radicals and Pro-oxidants
  - Freely enters the vessel wall

**What is MOST essential ??**

- Not that ‘my drug is superior to yours’
- Not that ‘this trial is better than that’
- Nor ‘this combination is better than that’
- But to get As Many People as we can to goal SBP < 140 & DBP < 90
- And prevent or halt TOD especially CAD
- Of course, tailor the treatment as per individual patient’s co-morbidities.

**What is the correct approach ?**

1. Are all patients screened for hypertension?
2. Are all hypertensives correctly identified?
3. Are they evaluated for co-morbidities/TOD?
4. Are they assessed for CHD risk factors?
5. Are the correct drug combinations prescribed?
6. What is the compliance for medicines & f/u?
7. Is the goal B.P. achieved and maintained?
8. Are there any complications/ side effects?
Macrophages and Foam Cells Express Growth Factors

HDL Promotes Cholesterol Molecule Expression

LDL
Monocyte
Adhesion Molecules
Cytokines
Cell Proliferation
Matrix Degradation
Growth Factors
Metalloproteinases
Fibrinolysis
Lipolysis

HDL and Reverse Cholesterol Transport

Bile
A-I
LCAT
A-I
SR-BI
CE
CE
Liver
Mature HDL
Nascent HDL
ABC1
Macrophage

CHD Risk Reduction — Statin Therapy

End points
Major coronary events
Coronary deaths
Cardiovascular deaths
Non CV events
Total mortality
Strokes
Intermittent claudication
Angina

Relative Risk Reduction (%)
+20 0
5 10 15 20 25 30 35 40 45 50

Time course of Statin effects

LDL-C lowered
Inflammation reduced
Vulnerable plaques stabilized & regressed
Endothelial function restored
Ischemic episodes reduced
Cardiac events reduced*

Endothelial Regulatory Functions

Vasodilation
NO, PGI₂, EDHF, BK, CNP
Thrombolysis
tPA, Protein C, TF-I, vonvWF
Platelet Disaggregation
NO, PGI₂, TGF-β, Hep
Antiproliferation
NO, PGI₂, TF, PGE₂

Vasoconstriction
ROS, ET-1, TXA₂, A-II, PGH₂
Thrombosis
PAI-1, TF, TXA₂
Adhesion Molecules
CAMs, Selectins
Growth Factors
ET-1, A-II, PDGF, TGF-β, Interleukins
Inflammation
ROS, NF-κB

Pathophysiology Vascular Disease

Risk Factors
Dyslipidemia, HT, Heredity, Smoking, Diabetes
Oxidative Stress
Xanthine Oxidase, NADH/NADPH, uncoupled eNOS
Endothelial Factors
NF-κB, Chemokines, GFs, sCAM, ICAM, ACE/AGT II
Function Alterations
↑ NO, ↓ VD, ↑ VC, Inflammation, Procoagulant state
Structural Alterations
↑ Tone, SmCP, Inflam. Cells, Plaque, Neg Remodel
↓ Fibrinolysis, ↓ Platelet aggregation, ↓ Inflammation
Clinical Sequelae
Ischemia, MI, CHF, Stroke, MACE, Death

Pepeine CJ, Am J Cardiol. 2001; 88 Supplement
Surrogate Markers of CVD

<table>
<thead>
<tr>
<th>Availability</th>
<th>Standardized Dx.</th>
<th>Accuracy</th>
<th>Severity</th>
<th>Rx. Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Micro Albuminuria</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Ankle Brachial Index</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Endothelial Damage</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Arterial Stiffness</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Serum Amyloid (SAP)</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

The Myths and Facts

<table>
<thead>
<tr>
<th>Myths</th>
<th>Facts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Of Men are more likely to have CAD</td>
<td>Heart disease is the #1 killer of men and women; 50,000 more women than men die of heart disease every year</td>
</tr>
<tr>
<td>Cancer is a bigger threat than CAD</td>
<td>Nearly twice as many women die from heart disease and stroke than from all cancers combined</td>
</tr>
<tr>
<td>Doctors are aware of women's risk for CAD and act</td>
<td>Under treatment and under diagnosis of heart disease in women contributes to excess mortality in women</td>
</tr>
</tbody>
</table>

Gender Differences in Presentation

Typical in both sexes
- Pain, pressure, squeezing, or stabbing pain in the chest
- Pain radiating to neck, shoulder, back, arm, or jaw
- Pounding heart, change in rhythm
- Difficulty breathing
- Heartburn, nausea, vomiting, abdominal pain
- Cold sweats or clammy skin
- Dizziness

Typical in women
- Milder symptoms (without chest pain)
- Sudden onset of weakness, shortness of breath, fatigue, body aches, or overall feeling of illness (without chest pain)
- Unusual feeling or mild discomfort in the back, chest, arm, neck, or jaw (without chest pain)

Women and CAD Risk Factors

- Higher prevalence of avoidable risk factors
  - ↑ blood cholesterol, ↑ TG
  - ↑ physical inactivity
  - ↑ overweight (body mass index, 25.0-29.9)
- Diabetes is a more powerful risk factor for CAD
  - 3- to 7-fold in women v/s 2- to 3-fold in men
- HDLc levels more predictive of CAD
- Women counseled less about nutrition, exercise, and weight control

Women CAD - Summary

- Presentation and Symptomatology
- Cardiac risk factors – differences
- Metabolic syndrome, Obesity – IR – T2DM
- Dyslipidemia patterns
- TMT – lower value
- Stress Echo, MPI, Sistemibi, Dobutamine
- CABG, PTCA risks, long term
- Above all need for greater clinical suspicion
- Drug Rx is not an antidote to an unhealthy lifestyle

Risk Factors for Future Cardiovascular Events

Lipoprotein(a)
Homocysteine
IL-6
TC
LDL-C
sICAM-1
SAA
Apo B
TC:HDL-C
hs-CRP
hs-CRP + TC:HDL-C