Metabolic Syndrome

- Definition: A constellation of metabolic risk factors that places a person at higher risk for cardiovascular disease
- Closely associated with Insulin Resistance – impaired tissue response to insulin
- Determined by:
  - Genetic factors
  - Metabolic factors: excess weight
  - Environmental factors: physical inactivity
**Metabolic Syndrome**

**Diagnosis**

Need at least 3 Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Criteria</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>Above 130/85 mm/Hg</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>150 mg/dL and above</td>
<td>Atherogenic dyslipidemia</td>
</tr>
<tr>
<td>Low HDL-C</td>
<td>Men – &lt; 40 mg/dL Women – &lt; 50 mg/dL</td>
<td>Atherogenic dyslipidemia</td>
</tr>
<tr>
<td>Glucose Levels</td>
<td>Above 100 mg/dL (fasting)</td>
<td>Impaired fasting glucose</td>
</tr>
<tr>
<td>Waist Circumference</td>
<td>Men – 40 inches plus Women – 35 inches plus</td>
<td>Central obesity</td>
</tr>
</tbody>
</table>

**Population at Risk for Insulin Resistance & Metabolic Syndrome**

- Obesity (central especially)
- Sedentary lifestyle
- Low birth weight
- Genetic predisposition
- Race/ethnicity
- Gestational DM
- Polycystic ovarian syndrome
- Hypertension
- TG > 250 and/or HDL < 40mg/dl

**Metabolic Syndrome Comorbidities**

- Sleep Apnea
- Ischemic Stroke
- Atrial Fibrillation
- Non-alcoholic Fatty Liver Disease
- Reproductive Abnormalities (PCOS)
- Musculoskeletal Disorders
- Cholelithiasis
- Gout

Metabolic Syndrome Risk

- Increased risk of Cardiovascular disease (CVD)*
- Increased risk of Type 2 Diabetes Mellitus


Metabolic Syndrome Impact on CVD

2.3 fold increase
Relative Risk on CV Health and Mortality

*Isomae et al. DM Care. 2001;24:683-690
(N=3606, ages 35-70, 6.9 yrs)
Effects of Increasing Total Cholesterol Levels in the Presence of Other Risk Factors

Schaefer EJ. Adapted from the Framingham Heart Study.

Insulin Resistance

- Defect in the ability of insulin to mediate glucose uptake (or disposal) by the muscle cells
- Beneficial compensatory mechanism in states of starvation in preventing hypoglycemia
- Disadvantage with states of overnutrition

Glucose & Insulin

- **Stimulus:** Increase in Blood Glucose
- **Pancreas**
  - Insulin Release
- **Decrease in** blood glucose
- **Insulin** stimulates glucose transport
- **Body Cells**
  - Glucose transport into cells
Inhibits glucose uptake
Skin
Premature aging
Fat Cells
Increased accumulation of fat cells
Expanded fat cells secrete cytokines (increases inflammation)

Arteries
Liver
Kidneys
Muscles
Inhibits glucose uptake
Skin
Premature aging
Fat Cells
Increased accumulation of fat cells
Expanded fat cells secrete cytokines (increases inflammation)

Hypertension
Systemic Inflammation

Visceral Obesity
Altered Vascular Reactivity
Diabetes Type II
Dyslipidemia
• High Triglycerides
• Low HDL
• Small Dense LDL

1st line = Therapeutic Lifestyle Changes
• Diet
• Physical Activity
• Weight Loss

2nd line
• Treat independent risk factors
• Pharmacological therapy
• Modify atherogenic dyslipidemia, hypertension & prothrombic state to reduce CHD risk
• Goal: Reduce the risk of CHD events and prevent or delay the onset of Type 2 DM
“Health behavior interventions in people identified at high cardio-metabolic risk are of critical importance given the emerging crisis of obesity and the consequent epidemic of type 2 diabetes”

Therapeutic Lifestyle Changes

Dietary Strategies

- Focus on a diet that can
  - Minimize post-prandial glucose
  - Minimize Triglyceride spikes
  - Sustain appetites
  - Reduce caloric intake
  - Restrict alcohol
  - Increase antioxidants and potassium
  - Increase MUFAs & PUFAs
  - Increase Omega 3 oils
Beneficial foods for Metabolic syndrome

- Antioxidants
  - Reduce oxidative stress

- MUFAs & PUFAs
  - Improve HTN, insulin Resistance and Hypertriglyceridemia

- Nuts
  - Improve lipid levels
  - Reduced risk of CHD and Diabetes
  - High in MUFA and PUFA
  - Rich in fiber, vitamins and minerals

- Olive oil
  - An excellent source of MUFA
  - High oleic acid content
  - Phenolic compounds
  - Antioxidant
  - Anti-inflammatory
  - Anti-thrombotic
  - Improve endothelial function
  - Prevent lipo-peroxidation
  - Change lipids favorably

Diet to Consider

- Mediterranean
- Dietary Approaches to Stop Hypertension (DASH)
- Carbohydrate restricted diet (Atkins)

The Mediterranean Diet

- Composition:
  - 45% carbohydrates
  - 35-40% fat (<10% saturated fat)
  - 15-20% protein
  - High in MUFAs and PUFAs & whole grains
  - Rich in fruits, vegetables, legumes, and fish
  - Low in red meats, processed meat, refined carbohydrates and whole fat dairy products
**Mediterranean Diet Effects**

- Improves
  - Lipid profile: HDL and oxidized LDL
  - Liver function tests
  - Endothelial function
  - Insulin resistance & sensitivity
- Reduces
  - Homocysteine concentrations
  - Body fat
  - Inflammation
  - Thrombotic risk (fibrinogen)

**The Mediterranean Diet, Endothelial Dysfunction & Inflammation**

- 180 Metabolic Syndrome subjects, 2 years
- Treatment group: Mediterranean diet
- Exercise increased 60% in both groups
- Treatment group achieved
  - Weight loss: 4.5 kg
  - Reduced hsCRP, Interleukin 6, 7 & 18
  - Reduced insulin resistance
  - Improved endothelial function
- 2 year f/u: Metabolic Syndrome incidence
  - Treatment group – 30 patients (reduced MS by 50%)
  - Control group – 73 patients


**PREDIMED: Prevention of Diabetes Mediterranean Diet Study**

- Pre-diabetic subjects: 1224
- 1 year duration
- Treatment group: Mediterranean diet
  - High in nuts and olive oil
- Outcomes:
  - Reduced waist circumference
  - Reduced incidence of Type 2 Diabetes
  - Metabolic syndrome prevalence was reduced by 14%

**ATTICA Trial**

- Greek subjects
- Adherence to the Mediterranean diet
- Reduced Metabolic syndrome incidence 20% (irrespective of age, sex, physical activity, lipids and blood pressure levels)
- Reduced all cause mortality rate
- Reduced concentrations of oxidized LDLs


**Dietary Approach to Stop Hypertension Diet: DASH**

- Macronutrients
- Low sodium
  - Caveat: Metabolic Syndrome is associated with high sensitivity to sodium
- Rich in fruits and vegetables
- High fiber
- Low fat dairy
- High in potassium & magnesium

**Dash Diet and the PREMIER Group**

- Subjects
- Elevated blood pressure
- 6 month duration
- Treatment group
- Outcomes
  - Weight lost
  - Improved blood pressure
  - Improved LDL
  - Improved endothelial function
  - Did not improve triglycerides or HDL

### Alternate Diet for Management of Metabolic Syndrome

- Carbohydrate Restriction Improves
- Excess weight
- Impaired glucose levels
- Hyper-insulinemia
- HDL deficiency
- Small dense LDLs
- Hypertriglyceridemia
- Elevated blood pressure

### Atkins Diet

- Restricted carbohydrate diet
- Week 1 & 2: 20 gm carbohydrates daily
  - 12-15 gm of the carbs must include non-starchy vegetables
- Then increase in 5 gm increments as long as achieving weight loss
- Unlimited fat and protein within reason
- Omega 3 and Multivitamin supplement

### Restrict Carbohydrates or Not?

- 40 subjects with atherogenic dyslipidemia
- 3 months duration
- Subjects were placed on 1 of 2 Diets (amount of carbs/fat/protein)
  - Carbohydrate restricted: 12/59/28%
  - Low fat diet: 56/24/20%
- Measured: Lipids, glucose, insulin levels, adiposity and insulin resistance
**Results from Low Carbohydrate Diet**

<table>
<thead>
<tr>
<th>Factors Measured</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>12%</td>
</tr>
<tr>
<td>Insulin</td>
<td>50%</td>
</tr>
<tr>
<td>2hr GTT</td>
<td>47%</td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>55%</td>
</tr>
<tr>
<td>Weight &amp; Adiposity</td>
<td>10%</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>14%</td>
</tr>
<tr>
<td>HDL</td>
<td>13%</td>
</tr>
<tr>
<td>Total Chol/HDL ratio</td>
<td>14%</td>
</tr>
<tr>
<td>ApoB/ApoA-1 ratio</td>
<td>16%</td>
</tr>
<tr>
<td>Retinol binding protein 4</td>
<td>20%</td>
</tr>
</tbody>
</table>


**A to Z Weight Loss Trial**

Premenopausal women were randomized to 1 of 4 diets for weight loss. Results are as follows:

<table>
<thead>
<tr>
<th>Group</th>
<th>Weight</th>
<th>LDL</th>
<th>Trigs</th>
<th>HDL</th>
<th>BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atkins</td>
<td>-9.9</td>
<td>+0.8</td>
<td>-29.3</td>
<td>+4.9</td>
<td>-4.4</td>
</tr>
<tr>
<td>Traditional</td>
<td>-5.5</td>
<td>+0.6</td>
<td>-14.6</td>
<td>-2.8</td>
<td>-2.2</td>
</tr>
<tr>
<td>Ornish</td>
<td>-3.3</td>
<td>-3.8</td>
<td>-14.9</td>
<td>0</td>
<td>-0.7</td>
</tr>
<tr>
<td>Zone</td>
<td>-3.3</td>
<td>0</td>
<td>-4.2</td>
<td>+2.2</td>
<td>-2.1</td>
</tr>
</tbody>
</table>


**Restricted Carbohydrate Diet Studies**

<table>
<thead>
<tr>
<th>Clinical Trial</th>
<th>Subjects</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nielsen &amp; Jensen (2008)</td>
<td>Type 2 DM</td>
<td>Reduced body weight</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Improved glycemic control</td>
</tr>
<tr>
<td>Boden, G et al (2005)</td>
<td>Obesity</td>
<td>Reduced fasting glucose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reduced insulin resistance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reduced appetite</td>
</tr>
<tr>
<td>Feinman, RD et al (2008)</td>
<td>Type 2 DM Mat Syndrome</td>
<td>Improved glycemic control*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Improved BP</td>
</tr>
<tr>
<td>Forsythe, et al(2008)</td>
<td>Type 2 DM</td>
<td>Reduced inflammation</td>
</tr>
</tbody>
</table>

* Subjects reduced insulin by up to 280 units in 3 weeks or eliminated their insulin
“As a society, the US spends billions on chronic disease treatments and interventions for risk factors. Although these are useful and important, a fraction of the investment to promote healthful lifestyles for primary prevention would yield greater benefit.

Eric Rimm, SCD
Meir J. Stapfer MD, DrPH

Exercise

- 2008 Federal guidelines for weekly exercise
- 150 minutes of moderate intensity cardio exercise
- 75 minutes of vigorous intense exercise
- Or a combination of the 2
- 2 days of strength training
- More successful when combined with dietary changes


Exercise Reduces Risk of Metabolic Syndrome

- Increases muscle insulin sensitivity
- Increases glucose transport
- Increases insulin sensitivity & uptake in adipose tissue
- Clears both free fatty acids and glucose
- Increases Nitric oxide providing an antioxidant protective effect and improved endothelial function
- Reduces body fat
Exercise

- “It is better to be fat and fit than to be thin and unfit”
- Increased physical activity considerably attenuates CVD risk associated with obesity
- Achieving weight loss and regular physical activity improves quality of life and reduces health care costs

Exercise & Metabolic Syndrome

- The association between physical activity and Metabolic Syndrome in rural Australians
- 1563 subjects, ages 25-74
- 1/5 inactive, 1/3 with Metabolic Syndrome
- Inactive men = 2 times more likely to develop Metabolic Syndrome
- Inactive women = 3 times as likely


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<table>
<thead>
<tr>
<th>Subjects</th>
<th>F/U</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ford, et al. 1991</td>
<td>492 diabetics</td>
<td>2 yrs</td>
</tr>
<tr>
<td>Kohl et al. 1992</td>
<td>8715 men</td>
<td>8.2 yrs</td>
</tr>
<tr>
<td>Makino Prevention Trial 1998</td>
<td>288 subjects with IGT*</td>
<td>10 yrs</td>
</tr>
<tr>
<td>Weis et al. 1999</td>
<td>200 subjects with IGT*</td>
<td>6 yrs</td>
</tr>
<tr>
<td>Wei et al. 2000</td>
<td>1263 diabetic men</td>
<td>12 yrs</td>
</tr>
<tr>
<td>Hu et al. 2001</td>
<td>5125 diabetic women</td>
<td>14 yrs</td>
</tr>
<tr>
<td>2001 Finnish DM Prevention Study</td>
<td>322 subjects</td>
<td>3.2 yrs</td>
</tr>
<tr>
<td>DM Prevention Program 2002</td>
<td>334 obese subjects</td>
<td>2.8 yrs</td>
</tr>
<tr>
<td>Panagotakos et al. 2004</td>
<td>2262 subjects CS+</td>
<td>Reduced odds of Metabolic Syndrome with any type of exercise</td>
</tr>
</tbody>
</table>
**Exercise & Landmark Diabetes Trials**

<table>
<thead>
<tr>
<th>Clinical Trial</th>
<th>Characteristics</th>
<th>Treatment</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Da Qing Study</td>
<td>577 Chinese IGT 45 y/o Exercise: 150-240 mins/week</td>
<td>3 Groups Diet Exercise Diet &amp; exercise</td>
<td>Reduced T2 DM by 31% 46% 42%</td>
</tr>
<tr>
<td>Finnish DM Prevention Study</td>
<td>522 Fins IGT 55 y/o</td>
<td>Reduced saturated fat &amp; high fiber diet Exercise: 210 mins/wk</td>
<td>3.5 kg weight loss Reduced DM incidence by 58%</td>
</tr>
<tr>
<td>DM Prevention Program</td>
<td>3,344 US subjects Different ethnicities IGT</td>
<td>3 Groups Placebo Metformin 850mg TID TLC: Diet &amp; exercise 150 mins/wk</td>
<td>TLC Group Reduced T2DM 58% 30% reverted to normal glucose tolerance HTN Risk reduction 33%</td>
</tr>
</tbody>
</table>


**Does Frequency & Length of Exercise Matter?**

- Acute vs Chronic exercise
- Chronic exercisers
  - Maintain lower weights
  - Train with greater intensity
  - Longer exercise periods
  - May achieve a 15-30%
  - Triglyceride reduction
- Intermittent vs Continuous exercise
  - Example:
  - 90 minutes vs 3 intervals of 30 minutes each
  - Both achieve the same reduction in Triglycerides

**Clinical Pedometry**

- Each step represents a muscle contraction that sensitizes insulin (like Glucophage)
- US Public Health recommendations for general health:
  - Walk a minimum of 3000 steps in 30 minutes 5 days weekly (3 mph pace for adults 5'7" to 6'0")
  - May separate this time into 3 ten minute sessions
- Weight loss recommendations:
  - > 11,000 steps/day for men
  - > 9,000 steps/day

Tudor-Locke 2008
**Pedometer Instructions**

1. Obtain a reliable pedometer
   - New Lifestyles, Accusplit, Omron
   - Validated to measure accurately with filters intact
2. Clip pedometer to tightly to waistband over mid-line of one leg or in-line over one foot
3. Measure daily steps for 5-7 days and average
4. Add steps based on state of fitness
   1. Add 1000-1500 steps if have a low fitness level
   2. Add 2000-3000 steps for higher fitness level
5. Every 2-4 weeks repeat step 4 building to a goal of ≥10,000 steps most days of the week
6. Goal for weight loss: 70-90,000 steps weekly
   (12,000 steps have resulted in significant weight loss)

**Resistance Training Benefits**

- Average person loses 5-7 lbs of lean muscle mass every decade after age 50
- Results in a declining basal metabolic rate (BMR)
- Moderate strength training 2-3 days weekly for at least 30-45 minutes is recommended
  - Rebuild 3 lbs muscle mass in 10 weeks
  - Increase BMR 7%
  - Reduce body fat by 4.6%
  - Increases daily energy and caloric requirements 15%

Peeke, P. “Fit for Life” www.DrPeeke.com
**Resistance Training**

A meta-analysis of the effect of resistance training on metabolic clustering in patients with abnormal glucose metabolism.

- 13 randomized controlled trials (1990-2007)
- All subjects had abnormal glucose levels
- Results: Resistance training (RT) reduced:
  - HbA1c by 0.48%
  - Fat mass by 2.33 kg
  - Systolic BP by 6.19 mm/Hg
- Recommendations: Use RT for the management of type 2 diabetes and metabolic disorders


**Exercise Recommendations**

- **Cardio exercise**
  - 30-60 minutes 5 days weekly
- **Cardio for weight loss**
  - 45-60 minutes 5 days weekly
- **Strength training**: 2-3 days weekly
  - Light weight lifting with high repetitions
  - Resistance exercises
  - Yoga & Pilates


“There is a growing consensus that a multi-disciplinary approach is needed to adequately address cardio-metabolic risk factors”
### Comprehensive Treatment for Metabolic Syndrome

- Identify those patients at risk
- Assess diet and physical activity routines
- Have a plan in place to address risk factors as a whole
- Initiate care through a multidisciplinary team
  - Physician, NPs, PAs, Nurses
  - Dietician/nutritionist
  - Exercise physiologist
  - Stress management
- Utilize the services in your community