Metabolic Syndrome: A window of opportunity

Presented by:
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Metabolic Syndrome (MetS): IDF definition

- Central Obesity: defined as waist circumference
  - Plus 2 other factors
    - Raised TG
    - Reduced HDL
    - Raised BP
    - Raised fasting glucose
Metabolic Syndrome

- Cluster of well-defined metabolic factors
- Frequently precedes the onset of Type 2 diabetes (T2DM) and cardiovascular disease
- San Antonio Heart Study concluded that metabolic syndrome predicts T2DM independently of other factors
Diabetes: Where are we heading?

• In the US alone, Boyle et al. predicted in 2001 that the incidence of T2DM would increase by 165%—from 11 million in 2000 to 29 million in 2050
  
  IN ONLY 12 YEARS, NOT 50

• In 2012, 29.1 million Americans had T2DM
What is the cost of T2DM?

• In 2012, T2DM cost the US $245,000,000,000$\textsuperscript{4}
  – $176$ billion in direct medical costs
  – $69$ billion in reduced productivity
Direct Medical Costs of T2DM - $176 billion

- Hospital inpatient
- Anti-diabetic agents/supplies
- Physician visits
- Other
What is the cost?

‘The prediction that diabetes incidence will double by 2025 indicates a parallel rise in cardiovascular-related illness and death, with an inevitable and profound impact on global healthcare systems’

- International Diabetes Federation, 2006¹
Some quick calculations...

$245 \text{ billion} \div 29.1 \text{ million people} = \$8419 \text{ per person per year}

1.7 \text{ million new cases of T2DM per year} \times \$8419 = \$14.3 \text{ billion per year in the US}

Intervention can prevent 60\% \times \$14.3 \text{ billion} = \$8.58 \text{ billion savings}
Prevention Model

- Clinical screening for MetS
- Central obesity defined as waist circumference\(^1\)
  - Waist circumference
  - Blood pressure
  - Random blood glucose
    - Use of capillary blood as screening only\(^7\)
- Easy, predictive of risk and low cost
- Yet rarely done in a clinical setting\(^6\)
- Missing the ‘window of opportunity’
Re-Defining ‘Normal’

- Waist Circumference

<table>
<thead>
<tr>
<th>Sex</th>
<th>At Risk</th>
<th>At HIGH Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>&gt;94cm</td>
<td>&gt;102cm</td>
</tr>
<tr>
<td>Female</td>
<td>&gt;80cm</td>
<td>&gt;88cm</td>
</tr>
</tbody>
</table>
Normal Fasting Blood Glucose and Risk of T2DM

46,578 subjects
4 groups according to fasting glucose (mg/dL):
1. < 85
2. 85-89
3. 90-94
4. 95-99

Monitored for 7 years
Adjusted for age, sex, BMI, BP, lipids, smoking, CVD

For every 1 mg/dL of fasting glucose = 6% increased risk of diabetes
Group 3 90-94 mg/dL were 49% more likely to develop diabetes compared to Group 1
Group 4 95-99 mg/dL were 2.33 times more likely of developing diabetes compared to Group 1

REMEMBER: these are normal fasting glucose results
Clinical Progression

Clinical Screening

Nutritional/Lifestyle interventions

Medical Intervention

Optimal health and wellbeing

Subjective feelings of fatigue and/or poor health

Chronic signs & symptoms

Clinical Pathology & Disease progression

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### Typical Clinical Progression

<table>
<thead>
<tr>
<th>1-5 years</th>
<th>5-10 years</th>
<th>10-20 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>Onset of diabetes</td>
<td>Microvascular; retinopathy, nephropathy, peripheral neuropathies</td>
</tr>
<tr>
<td>Poor wound healing</td>
<td>Increased weight</td>
<td>Poor immune function</td>
</tr>
<tr>
<td>Weight gain, central</td>
<td>Deterioration of joints</td>
<td>Macrovascular</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>Continuation of high blood pressure</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>Metabolic syndrome - undetected</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Prescription

<table>
<thead>
<tr>
<th>1-5 years</th>
<th>5-10 years</th>
<th>10-20 years</th>
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</thead>
<tbody>
<tr>
<td>Statin</td>
<td>Statin</td>
<td>Statin</td>
</tr>
<tr>
<td>Proton pump inhibitor</td>
<td>Proton pump inhibitor</td>
<td>Proton pump inhibitor</td>
</tr>
<tr>
<td>Diuretic</td>
<td>Diuretic</td>
<td>Diuretic</td>
</tr>
<tr>
<td>ACE inhibitor/ARB</td>
<td>ACE inhibitor/ARB</td>
<td>ACE inhibitor/ARB</td>
</tr>
<tr>
<td>Metformin</td>
<td>Metformin</td>
<td>Metformin</td>
</tr>
<tr>
<td>NSAID</td>
<td>NSAID</td>
<td>NSAID</td>
</tr>
</tbody>
</table>

To Medicine
Case Study

- 51 year female presented with osteopenia and poor weight management: 5kg weight gain in 3 years
- Currently restless legs with cramps at night
- 3 yrs prior – onset of peri-menopause
- 4 yrs prior – diagnosed with osteopenia
- 10 yrs prior – R knee injury impacting ability to exercise
Family Medical History

- Mother: Type 2 diabetes mellitus
- Mother and father: obesity
- Father: issues with high ferritin

Current Medications

- Evista (raloxifene hydrochloride) 60mg daily
- Calcium supplement – 1 tablet daily:
  - Calcium 250mg (as citrate and hydroxyapatite)
  - Magnesium 125mg (as oxide)
  - Vitamin D3 100IU
<table>
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<th>Nutritional/Lifestyle interventions</th>
<th>Medical Intervention</th>
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<tr>
<td>Optimal health and wellbeing</td>
<td>Subjective feelings of fatigue and/or poor health</td>
<td>Chronic signs &amp; symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinical Pathology &amp; Disease progression</td>
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</tbody>
</table>
## Standard Point of Care Screening

<table>
<thead>
<tr>
<th>Clinical Outcome</th>
<th>Initial Measurement</th>
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<tbody>
<tr>
<td>Height (cm)</td>
<td>155</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>81.5</td>
</tr>
<tr>
<td>BMI</td>
<td>33.9 (Obese)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>100</td>
</tr>
<tr>
<td>Random Blood Glucose (RBG)</td>
<td>155 mg/dL (8.7 mmol/L) 90 min pp</td>
</tr>
<tr>
<td>Random Total cholesterol (R T chol)</td>
<td>227 mg/dL (5.9 mmol/L)</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>146/95</td>
</tr>
<tr>
<td>Heart rate</td>
<td>65</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>NAD</td>
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**Initial Measurement**

- **Height (cm):** 155
- **Weight (kg):** 81.5
- **BMI:** 33.9 (Obese)
- **Waist circumference (cm):** 100
- **Random Blood Glucose (RBG):** 155 mg/dL (8.7 mmol/L) 90 min pp
- **Random Total cholesterol (R T chol):** 227 mg/dL (5.9 mmol/L)
- **Blood pressure:** 146/95
- **Heart rate:** 65
- **Urinalysis:** NAD
# Pathology Results

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>(US Units)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D</td>
<td>41</td>
<td>(16)</td>
<td>75-250 (30-100)</td>
</tr>
<tr>
<td>Ferritin</td>
<td>152</td>
<td></td>
<td>15-165 (pre-menopausal)</td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>5.7</td>
<td>(220)</td>
<td>&lt;5.5</td>
</tr>
<tr>
<td>LDL Cholesterol</td>
<td>2.8</td>
<td>(108)</td>
<td>&lt;2.5</td>
</tr>
<tr>
<td>TG</td>
<td>1.8</td>
<td>(160)</td>
<td>&lt;1.5 (&lt;150)</td>
</tr>
<tr>
<td>Fasting Glucose</td>
<td>5.7</td>
<td>(102)</td>
<td>3.0-5.4</td>
</tr>
<tr>
<td>ALT</td>
<td>45</td>
<td></td>
<td>&lt;41</td>
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Excluded thyroid and parathyroid disease
# Clinical Progression

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**Clinical Progression**

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Diet & Lifestyle Interventions

• Education on glycaemic index
• Implemented low glycaemic index diet: as described by CSIRO\(^8\) with emphasis on whole foods high in potassium, calcium and magnesium, plus ↓ salt intake
  – Woo et al (2009) found an association between low dietary magnesium and potassium with high sodium in terms of both hypertension and reduced bone density\(^9\)
  – Dietary magnesium intake has been found to be inversely related to the prevalence of metabolic syndrome in middle-aged women\(^10\)
• Get moving! 30 minutes 3 x per week
Diet & Lifestyle Interventions

• Fish oils: 800mg EPA/600mg DHA daily
  – Fish oil supplementation has been found to provide a modest reduction in blood pressure and consistent for lowering TG $^{11, 12}$

• Magnesium diglycinate: 150mg bd
  – Improving intracellular magnesium has been shown to improve insulin sensitivity, hyperglycaemia and vascular tone $^{13, 14}$
Diet & Lifestyle Interventions

• Vitamin D3: 5000IU/day
  – Improved vitamin D status with supplements has been shown to enhance glucose tolerance and insulin sensitivity\(^{15}\) plus beneficial for maintaining bone density

• Increase dietary calcium in conjunction with 500mg supplemented daily to achieve 1300mg/day (RDI)\(^{16}\)

• Cinnamon: 3g dietary consumption daily
Clinical Progression

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Clinical Outcomes

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<tr>
<th>Clinical Outcome</th>
<th>Initial</th>
<th>Post-12 weeks</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>155</td>
<td>155</td>
<td>0</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>81.5</td>
<td>71.9</td>
<td>-9.6</td>
</tr>
<tr>
<td>BMI</td>
<td>33.9 (Obese)</td>
<td>29.9 (Overweight)</td>
<td>-4.0</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>100</td>
<td>91.5</td>
<td>-8.5</td>
</tr>
<tr>
<td>RBG (mmol/L)</td>
<td>8.7 (90min pp)</td>
<td>5.8 (60min pp)</td>
<td>-2.9</td>
</tr>
<tr>
<td>R T Chol (mmol/L)</td>
<td>5.9</td>
<td>5.7</td>
<td>-0.2</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>146/95</td>
<td>125/85</td>
<td>-21/10</td>
</tr>
<tr>
<td>Heart rate</td>
<td>65</td>
<td>70</td>
<td>+5</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>NAD</td>
<td>NAD</td>
<td>N/A</td>
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*Resolution of restless legs and cramps at night and burning sensation in feet
Screening for Metabolic Disorders

- Point of Care screening can be utilised to improve compliance and client motivation\(^1\)
- Restrictions on ‘real world’ monitoring\(^6\)
- Redefining ‘normal’ range
- Don’t wait until it’s too late
Cinnamon

- Traditional use for dyspepsia, gastric complaints and diabetes
- Part used: bark
- Species: there are hundreds of species of Cinnamon. Most commonly used for therapeutic uses are Cinnamomum zeylanicum, Cinnamomum verum and Cinnamomum cassia
Herb in Chemistry

- Primary constituents of cinnamaldehyde; other phenols and terpenes, including eugenol.
- C. cassia seems to be the most favourable species for glucose management\(^{18}\)
- Polyphenols that possess insulin-like activity and have demonstrated a dose-dependent increase in glucose utilization in animal muscle tissue\(^{19}\)
- Varying sources of material and extraction techniques alter the chemical composition of the extracts
**Herb in Focus**

- **Cinnamon**
  - Short-term studies have shown that 3g cinnamon given orally caused a significant reduction in postprandial glucose and insulin response.
  - The effect was observed for 12 hours\(^\text{20}\)
  - No improvements were noticed with 1g given\(^\text{20}\)
  - 3g daily for 8 weeks showed improvements in fasting blood glucose, insulin, glycosylated haemoglobin, total cholesterol, LDL C, Apo lipoprotein 1 and B\(^\text{21}\)
  - Has shown to have hypotensive, anti-inflammatory and antioxidant properties\(^\text{19}\)
Cinnamon

- There have been conflicting reports
- Cochrane Review 2012 concluded that there was insufficient evidence to support the use of cinnamon in diabetes\textsuperscript{22}
- A later meta-analysis showed significant improvements in fasting glucose, total cholesterol, LDL-C and triglycerides. No impact on HbA1c\textsuperscript{23}
- Inconsistencies seem related to species/quality of cinnamon used, population, dose and duration of study.
Herb in

_Gymnema sylvestre_

- Traditional ayurvedic herb
- ‘sugar destroyer’
- Active constituents include triterpene saponins – gymnemic acids, gymnemasaponins and polypeptide, gurmarin
Herb in Focus

• Actions of *Gymnema sylvestre*
  – Blocks sweet reception on tongue
  – Reduction in absorption of glucose
  – Modulation of incretin
  – Increased regeneration of pancreatic beta cells
  – Enhanced cell uptake of glucose
  – Reduction of total cholesterol, LDL-C, TG$^{24}$
Herb in Focus

**Gymnema sylvestre**

- Regeneration of pancreatic islets in diabetic rats\(^{25,26}\)
  - Results showed a dose-dependant normalisation of blood glucose of 20-60 days
  - Both extracts doubled the number of islet beta-cells
- Human open label study\(^{28}\)
  - 500mg daily for 3 mths reduced polyphagia, fatigue, pp glucose and insulin, and beneficial shifts in lipid profiles
- Controlled Human trial given with oral hypoglycemic\(^{29}\)
  - 400mg for 18 mths
  - Additional benefit seen on glucose, Hb1Ac and insulin
Herb in Focus

- Place 3-4 drops onto tongue
- Coat mouth/tongue
- Wait 30 seconds
- Trial oral intake of sugar
- Dramatic, reliable, reversible
References


References

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17. Point of Care testing in General Practice, 2009.
http://www.appn.net.au/Data/Sites/1/SharedFiles/Publications/200901-poctfinalreport27jan09amended5feb09.pdf [accessed 28/05/14]


References


References


Thank you

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