A Dietary Approach to Insulin Resistance and Associated Conditions

Developed in partnership with the National Board of Physician Nutrition Specialists

Faculty

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Disclosures

Dr. Jampolis: Consultant – Prevention Pharmaceuticals; Board of Directors – TerraVia; Stock Shareholder—TerraVia

Learning Objectives

- Discuss the importance of dietary therapy in the prevention and treatment of insulin resistance (IR)
- Explain how specific macronutrients and foods affect IR
- Analyze the latest research on the role of phytonutrients, micronutrients, and the emerging importance of the microbiome in IR
- Discuss specific dietary approaches for diseases associated with IR

Factors Associated with IR

Extrinsic factors
- Diet
- Sedentary
- Obesity
- Toxins
- Medications
  - Immune
  - Psych
  - Statins
  - Thiazides
  - Beta-blockers
  - Anti-retrovirals

Intrinsic factors
- Genetics
- Microbiome
- Sarcopenia
- Aging
- Diseases
  - Pancreas
  - Liver
  - Endocrine
- Ovarian signaling
  - Menarche
  - Pregnancy
  - Menopause
  - PCOS

Does Diet Matter in IR?

VS

PCOS = polycystic ovary syndrome.
Calorie Contribution of Foods in US Diet

<table>
<thead>
<tr>
<th>Food</th>
<th>Calories (cumulative)</th>
</tr>
</thead>
<tbody>
<tr>
<td>French fries</td>
<td>32.4%</td>
</tr>
<tr>
<td>Beer</td>
<td>20.3%</td>
</tr>
<tr>
<td>Cheese</td>
<td>27.6%</td>
</tr>
<tr>
<td>Rolls, buns, muffins, bagels</td>
<td>25%</td>
</tr>
<tr>
<td>Rice</td>
<td>22.4%</td>
</tr>
<tr>
<td>Chips/Popcorn</td>
<td>19.7%</td>
</tr>
<tr>
<td>Pizza</td>
<td>16.8%</td>
</tr>
<tr>
<td>Burgers/Cheeseburgers</td>
<td>13.8%</td>
</tr>
<tr>
<td>Cakes, pastries, donuts</td>
<td>10%</td>
</tr>
<tr>
<td>Soda</td>
<td>7%</td>
</tr>
</tbody>
</table>

Courtesy of Dr. Zhaoping Li.

Healthful Dietary Indexes and IR

**Healthy Eating Index**: Waist circumference, HOMA-IR, CRP inversely related to adherence; adiponectin direct association

**Mediterranean Diet**: Strongly reduced risk of cardiometabolic disease

**Alternative Healthy Eating Index**: Greater adherence associated with MetS reversion mainly with central obesity and high TG

**DASH Diet**: Reduced fasting insulin independent of weight loss (no benefit FBG or HOMA-IR)

HOMA-IR = homeostasis model assessment of insulin resistance; CRP = C-reactive protein; MetS = metabolic syndrome; TG = triglyceride; FBG = fasting blood glucose.

Macronutrients and IR

Dietary Fat: Composition of Oils

Common Sources of Saturated Fat

Common Sources of Unsaturated Fat

N3 PUFAs
- fatty fish (salmon, mackerel, and sardines)
- flaxseeds
- walnuts
- canola oil

N6 PUFAs
- vegetable oils: sunflower, soybean

MUFAs
- olive oil
- peanut oil
- canola oil
- avocados
- most nuts

PUFA = polyunsaturated fatty acid; MUFA = monounsaturated fatty acid.

Dietary Fat and IR

- Many observational studies do not show an association between total fat intake and insulin sensitivity or risk of diabetes mellitus
- Excess saturated fat induces IR
- Trans fats strongly increase IR
- Unsaturated fats (PUFA, MUFA), especially when substituted for SFA or CHO, improve insulin sensitivity

Avocados and Metabolic Syndrome

MUFA and Diabetes Mellitus

Omega-3 Fatty Acids and IR

Fat Modification and HOMA-IR Status

Effect of dietary fat modification on fasting glucose, insulin and markers of insulin sensitivity and secretion according to tertiles of low, medium, and high HOMA-IR status

**Dietary Carbohydrates**

- Quantity **and** quality matter
- Added sugar controversial but may contribute to or exacerbate IR
- Fiber improves insulin sensitivity
- Poor diet induces changes in the microbiome, which may increase inflammation, IR, and obesity

**Cereal Fiber, GI/GL, and Diabetes Mellitus**

**Resistant Starch and IR**

**SSBs and IR**

**Dietary Protein**

- **Protein has weight loss** benefits
  - Satiety, blood sugar control (reduced HOMA-IR), preserves LBM during weight loss
  - Diet x phenotype interaction
  - Protein source matters

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Red Meat and IR

<table>
<thead>
<tr>
<th>Fasting Insulin (μU/mL)</th>
<th>Unprocessed Red Meat</th>
<th>Processed Red Meat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median intake (g/d)</td>
<td>Median intake (g/d)</td>
<td></td>
</tr>
<tr>
<td>16 (n=446)</td>
<td>0 (n=429)</td>
<td></td>
</tr>
<tr>
<td>38 (n=442)</td>
<td>3 (n=475)</td>
<td></td>
</tr>
<tr>
<td>62 (n=475)</td>
<td>6 (n=437)</td>
<td></td>
</tr>
<tr>
<td>103 (n=420)</td>
<td>12 (n=442)</td>
<td></td>
</tr>
<tr>
<td>Model 1 4.66 4.93 4.81 5.38 .0003</td>
<td>Model 1 4.58 4.68 5.25 5.26 &lt;.0001</td>
<td></td>
</tr>
</tbody>
</table>


Red Meat Substitutions

- Effect estimates for changes in biomarkers corresponding to substitution of 1 serving of red meat (total, unprocessed, or processed) with alternative protein foods.

Yogurt and Metabolic Syndrome

<table>
<thead>
<tr>
<th>Associations between yogurt consumption and levels of metabolic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-consumers</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Median energy contribution from yogurt (kcal)</td>
</tr>
<tr>
<td>HDL 53 53 53.4 .29 .53</td>
</tr>
<tr>
<td>TG 111.2 109.5 104.3 &lt;.001 .01</td>
</tr>
<tr>
<td>Cholesterol 98.7 97.9 96.5 &lt;.001 &lt;.001</td>
</tr>
<tr>
<td>Glucose 83.8 83.2 70.4 &lt;.001 &lt;.001</td>
</tr>
<tr>
<td>HOMA-IR 121.7 120.5 119.8 &lt;.001 &lt;.001</td>
</tr>
<tr>
<td>3.42 3.37 3.17 &lt;.001 &lt;.001</td>
</tr>
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Micronutrients and More

Polyphenols and IR

Green Tea and Glucose Control

Courtesy of Bill Lagakos, PhD.

Resveratrol and IR


Spices and IR


Magnesium and IR


Vitamin D and IR


Probiotics and IR


Advanced Glycation End-Products

Diseases Associated with IR

- Nonalcoholic fatty liver disease
- Polycystic ovarian syndrome
- Obstructive sleep apnea
- Atherogenic dyslipidemia
- Type 2 diabetes mellitus
- Hypoandrogenemia
- Cancer

Diet and Type 2 Diabetes Mellitus

- Diets rich in whole grains, fruits, vegetables (especially leafy greens), legumes, nuts, moderate amount of dairy, and lower in refined grains, red/processed meats, and SSB reduce risk of diabetes mellitus and improve glycemic control in patients with diabetes mellitus.
- Moderate alcohol consumption.
- Optimal macronutrient ratio has not been clearly established
  - Wide range of diet patterns that include nutrient-dense foods suitable.

Diet and Type 2 Diabetes Mellitus

- Foods high in sugar/refined flour (CHO) may induce or amplify
- Replacing those CHO with protein is beneficial
- High-fiber, low sugar/refined CHO
- PREDIMED study

Atherogenic Dyslipidemia

- Values are mean ± SD, = 40. Means without a common letter differ, P < 0.05. The following traits were log-transformed prior to statistical analysis: TG, HDL-C, large VLDL, medium VLDL, small VLDL, total LDL, large LDL, medium LDL, small LDL, and very small LDL. HDL-C = HDL cholesterol; LCHSF = lower carbohydrate, high-saturated fat; LCLSF = lower carbohydrate, low-saturated fat; LDL-C = LDL cholesterol; non-HDL-C = non-HDL cholesterol; TC = total cholesterol.

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- Significantly different between groups, P<0.05 (one-way ANOVA). ADMF = alternate-day modified fasting.

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Diet and NAFLD

- No consensus what diet best but moderate carbohydrates (40%-45%) + with increased MUFA and omega-3 PUFA + reduced SFAs may be beneficial
- Reduce SSB and added sugar and refined carbohydrates
- Vitamin E: Benefit in non-diabetic patients with NASH
- Polyphenols: Reduce liver fat accumulation


NAFLD, Diet, and Microbiome

- Lifestyle management first-line therapy, but optimal diet composition uncertain
- Weight loss MOST important
  - Greater weight loss with MUFA-enriched diet
  - Improved menstrual cycle with low GI diet
  - Increased free androgen index for high CHO diet
  - Greater reductions in IR, fibrinogen, total and HDL cholesterol
  - Improved QOL with low GI diet
  - Improved depression and self-esteem with high-protein diet


Diet and PCOS

- Healthful dietary patterns play an important role in the prevention and treatment of IR and associated conditions
- The optimal macronutrient composition of a healthful diet for IR and associated diseases has not been established, allowing for some flexibility in dietary approaches, which is helpful for compliance
- A healthful dietary pattern is naturally rich in beneficial micronutrients and phytoneutrients, although supplementation may be beneficial in some situations


Other Lifestyle Considerations for IR

- Sit less
- Boost exercise intensity (HIIT, HIRT)
- Sleep better
- Avoid tobacco
- Manage stress (meditation)
- Medications


What’s the “Take Home”?

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Questions?

Special thanks to Drs. Zhaoping Li (VP, NBPNLS) and Mike Rothkopf (President, NBPNLS) for their assistance with this presentation.