Role of Nutrition in Diabetes

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You have diabetes, dyslipidemia and gout. No problem! Just avoid any food that contains carbohydrates, fat or protein and you will be fine!
The Impact of Diet on Diabetes: Known Before the Era of Diabetes Medications

1869–1962
Joslin Clinic
Boston, MA

1879–1964
Physiatric Institute
Morristown, NJ

Die of diabetes or risk "inanition": “Starvation due to inability to acquire tolerance for any living diet.”
Historically Food Myths, Fad Diets and Dietary Trends Have Always Been Popular

1900 1915 1910 1922 1970 2012

- Single Food Fad Diets
  - Oat Diet
  - Grapefruit Diet
  - Milk Diet
  - Potato Therapy
- The Allen Diet (a starvation diet)
- The Soup Diet
  - Low Carbs & high fat Diet (40% fat, 40% carbs, 20% protein)
- The Atkins Diet
  - The Blood Type Diet
  - High Carbs Diet (30% Fat, 50-55% Carbs, 15-20% protein)
Objectives

• Nutrition targets in diabetes management
• Current recommendations and the slow adaptation of evidence
• Looking Ahead
  – Macronutrients
    • Protein content
    • Carbohydrates
  – Micronutrients
Major Problems in Patients with Type 2 DM (Nutrition Targets)

- Overweight or obese (+ large waist line)
- Postprandial hyperglycemia
- Postprandial hypertriglyceridemia
- Insulin resistance (increased HGP and decreased PGD)
- Hyperinsulinemia (pre- and early diabetes)
- Low HDL
- Increased cytokines (inflammatory, coagulation)
- Endothelial dysfunction
- High risk for coronary and cerebral vascular disease
- Continue to gain weight on medications
- Decreased EE (decreased PA and TEF)

- Hypertension
- +
- High small dense-LDL
## Current Dietary Recommendations

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>EASD [% Energy]</th>
<th>American Diabetes Association [% Energy]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>10-20</td>
<td>15-20</td>
</tr>
<tr>
<td>Fat</td>
<td>35</td>
<td>-</td>
</tr>
<tr>
<td>SFA</td>
<td>SFA + trans fats &lt; 10, individually tailor MUFA</td>
<td>&lt;7, limit trans fats Cholesterol &lt; 200 mg/day, individually tailor MUFA</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>45-60</td>
<td>At least 130 g/day</td>
</tr>
</tbody>
</table>

- MNT is important in preventing diabetes, managing existing diabetes, and preventing or slowing the rate of complications
- MNT includes counseling about general healthy eating and also nutrition support when appropriate

Current Protein Recommendations

• Diabetes and normal renal function: 15-20% of total energy intake (E)

• Diabetes with early stages of CKD: 0.8-1 gm/kg/day (B)

• Diabetes with later stages of CKD: 0.8 gm/kg/day (B)

• High protein diet are not recommended as method for weight loss at this time (E)

• MNT that favorably affects cardiovascular risk factors may improve microvascular complications (retinopathy, nephropathy) (C)
What About Protein?

“Oh hey! I just love these things!... Crunchy on the outside and a chewy center!”
## Protein Content of Diabetes Diet

### Is it a Percentage or an absolute amount?

<table>
<thead>
<tr>
<th>Status</th>
<th>gm/Kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low</td>
<td>&lt;0.6</td>
</tr>
<tr>
<td>Low</td>
<td>0.6-0.8</td>
</tr>
<tr>
<td>Moderately low</td>
<td>0.8-1</td>
</tr>
<tr>
<td>Average</td>
<td>1-1.5</td>
</tr>
<tr>
<td>Moderately high</td>
<td>1.5-2</td>
</tr>
<tr>
<td>High</td>
<td>&gt;2</td>
</tr>
</tbody>
</table>
Type 1 DM:
Many RCTs showed that reducing protein intake to 0.8 gm/kg/day in patients with overt nephropathy decreases proteinuria, reduces the decline in GFR, risk of renal failure and death.

Type 2 DM:
Very little or no data

No evidence to show that increased protein intake in patients with normal kidney function will induce microalbuminuria or cause decline in GFR.
TABLE 3
Relative risks (RR) of ischemic heart disease and 95% CIs according to quintiles of protein intake

<table>
<thead>
<tr>
<th>quintiles of total protein intake</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total protein intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (% of energy)</td>
<td>14.7</td>
<td>17.1</td>
<td>18.8</td>
<td>20.6</td>
<td>24.0</td>
</tr>
<tr>
<td>Number of cases</td>
<td>211</td>
<td>184</td>
<td>182</td>
<td>193</td>
<td>169</td>
</tr>
<tr>
<td>Person-years</td>
<td>211420</td>
<td>218846</td>
<td>215949</td>
<td>209797</td>
<td>201258</td>
</tr>
<tr>
<td>Age-adjusted RR</td>
<td>1.0</td>
<td>0.82</td>
<td>0.81</td>
<td>0.86</td>
<td>0.75 (0.61, 0.92)</td>
</tr>
<tr>
<td>Multivariate RR</td>
<td>1.0</td>
<td>0.86</td>
<td>0.84</td>
<td>0.91</td>
<td>0.72 (0.57, 0.91)</td>
</tr>
<tr>
<td>Additional adjustment for specific fats</td>
<td>1.0</td>
<td>0.86</td>
<td>0.84</td>
<td>0.92</td>
<td>0.74 (0.59, 0.95)</td>
</tr>
<tr>
<td><strong>Animal protein intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (% of energy)</td>
<td>11.6</td>
<td>13.3</td>
<td>15.2</td>
<td>17.2</td>
<td>20.6</td>
</tr>
<tr>
<td>Number of cases</td>
<td>195</td>
<td>197</td>
<td>174</td>
<td>201</td>
<td>172</td>
</tr>
<tr>
<td>Age-adjusted RR</td>
<td>1.0</td>
<td>0.97</td>
<td>0.85</td>
<td>0.99</td>
<td>0.84 (0.68, 1.03)</td>
</tr>
<tr>
<td>Multivariate RR</td>
<td>1.0</td>
<td>1.01</td>
<td>0.92</td>
<td>0.87</td>
<td>0.86 (0.68, 1.09)</td>
</tr>
<tr>
<td>Additional adjustment for specific fats</td>
<td>1.0</td>
<td>1.01</td>
<td>0.91</td>
<td>0.85</td>
<td>0.85 (0.67, 1.09)</td>
</tr>
<tr>
<td>Further adjustment for vegetable protein</td>
<td>1.0</td>
<td>1.00</td>
<td>0.90</td>
<td>0.84</td>
<td>0.84 (0.65, 1.07)</td>
</tr>
<tr>
<td><strong>Vegetable protein intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (% of energy)</td>
<td>2.4</td>
<td>3.0</td>
<td>3.5</td>
<td>4.1</td>
<td>5.0</td>
</tr>
<tr>
<td>Number of cases</td>
<td>219</td>
<td>197</td>
<td>187</td>
<td>173</td>
<td>163</td>
</tr>
<tr>
<td>Age-adjusted RR</td>
<td>1.0</td>
<td>0.87</td>
<td>0.81</td>
<td>0.77</td>
<td>0.74 (0.60, 0.90)</td>
</tr>
<tr>
<td>Multivariate RR</td>
<td>1.0</td>
<td>0.95</td>
<td>0.95</td>
<td>0.85</td>
<td>0.84 (0.66, 1.08)</td>
</tr>
<tr>
<td>Additional adjustment for specific fats</td>
<td>1.0</td>
<td>0.98</td>
<td>1.00</td>
<td>0.92</td>
<td>0.94 (0.71, 1.23)</td>
</tr>
<tr>
<td>Further adjustment for animal protein</td>
<td>1.0</td>
<td>0.96</td>
<td>0.97</td>
<td>0.89</td>
<td>0.89 (0.68, 1.18)</td>
</tr>
</tbody>
</table>
The Metabolic Relation of Different Proteins to Glucose

Response to 50 gm of Glucose + 25 gm of Protein

Mean Decrease= 21%
Cottage C= 38%
* p<0.05

Adapted from Gannon MC et al. Metabolism 1988;37:1081-1088
The Metabolic Effect of Different Protein Ratios in Type 2 DM

Change in HbA1c after 5 weeks

- Pioglitazone 45 mg 16 weeks -0.7%
- Metformin 2500 mg 29 weeks -1.4%
- 30% protein diet 5 weeks -0.8 (1.6%)

n=12

Adapted from Gannon MC et al. Amer J Clin Nutr 2003;78:734-741
### Effect of High Protein Intake on Renal Function (Nurses Health Study)

<table>
<thead>
<tr>
<th></th>
<th>Normal Renal Function</th>
<th>Mild Renal Insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=1153</td>
<td>n=489</td>
</tr>
<tr>
<td>Decline of estimated GFR/10 grams of protein increase</td>
<td>-0.25</td>
<td>-1.69</td>
</tr>
<tr>
<td>(ml/min/1.73 m²)</td>
<td>(95%CI, -0.78-1.28)</td>
<td>(95%CI, -2.93 -0.45)</td>
</tr>
<tr>
<td>Unadjusted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decline of estimated GFR/10 grams of protein increase</td>
<td>-1.14</td>
<td>-7.72*</td>
</tr>
<tr>
<td>(ml/min/1.73 m²)</td>
<td>(95%CI, -3.83-4.75)</td>
<td>(95%CI, -15.52-0.08)</td>
</tr>
<tr>
<td>Adjusted</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Study Conclusion:** High protein intake was not associated with renal function decline in women with normal kidney function.

*p < 0.05
Knight et al, Ann Intern Med. 2003;138:460-467
Origin of the Protein Recommendations

EURODIAB IDDM

Cross-sectional study, clinic-based
30 centers, 16 European countries
2696 Type 1 Diabetic patients
3-day dietary records, urinary AER

Protein intake <20% → AER < 20 mg/min
Protein intake >20% → AER > 20 mg/min

Conclusion:
It is recommended that people with diabetes don’t exceed a protein intake of 20%

Monitoring and adjusting of protein intake appears particularly desirable for individuals with AER exceeding 20 \( \mu \text{g/min} \) (30mg/24 hr), especially when BP is raised and/or diabetic control is poor

The test for a linear relationship between protein intake and AER revealed a significant trend of energy adjusted AER to rise with higher intakes of total protein (% of energy, $\beta = 0.02$ [CI 0.01, 0.04], $p = 0.01$) or animal protein (% of energy, $\beta = 0.02$ [CI 0.003, 0.03], $p = 0.02$), while trends were not significant for vegetable protein (% of energy, $\beta = 0.01$ [CI -0.04, 0.05], $p = 0.83$) or protein related to body weight (g/kg body weight, $\beta = 0.1$ [CI -0.1, 0.3], $p = 0.38$). After inclusion of diabetes duration, age, HbA1c, diastolic blood pressure (mean ± SD: 

**Toeller M et al. Diabetologia. 1997; 40:1219-1226**

The association between higher AER and higher dietary protein intake that we demonstrated was of particular importance for patients with hypertension and/or higher HbA1c values, with the presence of hypertension having a greater impact than that of a poorer diabetes control.
Higher Dietary Fat Correlates with Microalbuminuria whereas Higher Protein Correlates with Lower Urine Albumin Levels

TABLE 4
Odds ratios and 95% CIs for microalbuminuria in subjects with insulin-dependent diabetes mellitus according to quintile of energy-adjusted macronutrient intake

<table>
<thead>
<tr>
<th>Dietary quintile</th>
<th>Unadjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td><strong>Saturated fat</strong></td>
<td></td>
<td>(P)</td>
</tr>
<tr>
<td>1 (lowest)</td>
<td>1.0</td>
<td>Referent</td>
</tr>
<tr>
<td>2</td>
<td>1.9</td>
<td>0.51, 6.7 (0.34)</td>
</tr>
<tr>
<td>3</td>
<td>1.0</td>
<td>0.25, 4.0 (1.00)</td>
</tr>
<tr>
<td>4</td>
<td>1.3</td>
<td>0.33, 4.8 (0.74)</td>
</tr>
<tr>
<td>5 (highest)</td>
<td>2.8</td>
<td>0.82, 9.9 (0.10)</td>
</tr>
<tr>
<td><strong>Protein</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (lowest)</td>
<td>1.0</td>
<td>Referent</td>
</tr>
<tr>
<td>2</td>
<td>0.96</td>
<td>0.36, 2.6 (0.93)</td>
</tr>
<tr>
<td>3</td>
<td>0.48</td>
<td>0.16, 1.4 (0.18)</td>
</tr>
<tr>
<td>4</td>
<td>0.84</td>
<td>0.31, 2.3 (0.74)</td>
</tr>
<tr>
<td>5 (highest)</td>
<td>0.38</td>
<td>0.12, 1.2 (0.09)</td>
</tr>
</tbody>
</table>

1Quintiles adjusted for age at diagnosis (protein: n = 178) and for BMI and serum HDL cholesterol (saturated fat: n = 136).
Improvement in BP & GFR in Patients with ESRD on Low Protein Diet is Related to Decreased Sodium Intake

Table 4 | Multiple regression analysis with mean BP at the end of the study as dependent variable in stages 4 and 5 CKD patients

<table>
<thead>
<tr>
<th></th>
<th>β Coefficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>94.817</td>
<td>0.0001</td>
</tr>
<tr>
<td>Age</td>
<td>0.075</td>
<td>0.119</td>
</tr>
<tr>
<td>Gender (female as reference)</td>
<td>-0.302</td>
<td>0.845</td>
</tr>
<tr>
<td>eGFR</td>
<td>-0.134</td>
<td>0.175</td>
</tr>
<tr>
<td>Number of antihypertensive drugs</td>
<td>1.256</td>
<td>0.101</td>
</tr>
<tr>
<td>Diuretic use</td>
<td>-0.191</td>
<td>0.900</td>
</tr>
<tr>
<td><strong>Protein intake</strong></td>
<td>-3.882</td>
<td>0.397</td>
</tr>
<tr>
<td><strong>Supplemented VLPD</strong></td>
<td>-6.692</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Sodium intake</strong></td>
<td>0.696</td>
<td>0.023</td>
</tr>
</tbody>
</table>

BP, blood pressure; CKD, chronic kidney disease; eGFR, GFR estimated by Cockroft-Gault equation; VLPD, very low protein diet.
Model summary: $R^2=0.270$, $P=0.0001$.

Figure 1 | Percent changes of protein intake, salt intake, FENa from baseline to 6 months, in patients at VLPD (white bars), LPD (black bars), and FD (gray bars). *$P<0.001$ vs LPD and FD.
What about Carbohydrates?

“I’m practically a vegetarian. I eat plenty of grains after they’ve been turned into cows, pigs and chickens.”
General Carbohydrates Recommendations

- 50-60% of total kcal
- Three types of carbohydrates (sugars, starch, and fiber) with different impact on blood glucose level
- Consume at least 7-10 servings/day of healthy carbohydrates (fresh fruits, vegetables, pulses [legumes, beans, and peas], and whole grains)
- Low glycemic index foods (< 55) facilitate glycemic control
- Fiber intake should be 14 g/1000 kcal/d or 25-30 g/d
- Sugar substitutes are safe within ranges provided by the U.S. F.D.A.
The Metabolic Effect of Different Protein/Carbohydrates Ratios in Type 2 DM

Protein to carbohydrate to fat: 30:40:30 Versus 15:55:30
-40% Reduction

Twenty-four-hour plasma glucose response of subjects to the control (15% protein) and high-protein (30% protein) diets

*Significantly different from control diet, P < 0.05

Twenty-four-hour triacylglycerol response of subjects to the control (15% protein) and high-protein (30% protein) diets.

*Significantly different from the fasting control value, P < 0.03

Adapted from Gannon MC et al. Amer J Clin Nutr 2003;78:734-741
Effects of Lower % Carbohydrates in Low Calorie Diet on Visceral Fat and Basal Insulin in Obese Patients with Type 2 Diabetes

<table>
<thead>
<tr>
<th></th>
<th>C</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Carbs</td>
<td>39</td>
<td>35</td>
<td>25</td>
</tr>
<tr>
<td>High Carbs</td>
<td>62</td>
<td>10</td>
<td>26</td>
</tr>
</tbody>
</table>

Visceral Fat (cm²)

- No Difference in Reduction of Weight, Lean Mass, Total Fat

% Decrease in basal Insulin

- High Carbohydrates
- Low Carbohydrates

% Change in HDL-C

- No Difference in Reduction of Weight, Lean Mass, Total Fat

n= 22

* p<0.05
** p<0.01

Lowering the Glycemic Index (GI) of Carbohydrates Improves PP Plasma Glucose Response

The glucose responses to 30 g of carbohydrate from three treatments (DEX, RS2 and RS4_{XL}).

Haub MD et al. J Nutr Metab. 2010
Diets with High or Low Protein Content and Glycemic Index for Weight-Loss Maintenance (26 weeks)

13% protein (LGI/HGI) versus 25% protein (LGI/HGI)

n = 773

Initial weight loss >8%

What about Weight Reduction?
Weight Reduction Improves Metabolic and CV Risk Factors

- Maintenance of body weight requires 25-30 kcal/kg/day

- Weight reduction of 5-10% has significant impact on metabolic and cardiovascular risk factors in overweight and obese patients with diabetes. Aim for a BMI of 20-25 kg/M²

- Modest caloric reduction of ~500 kcal/d results in a weight loss of 1 pound/wk

- Reduction of total carbohydrates to ~40% of the caloric intake and increase of protein to 1.5-2 gm/adjusted body weight are effective dietary tools

- Diabetes specific meal replacements are useful tools (1-2/day)

- Increase of physical activity to 175-300 min/week in short bouts of 10 min each with emphasis on strength training are effective for weight reduction and maintenance.
Strong Correlation Between Meal Replacements and Weight Loss in the Look AHEAD Study

Quartile of meal replacements (MR) based on Avg. # of MR used

**1st Quartile**
- **117 MRs**
- **5.9%** reduction in initial weight in ill participants
  - (~2 MR per week)*

**2nd Quartile**
- **277 MRs**
- **7.2%** reduction in initial weight in ill participants
  - (~1 MR every other day)*

**3rd Quartile**
- **406 MRs**
- **9.4%** reduction in initial weight in ill participants
  - (~1 MR per day)*

**4th Quartile**
- **608 MRs**
- **11.2%** reduction in initial weight in ill participants
  - (1 - 2 MRs per day)*

Take Home Message

1. Medical Nutrition Therapy is a key component of overall diabetes management
2. Many targets in comprehensive diabetes care are missed with the current diabetes nutrition recommendations
3. Protein intake may be increased in the nutrition plan of patients with type 2 diabetes and normal kidney function
4. Protein should be calculated as gm/kg, especially when hypocaloric diet is recommended
5. Reduction of carbohydrates load to ~40-45% may improve diurnal plasma glucose and triglycerides, increase HDL-cholesterol and reduce visceral fat
6. Meal replacement is a key component of weight reduction for overweight and obese patients with type 2 diabetes
7. Adequacy of micronutrients is integral part of MNT for patients with diabetes
“They revised the Food Pyramid again.”