Diabetes Care in the U.S. A 2009 vision

Enrique Caballero MD
Director, Latino Diabetes Initiative
Director, Medical Affairs, Professional Education
Joslin Diabetes Center
Harvard Medical School
Glycemic Control Has Improved – But Many Patients Still Not at Goal A1C <7%

N=1334
NHANES=National Health and Nutrition Examination Survey
Why Can’t We Get There Yet?

- Diabetes is a progressive and difficult to treat disease
- It is a very expensive disease
- Proper diabetes care requires effective and sustained education and a team approach
- Social and cultural challenges
- Failure to implement timely and appropriate interventions
Why Can’t We Get There Yet?

- Low adherence to treatment plans
- Confusion in who, when and how to treat diabetes
- Unmet needs in treatment approaches
- Difficult climate to implement therapies due to pressure of media and possible legal problems
- Lack of reimbursement for preventive strategies
Natural History of Type 2 diabetes

- Genetic susceptibility
- Environmental factors
  - Nutrition
  - Inactivity
  - Weight gain

- Insulin Resistance
  - Beta Cell dysfunction

- normoglycemia
- IFG
- IGT
- hyperglycemia

Diagnosis of Diabetes

Appearance of Complications

Disability

Death

- Atherosclerosis
- CHD
- Blindness
- ESRD/dialysis/transplantation
- Stroke
- Amputation

Complications:
- Retinopathy
- Nephropathy
- Neuropathy
Current view of the Pathophysiology of Type 2 Diabetes

- Decreased peripheral glucose uptake
- Increased glucose production in the liver
- Hyperglucemia
- Beta and Alpha Cell dysfunction
Pharmacologic Approaches in DM2

• Improve insulin resistance
  – Biguanides
  – Thiazolidinediones

• Enhance insulin secretion/β-cell function
  – Sulfonylureas
  – Short-acting secretagogues

• Reduce glucose absorption
  – Alpha-glucosidase inhibitors

• Incretin-based therapies
  – Incretin mimetics: GLP-1 analogs (exenatide, liraglutide, taspoglutide)
  – Incretin enhancers: DPP-IV inhibitors (sitagliptin, vildagliptin, saxagliptin, alogliptin and others in development)

• Insulin replacement
  – Basal insulins
  – Preprandial insulins

• Bile-acid sequestrants
  – Colesevelam
Drugs that enhance insulin action in peripheral tissues

- **Thiazolidinediones**

Drugs that suppress endogenous glucose production

- **Metformin**

Drugs that enhance endogenous insulin secretion

- **Sulfonylureas**
  - Repaglinide, Nateglinide
  - Exenatide, Liraglutide, Taspoglutide

DPP-IV inhibitors

Drugs that delay the absorption of carbohydrate from the GI Tract

- **Alpha glucosidase inhibitors**

- **Colesevelam**

**Medications to Treat Type 2 Diabetes**
Downloadable Glucometers


<table>
<thead>
<tr>
<th>Time</th>
<th>Tests</th>
<th>Percent</th>
<th>BG Range (mg/dL)</th>
<th>Highest BG (mg/dL)</th>
<th>Lowest BG (mg/dL)</th>
<th>Average BG (mg/dL)</th>
<th>Number of Hls</th>
<th>Number of LOs</th>
<th>Total # of Tests</th>
<th>Avg. # Tests per Day</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Night</td>
<td>0</td>
<td>0%</td>
<td>&gt; 140 mg/dL</td>
<td>341</td>
<td>21</td>
<td>137.2</td>
<td>0</td>
<td>0</td>
<td>56</td>
<td>4.0</td>
<td>50.6</td>
</tr>
<tr>
<td>Before Breakfast</td>
<td>13</td>
<td>50.0%</td>
<td>70 - 140 mg/dL</td>
<td></td>
<td></td>
<td>140.8</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>4.0</td>
<td></td>
</tr>
<tr>
<td>After Breakfast</td>
<td>1</td>
<td>5.4%</td>
<td>50 - 69 mg/dL</td>
<td></td>
<td></td>
<td>131.0</td>
<td>0</td>
<td>0</td>
<td>15</td>
<td>10.0</td>
<td></td>
</tr>
<tr>
<td>Before Lunch</td>
<td>12</td>
<td>42.9%</td>
<td>&lt; 50 mg/dL</td>
<td></td>
<td></td>
<td>140.8</td>
<td>2</td>
<td>0</td>
<td>15</td>
<td>10.0</td>
<td></td>
</tr>
<tr>
<td>After Lunch</td>
<td>2</td>
<td>1.8%</td>
<td></td>
<td></td>
<td></td>
<td>223.5</td>
<td>15</td>
<td>0</td>
<td>15</td>
<td>10.0</td>
<td></td>
</tr>
<tr>
<td>Before Dinner</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>145.1</td>
<td>3</td>
<td>0</td>
<td>15</td>
<td>10.0</td>
<td></td>
</tr>
<tr>
<td>After Dinner</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>125.0</td>
<td>15</td>
<td>0</td>
<td>15</td>
<td>10.0</td>
<td></td>
</tr>
<tr>
<td>Evening</td>
<td>15</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>126.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Continuous Glucose Monitors
Continuous Sensor Data

Glucose Sensor Profile: 03-29-01

* This day does not satisfy the criteria for optimal accuracy as indicated by the shaded entries in the summary table. Please use your clinical judgement in evaluating the graph.

Patient: P000-0004@03-30-2001@09-51-56

- 300 mg/dl
- 50 mg/dl
Pancreas Transplantation
Islet Cell Transplantation
Embryonic Stem Cells (ESC)

Ectoderm

Mesoderm

ESC  Endoderm  Pancreas  Islet Precursor \( \beta \)-cell Cell

We need to understand mechanisms
The Basic Triad in Diabetes Care

The Patient:
Medical, Socio-economic, Cultural factors

The Health Care Provider:
Suboptimal implementation of basic diabetes care
Lack of cultural competence

The Health Care System:
Insufficient:
Time and support with patients
Support to Education and Prevention
Culturally Oriented Programs
Professional education
Cultural diversity
Health care access

Modified from Caballero AE. Current Diabetes and Endocrinology Reports 2007. 14:151-157
Genes, Environment and Social/Cultural Factors in the development and course of Diabetes in Minorities

Socio-economic and Cultural factors + Thrifty Genes + Inadequate Lifestyle

Insulin Resistance and Abdominal Obesity

Beta Cell Dysfunction

Other defects Incretin function?

Type 2 Diabetes

Frequent Chronic Complications

Increased Mortality rates

Socio-economic and Cultural factors

The Latino Diabetes Initiative

The overall goal of the Initiative is to improve the lives of Latinos affected by diabetes or at risk for the disease through culturally oriented patient care, education and research.

www.joslin.org/latino
The Latino Diabetes Initiative

Patient Care and Education

Research

Community Outreach

Professional Education

www.joslin.org/latino
The Diabetes Care Team

- Physician
- Nutritionist
- Family
- Endocrinologist
- Pharmacy
- Diabetes Nurse
- Patient
Incidence of Diabetes in the DPP

- Placebo (n=1082)
- Metformin (n=1073, p<0.001 vs. Placebo)
- Lifestyle (n=1079, p<0.001 vs. Metformin, p<0.001 vs. Placebo)

Risk reduction
- 31% by metformin
- 58% by lifestyle
## Main Characteristics in both Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls (n=17)</th>
<th>At risk (n=21)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>14.18±2.3</td>
<td>13.33±2.7</td>
<td>0.31</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.79±0.08</td>
<td>0.88±0.11</td>
<td>0.003</td>
</tr>
<tr>
<td>Total % fat</td>
<td>24±6</td>
<td>42±9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Trunk fat</td>
<td>19±5</td>
<td>42±9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>101.5±7</td>
<td>116.6±12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>68.6±6</td>
<td>70.9±6</td>
<td>0.23</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>142.06</td>
<td>149.76</td>
<td>0.318</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>58.82</td>
<td>108.29</td>
<td>0.004</td>
</tr>
<tr>
<td>HDL</td>
<td>42.00</td>
<td>37.52</td>
<td>0.162</td>
</tr>
<tr>
<td>LDL</td>
<td>89.24</td>
<td>93.50</td>
<td>0.484</td>
</tr>
</tbody>
</table>

Demographic and clinical characteristics between both groups, comparisons were done with t test in case of continuous variables and x² in case of dichotomous variables.
Glucose and Insulin curves during OGTT

Panel A

Panel B

Caballero AE. Diabetes Care. 2008; 31:1-7
THANK YOU