New Thinking and Approaches in the Management of Type 2 Diabetes

M. Susan Burke, MD, FACP
Clinical Associate Professor of Medicine
Sidney Kimmel Medical College at Thomas Jefferson University
Senior Advisor, Lankenau Medical Associates
Lankenau Medical Center
Wynnewood, PA

Ellen H. Miller, MD
Professor of Science Education & Medicine
Hofstra Northwell School of Medicine
Senior Medical Director
North Shore - LIJ CareConnect
East Hills, NY

Diabetes Prevalence in the US, 2012

Obesity and T2D: A Common Burden

ADA: Foundations of Care

Self-management Education

Nutrition
- Promote healthy eating patterns, appropriate portion sizes, address personal and cultural preferences
- Achieve and maintain body weight goals and individualized glycemic, blood pressure, and lipid goals

Physical Activity
- Adults with diabetes: at least 150 min/wk of moderate-intensity aerobic activity over at least 5 days/week; resistance training at least twice weekly

Smoking Cessation
- Advise all patients not to use cigarettes, other tobacco products, or e-cigarettes; diabetes care should include routine smoking cessation counseling

New Thinking and Approaches in the Management of Type 2 Diabetes

### ADA: Foundations of Care

#### Immunizations in Diabetes

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Frequency of administration</th>
<th>Patient age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>Annually</td>
<td>≥6 months</td>
</tr>
<tr>
<td>PPSV23, 1 injection before age 65</td>
<td>19-64 years</td>
<td></td>
</tr>
<tr>
<td>PCV13 plus PPSV23</td>
<td>1 injection each, in series ≥1 year apart</td>
<td>≥65 years</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>3 injection series</td>
<td>20-59 years 1 year apart ≥65 years</td>
</tr>
<tr>
<td>Td (or Tdap)</td>
<td>every 10 years</td>
<td>≥19 years</td>
</tr>
<tr>
<td>Zoster vaccine</td>
<td>200 years</td>
<td></td>
</tr>
</tbody>
</table>


### Diabetes Mellitus: A Constellation of Complications

- Erectile Dysfunction
- Renal Disease
- Peripheral Vascular Disease
- Retinopathy/Macular Edema
- Gastropathy
- Dystipemia
- Cardiovascular Disease
- Hypertension
- Autonomic Neuropathy
- Peripheral Neuropathy

### Looking Beyond Glucose Control

#### BP Targets

- People with T2DM and hypertension should be treated to a systolic blood pressure goal of <140 mmHg; lower targets may be appropriate for certain individuals
- Consider aspirin therapy (75-162 mg/day)
- As a primary prevention strategy in those at increased cardiovascular risk (10-year risk >10%)
- Includes most men or women with DM age ≥50 years who have ≥1 major risk factor

Remember to use moderate or high dose statins in most diabetics >40, depending on risk


### Screening Recommendations

- Nephropathy
  - At least yearly, assess urine albumin excretion and estimated glomerular filtration rate (eGFR)
- Retinopathy
  - Dilated exam by ophthalmologist at diagnosis and Q 1-2 years
- Regular foot care
- Neuropathy, including monofilament testing
  - At time of diagnosis and annually

### NQS Priorities

Mandated by the Patient Protection and Affordable Care Act, the National Quality Strategy (NQS) was developed to improve patient health and health care quality. The NQS priorities address the most common health concerns among patients:

1. Patient safety
2. Engaging patients and caregivers
3. Coordinating patient care
4. Disseminating effective prevention and treatment practices for leading causes of mortality
5. Promoting use of best practices to enable healthy living within communities
6. Developing new health care delivery models to provide affordable quality care for individuals, families, employers, and governments

http://www.ahrq.gov/workingforquality/nqs/overview.htm

### CMS National Quality Measures in Diabetes

- Diabetes: Hemoglobin A1C Poor Control
- Diabetes: Low Density Lipoprotein (LDL-C) Control (<100 mg/dL)
- Diabetic Retinopathy: Documentation of Presence or Absence of Macular Edema and Level of Severity of Retinopathy
- Diabetic Retinopathy: Communication with the Physician Managing Ongoing Diabetes Care
- Diabetes: Medical Attention for Nephropathy
- Diabetes Mellitus: Diabetic Foot and Ankle Care, Peripheral Neuropathy – Neurological Evaluation
- Diabetes Mellitus: Diabetic Foot and Ankle Care, Ulcer Prevention – Evaluation of Footwear
- Diabetes: Foot Exam

https://www.cms.gov
New Thinking and Approaches in the Management of Type 2 Diabetes

**Goal Achievement in Diabetes—How Well Are We Doing?**

![Graph](image)

*Data from separate studies.

BP = blood pressure; LDL-C = low-density lipoprotein cholesterol; NHANES = National Health and Nutrition Examination Survey.


**Diabetes Management Is Changing...**

- New oral agents:
  - DPP-4 inhibitors, SGLT-2 inhibitors, multiple combinations (metformin, SU, TZD)
- Additional injectable options:
  - New insulins: basal, long-acting basal, ultra rapid
  - New GLP-1 RA with longer half-life
  - New insulin GLP-1 RA combinations

**Goals of today’s discussion:**
- Review the most current understanding of T2DM pathophysiology and its implication on treatment options
- Apply treatment strategies to patient scenarios
- Explore patient engagement techniques to help with medication and goal selection, and improve adherence

**Current Understanding of the Pathophysiology of T2DM and the Targets of Available Anti-Hyperglycemic Agents**

**Insulin and Glucagon Dynamics in Response to Meals Are Abnormal in Type 2 Diabetes**

![Graph](image)

**The Pathophysiology of Type 2 Diabetes Includes Islet Cell Dysfunction and Insulin Resistance**

![Diagram](image)

**Multiple Metabolic Abnormalities Contribute to Hyperglycemia in T2DM**

![Diagram](image)
Proximal tubule

- None, unless used with
  - Facilitated glucose transporters (GLUTs) transport glucose down gradient
  - Neutral
  - HbA1C ~0.5%
  - Many other tissue effects
  - Two predominant incretins
    - Glucagon-like peptide-1 (GLP-1)
    - Glucose-dependent insulinotropic peptide (GIP)
  - Rapidly inactivated by dipeptidyl peptidase-4
  - Incretin effect is impaired in type 2 diabetes

- Reduced Incretin Effect in Type 2 Diabetes Patients

- DPP-4 Inhibitors and GLP-1 RAs: Summary of Efficacy and Other Considerations

- Role of Incretins in Glucose Homeostasis

- Incretin Therapies to Treat T2DM

- Glucose Control by the Kidney

- New Thinking and Approaches in the Management of Type 2 Diabetes

New Thinking and Approaches in the Management of Type 2 Diabetes

SGLT-2 Inhibitors: FDA Approved or in Clinical Development

<table>
<thead>
<tr>
<th>Compounds in development</th>
<th>Development status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dapagliflozin</td>
<td>FDA APPROVED</td>
</tr>
<tr>
<td>Canagliflozin</td>
<td>FDA APPROVED</td>
</tr>
<tr>
<td>Empagliflozin</td>
<td>FDA APPROVED</td>
</tr>
<tr>
<td>Ipragliflozin</td>
<td>US – Phase III clinical trials Approved for use in Japan</td>
</tr>
<tr>
<td>LX4211</td>
<td>Phase II clinical trials</td>
</tr>
</tbody>
</table>

SGLT-2 Inhibitors for Treatment of Type 2 Diabetes

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Insulin-independent action</td>
<td>• Recurrent UTI</td>
</tr>
<tr>
<td>• Calorie loss – possible weight loss</td>
<td>• Genital fungal infection</td>
</tr>
<tr>
<td>• Low hypoglycemia</td>
<td>• Decreased blood pressure</td>
</tr>
<tr>
<td>• Complement action of other anti-diabetic agents</td>
<td>• Worsening of renal function</td>
</tr>
<tr>
<td>• Can be used regardless of diabetes duration</td>
<td>• Increased hematocrit*</td>
</tr>
<tr>
<td></td>
<td>• Increased LDL-C*</td>
</tr>
</tbody>
</table>

Pathophysiology and Pharmacologic Targets: Summary

- Several new agents have hit the market in recent years, providing increased ability to tailor treatments based on patient profiles
- Expanded treatment armamentarium allows for more personalized shared decision-making between PCP and patient

* Specific considerations for individuals with existing renal insufficiency, the elderly, and those receiving loop diuretics
* Specific considerations for individuals with existing renal insufficiency, the elderly, and those receiving loop diuretics
* Significance on patient outcomes is unclear at this time