Clinical approach
to the Patient
with Type II Diabetes Mellitus

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Objectives of lecture
1. Describe the scope of DM epidemic
2. List types of Diabetes
3. List the classic symptoms of DM
4. Define how to diagnosis Diabetes Mellitus and prediabetes using A1C, FBS, random BS
5. List major complications of DM
6. List targets for therapy, lab testing with frequency for Type 2 DM.
7. List standards of care for Type 2 DM

Scope of the problem
• 29.1 million people – 9.3% of the population
  – Diagnosed: 21.0 million people.
  – Undiagnosed: 8.1 million people
    • (27.8% of people with diabetes are undiagnosed).
• #7 Cause of death in USA - 75,535; 2.9% (2015)
• Increased risk with Obesity “epidemic”
**Age-adjusted** percentage of people aged 20 years or older with diagnosed diabetes, by race/ethnicity, United States, 2010–2012

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Percentage of People with Diagnosed Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic whites</td>
<td>7.6</td>
</tr>
<tr>
<td>Asian Americans</td>
<td>9.0</td>
</tr>
<tr>
<td>Hispanics</td>
<td>12.8</td>
</tr>
<tr>
<td>Non-Hispanic blacks</td>
<td>13.2</td>
</tr>
<tr>
<td>American Indians/Alaska Natives</td>
<td>15.9</td>
</tr>
</tbody>
</table>

*Based on the 2000 U.S. standard population.

**Diagnosed and undiagnosed diabetes among people aged 20 years or older, United States, 2012**

<table>
<thead>
<tr>
<th>Category</th>
<th>Number with Diabetes (Million)</th>
<th>Percentage with Diabetes (Unadjusted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>28.3</td>
<td>12.3</td>
</tr>
<tr>
<td>20 years or older</td>
<td></td>
<td></td>
</tr>
<tr>
<td>By age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-44</td>
<td>4.3</td>
<td>4.1</td>
</tr>
<tr>
<td>45-64</td>
<td>13.4</td>
<td>16.2</td>
</tr>
<tr>
<td>65 years or older</td>
<td>11.2</td>
<td>25.9</td>
</tr>
<tr>
<td>By sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>15.3</td>
<td>13.6</td>
</tr>
<tr>
<td>Women</td>
<td>13.6</td>
<td>11.2</td>
</tr>
</tbody>
</table>


**DIABETES**

29.1 million people have diabetes
That's about 1 out of every 5 people

1 out of 4 do not know they have diabetes

**COST**

$245 billion
Total medical costs and lost work and wages for people with diagnosed diabetes

Medical costs for people with diabetes are twice as high as for people without diabetes.
34.9% or 78.6 million of U.S. adults are obese.
What's in a Name?

**Etymology of Diabetes Mellitus**

- Diabetes = Greek to pass through, a siphon
  - Greek from dia (through)
  - Greek from bainein (to go)
  - any disorder characterized by polyuria

- Mellitus (vs. Insipid: lacking flavor)
  - Greek (mel referring to the sweetness of honey)

**Types of Diabetes**

- Diabetes Insipidus
  - Nephrogenic
  - Central

- **Diabetes Mellitus (hyperglycemia)**

**Types of Diabetes Mellitus**

- Diabetes Mellitus (hyperglycemia)
  - Type 1 (5-10%)
    - Juvenile DM, Insulin dependent DM
  - **Type 2 (90-95%)**
    - Adult onset DM, Non-insulin dependent DM (initially)
    - Gestational Diabetes
    - Other (1-5%)
      - Genetic defects of beta cell fx or insulin action
      - Defects of exocrine pancreas (Cystic Fibrosis)
      - Drug or chemical induced
Symptoms of DM

- Polyuria
- Polydipsia
- Rarely, weight loss
- Intermittent blurred vision
- Majority are asymptomatic

The Case of Mr. DM

D.M. is a 44 year old obese man with a BMI of 34 who presents to establish care and routine physical exam. His past medical and surgical history are unremarkable. He takes no medications and he has no allergies. His father was diagnosed with diabetes in his 70's and had a coronary artery bypass surgery at age 72.

D.M. drinks alcohol in moderation and does not smoke tobacco. He rarely exercises. His review of systems is negative. On exam he has truncal obesity but otherwise the exam is unremarkable. His blood pressure is 146/92.

Fasting labs are ordered and are significant for total cholesterol 216mg/dL; LDL 133mg/dL; HDL 34mg/dL; TG 243 mg/dL; and fasting blood glucose of 112mg/dL.
Screening for Type 2 DM in Adults

ADA
• BMI > 25, with 1 or more risk factors
  – Or, begin at age 45 if no risk factors
  – Rec 3 yr interval
  – If IFG, you would follow more frequently

Risk Factors
• Age > 45
• BMI >25, >30
• A1C > 5.7
• HTN (>140/90)
• HDL < 35 mg/dl and/or TG > 250 mg/dl
• Physical inactivity
• First degree relative with DM
• Give birth to baby weighing >9 lb or gestational DM
• Polycystic Ovarian Syndrome
• Ethnicity (non-white)
• History of CVD or PVD

Screening for Type 2 DM in Adults

USPSTF
• BP >135/80
  – If BP <135/80

• 40 to 70 years who are overweight or obese
  – Or earlier if:
    ...have a family history of diabetes, have a history of gestational diabetes or PCOS, or are members of certain racial/ethnic groups
    (African Americans, American Indians or Alaskan Natives, Asian Americans, Hispanics or Latinos, or Native Hawaiians or Pacific Islanders)
The Case of Mr. DM

What is the clinical diagnosis?
   – Impaired fasting glucose or pre-diabetes with hyperlipidemia and hypertension (unconfirmed)

These form the constellation known as the metabolic syndrome: which is significant in predicting high risk patients to develop DMII and CVD

Risk Factors

- Age > 45
- BMI >25, >30
- A1C > 5.7
- HTN (≥140/90)
- HDL < 35 mg/dl and/or TG > 250 mg/dl
- Physical inactivity
- First degree relative with DM
- Give birth to baby weighing >9 lb or gestational DM
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Metabolic Syndrome

Co-occurrence of metabolic risk factors for both type 2 diabetes and CVD

- Abdominal obesity
- Hyperglycemia
- Dyslipidemia
- Hypertension

Diagnosis of Diabetes Mellitus

1. Fasting Blood Sugar (8 hours)
2. Random Blood Sugar with symptoms
3. Hemoglobin A1C
4. Oral Glucose Tolerance Test (75 gm)

Diagnosis of Diabetes Mellitus

<table>
<thead>
<tr>
<th>Pre-diabetes</th>
<th>Diabetes Mellitus</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS 101 – 125</td>
<td>FBS ≥ 126</td>
</tr>
<tr>
<td>A1C* 5.7 – 6.4%</td>
<td>A1C ≥ 6.5%</td>
</tr>
<tr>
<td>OGTT with BS 140-199</td>
<td>OGTT with BS &gt; 200</td>
</tr>
<tr>
<td>AKA</td>
<td>Random BS ≥ 200 + sx</td>
</tr>
<tr>
<td>- Impaired glucose tolerance</td>
<td></td>
</tr>
<tr>
<td>- Impaired fasting glucose</td>
<td></td>
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</table>
5 – 10% of prediabetes progress to DM per year

The Case of Mr. DM

What interventions have proven to be useful at this stage?

– Aggressive lifestyle modifications (diet, exercise, weight loss)
  • reduce the incidence of DM by 58%

– Metformin
  • Reduce the incidence of DM by 31%

The Case of Mr. DM

After six months he has lost 10% of his body weight from diet and exercise efforts – labs look better (LDL lower, FBG 103) and his BP dropped below 140/90. You encourage him to keep going. He does not return to clinic for two years. His weight is back up, his cholesterol is elevated again. A HgA1c is drawn and is 10.2%. FBG is 244 mg/dL.
So What?

Clinical significance of hyperglycemia?
- Acute: dehydration, immunosuppression
  - Chronic: Long term complications

Not nearly as dangerous as hypoglycemia

Complications of DM
- Microvascular
  - Retinopathy (blindness)
  - Neuropathy (non-healing ulcer amputation)
  - Nephropathy (ESRD—dialysis/transplant)

- Macrovascular (accelerated atherosclerosis)
  - Myocardial infarction
  - Stroke
  - Peripheral Vascular Disease
The Case of Mr. DM

Question 4

a. Microvascular:
   nephropathy, retinopathy, neuropathy

b. Macrovascular:
   cardiovascular disease and stroke

Complications of DM

- Glucotoxicity is key mediator
- 2-4x incidence of CAD death and stroke compared to non-diabetics
- 75% have HTN
- 15-20 yrs after onset of hyperglycemia
  - Retinopathy, Nephropathy, Neuropathy

Retinopathy

- 60-80%
  - some form of retinopathy 15-20 yrs after dx
- Hypoxia induced overexpression of VEGF in retina,
- Rx Intravitreous injection of antiangiogenic agents
### Nephropathy
- 30-40% develop clinical evidence of nephropathy (proteinuria), but only a smaller % progressed to ESRD
- Native Americans/AA/Hispanics have higher risk of ESRD than whites
- By 20 yrs, about 20% with overt nephropathy will develop ESRD needing dialysis or transplant

### Neuropathy
- Stocking/glove = distal, symmetric, polyneuropathy
- Also mononeuropathy – sudden foot drop, wrist drop, or isolated CN palsies
- Also autonomic neuropathy – gastroparesis, erectile dysfunction

### Complication Screening
- **Annual:**
  - Retinal Exam*: detecting / treating eye disease can reduce severe vision loss by 50 – 60%
  - Microalbuminuria: detecting nephropathy early, treat with ACE-I
  - Foot Exam: monofilament along with comprehensive foot care can reduce amputation rates by 45 – 85%
Lifestyle Modifications

• Dietary Change
  – Reduce overall daily calorie intake
  – Reduce carbohydrates, especially simple
  – Increase in nutrient dense food

• Physical Activity / Exercise
  – Cardiopulmonary exertion

• Weight Loss

Lifestyle Modifications

• Diabetes Prevention Program
  – Now covered by Medicare!
  – 5-7% weight loss and physical activity of 150 min per week (30 min daily, 5 days per week)

• Diabetes Self Management Training
  – Also covered by Medicare
  – Four critical time points for referral
  – Review of 7 Self-Care Behaviors*
  – DSMT is associated with improved diabetes knowledge and self care behaviors, lower A1c, lower self reported weight, improved quality of life, healthy coping, and reduced health care costs.

*Monitoring, Healthy Eating, Reducing Risks, Physical Activity, Problem Solving, Healthy Coping, Taking Medication

Basic nutrition

• No one-size-fits-all eating pattern
  • Medication Nutrition Therapy (MNT) by a Registered Dietitian (RD) decreases A1c, 3-1.0% in people with type 1 diabetes and 0.5-2.0% for people with type 2 diabetes

• Focus on: Nutrient-dense high-quality foods versus “avoiding” specific nutrients
  • Limit simple sugars/processed foods and focus on whole grains, vegetables, fruits, legumes and dairy

• Stage of care:
  • Flexible Insulin Therapy Program: Carbohydrate Counting
  • Fixed Mealtime Insulin Dosing: Consistent Carbohydrate Pattern
  • Diabetes on oral medication or no medication: MyPlate and 3 – 6 small meals with controlled carbohydrate portions
Basic nutrition

• CVD Risk: Mediterranean-style diet rich in monounsaturated fats and 1,500 – 2,300 mg sodium restriction pending existing hypertension
  – Emphasize: nuts, seeds, fatty fish, healthy oils... What else has monounsaturated fat?

• OTC micronutrients and herbal supplements:
  What are your patients given taking and is it FDA approved?
  – No clear evidence that supplementation with vitamins, minerals, herbs or spices can improve outcomes in patients with diabetes who do not have underlying deficiency (i.e. think pre-existing conditions or meds predisposing to a deficiency such as metformin and Vitamin B12)

• Alcohol?
  – May place people with diabetes at increased risk for hypoglycemia, especially with insulin or insulin secretagogues

Basic Nutrition

• Weight Loss
  Diet, physical activity and behavioral activity should be prescribed for overweight and obesity in type 2 diabetes ready to achieve weight loss

<table>
<thead>
<tr>
<th>Treatment</th>
<th>BMI categories (kg/m²)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>21.5&lt; or 25.0–26.9</td>
</tr>
<tr>
<td>Diet, physical activity, and behavioral therapy</td>
<td>+</td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>+</td>
</tr>
<tr>
<td>Metabolic surgery</td>
<td>+</td>
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</table>

*Cut-off points for Asian American individuals. Treatment may be indicated for selected overweight patients.

Treatment Targets

• Blood Glucose: A1C – 7%
  – every 1% drop in A1C lowers risk of microvascular complications by 40%

• Blood Pressure: <140/90*
  – Every 10 mmHg drop of sys BP lowers CV risk of complications by 12%

• Cholesterol:
  – Improved control of LDL can reduce CV complications by 20 – 50%
Medical Therapy

- Oral Hypoglycemic Therapy
- Insulin Therapy
- Statin Therapy

The Case of Mr. DM

What type of pharmacologic therapy would you start now? (HgA1c of 10.2%)
- Metformin
- CV risk
  - glucagon-like peptide-1 (GLP-1) receptor agonist
  - sodium-glucose co-transporter 2 (SGLT2) inhibitor
- Combination of metformin and sulfonylurea
- Consider DPP-4
Average Cost:

- $7 - $20 / 30 days
- $10 - $30 / 90 days

For glipizide:

- $4 - $20 / 30 days
- $10 - $30 / 90 days
<table>
<thead>
<tr>
<th>Average Cost: sitagliptin</th>
</tr>
</thead>
<tbody>
<tr>
<td>$300+ / 30 days</td>
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</table>

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Strength (mg)</th>
<th>Quantity</th>
<th>Cost per 30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitaglipin</td>
<td>100 mg</td>
<td>30 tablets</td>
<td>$300+</td>
</tr>
<tr>
<td></td>
<td>25 mg</td>
<td>30 tablets</td>
<td>$150+</td>
</tr>
<tr>
<td></td>
<td>5 mg</td>
<td>30 tablets</td>
<td>$50+</td>
</tr>
</tbody>
</table>

Note: The quantities and costs are approximate and subject to change. Always consult a healthcare professional for the latest information.
Insulin

Cost ranges greatly:
- Formulation: long acting, short acting
- Delivery; syringes, quick pen

Preventive Measures

- Daily aspirin risk/benefit
- Statin therapy
- Ophthalmology; retinal exam
- Foot Exam: monofilament w/ pulse check
- Microalbumin yearly
- Pneumococcal vaccine, Hep B vaccine, Flu
- Smoking cessation

Question 6
Key EBM studies and DM

• DCCT (type 1 DM)
• UKPDS (type 2 DM)
• Kumamato (type 2 DM)
• ADVANCE
• ACCORD
• VADT