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DIAGNOSIS AND CLASSIFICATION OF DIABETES
Objectives

▶ At conclusion of the lecture the participant will be able to:

1. Differentiate between the classifications of diabetes
2. Discuss screening for diabetes
3. List diagnostic criteria for diabetes
4. Describe the components of a comprehensive diabetes evaluation
Classification of Diabetes

- Type 1 diabetes
  - $\beta$-cell destruction
- Type 2 diabetes
  - Progressive insulin secretory defect
- Other specific types of diabetes
  - Genetic defects in $\beta$-cell function, insulin action
  - Diseases of the exocrine pancreas
  - Drug- or chemical-induced
- Gestational diabetes mellitus (GDM)

ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S8
Criteria for the Diagnosis of Diabetes

• A1C ≥6.5%

  OR

• Fasting plasma glucose (FPG) ≥126 mg/dL (7.0 mmol/L)

  OR

• 2-h plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT

  OR

• A random plasma glucose ≥200 mg/dL (11.1 mmol/L)

ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S9; Table 2.1
Criteria for the Diagnosis of Diabetes

A1C ≥ 6.5%

- The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.

ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S9; Table 2
Fasting plasma glucose (FPG) ≥126 mg/dL (7.0 mmol/L)

Fasting is defined as no caloric intake for at least 8 h*

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.
Criteria for the Diagnosis of Diabetes

• 2-h plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT

• The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water*

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.

ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S9; Table 2.1
Criteria for the Diagnosis of Diabetes

• In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis,
  • a random plasma glucose $\geq 200$ mg/dL (11.1 mmol/L)

ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S9; Table 2.1
### Diabetes and Prediabetes

<table>
<thead>
<tr>
<th></th>
<th>Prediabetes</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FBG</strong></td>
<td>100-125 mg/dl</td>
<td>≥126 mg/dl</td>
</tr>
<tr>
<td>Casual (random) plasma glucose, if classic symptoms of hyperglycemia</td>
<td>140 – 199 mg/dl</td>
<td>&gt; 200 mg/dl</td>
</tr>
<tr>
<td><strong>A1C</strong></td>
<td>5.7% - 6.4%</td>
<td>≥ 6.5%</td>
</tr>
</tbody>
</table>
Advantages and disadvantages of screening tests

Fasting Blood Glucose

- Advantages
  - Low cost
  - Extensive experience
  - Widespread availability
Disadvantages

- Fasting required
- Only reflects glycemic status at time of test
- Variability due to sample source
- Samples less stable
- Can be effected by acute illness
- Not good predictor of chronic complications
- Not globally standardized
Advantages

- Fasting not necessary
- Low biological variability
- Marker of long-term glycemia
- Stable during acute illness
- Greater sample stability
- Better predictor of chronic complications
- Globally standardized
A1C

- index of average glucose over the preceding weeks to months
- life-span averages about 120 days average glucose (AG) over the preceding weeks-to-months
- The level of HbA1c at any point in time is contributed to by all circulating erythrocytes, from the oldest (120 days old) to the youngest
A1C Cont’d

- HbA1c

- Weighted Average

- A1c can increase or decrease relatively quickly with large changes in glucose
A1C Disadvantages

- Not accurate with hemoglobinopathies
- Not reliable with anemia
- Nor reliable if there was a recent transfusion
- False lows in advanced renal disease
- Racial and ethnic differences
- Higher cost
Correlation with A1C and Blood Glucose

- The relationship between A1C and eAG is described by the formula 28.7 X A1C – 46.7 = eAG

<table>
<thead>
<tr>
<th>HbA1c (%)</th>
<th>eAG (mg/dL)</th>
<th>eAG (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>97</td>
<td>5.4</td>
</tr>
<tr>
<td>6</td>
<td>126</td>
<td>7.0</td>
</tr>
<tr>
<td>7</td>
<td>154</td>
<td>8.6</td>
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<tr>
<td>8</td>
<td>183</td>
<td>10.2</td>
</tr>
<tr>
<td>9</td>
<td>212</td>
<td>11.8</td>
</tr>
<tr>
<td>10</td>
<td>240</td>
<td>13.4</td>
</tr>
<tr>
<td>11</td>
<td>269</td>
<td>14.9</td>
</tr>
<tr>
<td>12</td>
<td>298</td>
<td>16.5</td>
</tr>
</tbody>
</table>
2-hour plasma glucose during 75-gram OGTT

Advantages

- Most sensitive test
- Earliest marker of glucose dysregulation
2-hour plasma glucose during 75-gram OGTT

Disadvantages
- Fasting required
- Significant biological variability
- Not good predictor of chronic complications
- Time consuming
- Higher cost
- Not globally standardized
Components of the Comprehensive Diabetes Evaluation (4)

Physical examination (1)
- Height, weight, BMI
- Blood pressure determination, including orthostatic measurements when indicated
- Fundoscopic examination
- Thyroid palpation
- Skin examination (for acanthosis nigricans and insulin injection sites)

Inform type 1 diabetes patients of the opportunity to have their relatives screened for type 1 diabetes risk in the setting of a clinical research study.

ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S9; Table 2.1
Categories of Increased Risk for Diabetes (Prediabetes)*

- FPG 100–125 mg/dL (5.6–6.9 mmol/L): IFG
- OR
- 2-h plasma glucose in the 75-g OGTT 140–199 mg/dL (7.8–11.0 mmol/L): IGT
- OR
- A1C 5.7–6.4%

*For all three tests, risk is continuous, extending below the lower limit of a range and becoming disproportionately greater at higher ends of the range.

ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S10; Table 2.3
Recommendations: Testing for Diabetes in Asymptomatic patients

➢ Consider testing overweight/obese adults (BMI ≥25 kg/m² or ≥ 23 kg/m² in Asian Americans) with one or more additional risk factors for type 2 diabetes; for all patients, particularly those who are overweight, testing should begin at age 45 years B

➢ If tests are normal, repeat testing at least at 3-year intervals is reasonable C

➢ To test for diabetes/prediabetes, the A1C, FPG, or 2-h 75-g OGTT are appropriate B

➢ In those with prediabetes, identify and, if appropriate, treat other CVD risk factors B

ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S11
Testing should be considered in all adults who are overweight (BMI ≥25 kg/m²* or ≥23 kg/m² in Asian Americans) and have additional risk factors:

- Physical inactivity
- First-degree relative with diabetes
- High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
- Women who delivered a baby weighing >9 lb or were diagnosed with GDM
- Hypertension (≥140/90 mmHg or on therapy for hypertension)
Recommendations: Testing for Diabetes in Asymptomatic Patients (cont’d)

- HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
- Women with polycystic ovarian syndrome (PCOS)
- A1C ≥5.7%, IGT, or IFG on previous testing
- Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
- History of CVD
In the absence of criteria (risk factors on previous slides), and particularly in those who are overweight or obese, testing for diabetes should begin at age 45 years.

If results are normal, testing should be repeated at least at 3-year intervals, with consideration of more frequent testing depending on initial results (e.g., those with prediabetes should be tested yearly), and risk status.

ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S10; Table 2.2
Testing to detect type 2 diabetes and prediabetes should be considered in children and adolescents who are overweight and who have two or more additional risk factors for diabetes.

ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S11
Recommendations: Detection and Diagnosis of GDM (1)

- Screen for undiagnosed type 2 diabetes at the first prenatal visit in those with risk factors, using standard diagnostic criteria B

- Screen for GDM at 24–28 weeks of gestation in pregnant women not previously known to have diabetes A

- Screen women with GDM for persistent diabetes at 6–12 weeks postpartum, using OGTT, nonpregnancy diagnostic criteria E

ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S13
Recommendations: Detection and Diagnosis of GDM (2)

- Women with a history of GDM should have lifelong screening for the development of diabetes or prediabetes at least every 3 years \textbf{B}

- Women with a history of GDM found to have prediabetes should receive lifestyle interventions or metformin to prevent diabetes \textbf{A}

\textit{ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S13}
Screening for and Diagnosis of GDM
One-step Strategy

- Perform a 75-g OGTT, with plasma glucose measurement fasting and at 1 and 2 h, at 24–28 weeks of gestation in women not previously diagnosed with overt diabetes

- Perform OGTT in the morning after an overnight fast of at least 8 h

ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S14; Table 2.5
Screening for and Diagnosis of GDM One-step Strategy

- GDM diagnosis: when any of the following plasma glucose values are exceeded
  - Fasting: 92 mg/dL (5.1 mmol/L)
  - 1 h: 180 mg/dL (10.0 mmol/L)
  - 2 h: 153 mg/dL (8.5 mmol/L)
Step 1: Perform 50-g GLT (nonfasting) with plasma glucose measurement at 1 h at 24–28 weeks of gestation in women not previously diagnosed with overt diabetes.

If plasma glucose level measured at 1 h after load is $\geq 140$ mg/dL* (7.8 mmol/L), proceed to step 2, 100-g OGTT.

*ACOG recommends 135 mg/dL in high-risk ethnic minorities with higher prevalence of GDM.
Screening for and Diagnosis of GDM
Two-step Strategy (2)

**Step 2:** 100-g OGTT is performed while patient is fasting. The diagnosis of GDM is made if 2 or more of the following plasma glucose levels are met or exceeded:

<table>
<thead>
<tr>
<th>Carpenter/Coustan</th>
<th>or</th>
<th>NDDG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fasting</strong></td>
<td>95 mg/dL (5.3 mmol/L)</td>
<td>105 mg/dL (5.8 mmol/L)</td>
</tr>
<tr>
<td><strong>1h</strong></td>
<td>180 mg/dL (10.0 mmol/L)</td>
<td>190 mg/dL (10.6 mmol/L)</td>
</tr>
<tr>
<td><strong>2h</strong></td>
<td>155 mg/dL (8.6 mmol/L)</td>
<td>165 mg/dL (9.2 mmol/L)</td>
</tr>
<tr>
<td><strong>3h</strong></td>
<td>140 mg/dL (7.8 mmol/L)</td>
<td>145 mg/dL (8.0 mmol/L)</td>
</tr>
</tbody>
</table>

ADA. 2. Classification and Diagnosis. Diabetes Care 2015;38(suppl 1):S14; Table 2.5
Recommendations: Cystic Fibrosis–Related Diabetes (CFRD) (1)

- Annual screening for CFRD with OGTT should begin by age 10 years in all patients with cystic fibrosis who do not have CFRD. A1C as a screening test for CFRD is not recommended.

- In patients with cystic fibrosis and IGT without confirmed diabetes, prandial insulin therapy should be considered to maintain weight.
A complete medical evaluation should be performed to:

- Classify the diabetes
  - Detect presence of diabetes complications
  - Review previous treatment, risk factor control in patients with established diabetes
  - Assist in formulating a management plan
  - Provide a basis for continuing care

- Perform laboratory tests necessary to evaluate each patient’s medical condition

Screening Recommendation

- Consider screening those with type 1 diabetes for other autoimmune diseases (thyroid, vitamin B12 deficiency, celiac) as appropriate.
Establishing a Diagnosis of Type 1 DM

C peptide
- reflects the amount of endogenous insulin
- T1DM – low
- T2DM - normal to high levels

The hormone insulin is formed by chemical modification and cleavage of a precursor molecule. The cleaved "C-peptide" is useful for monitoring residual beta cell function in people with diabetes who are on insulin therapy.
T1DM

Autoantibodies
- Islet cell autoantibodies
- Insulin autoantibodies
- Glutamic acid decarboxylase (GAD)
- Zinc transporter autoantibodies
LADA

- Latent autoimmune diabetes in adults includes
  - Heterogeneous group of conditions that are phenotypically similar to type 2 diabetes,
  - Autoantibodies that are common with T1DM
- Diagnostic criteria
  - More common in adults usually Age \( \geq 30 \)
  - No insulin treatment for six months after diagnosis – eventually will need insulin
Antibodies

- Presence of autoantibodies to:
  - glutamic acid decarboxylase
  - islet cells,
  - tyrosine phosphatase
  - (IA-2α and IA-2β)
  - insulin.
LADA

~ 10% to 15% of patients classified as T2DM
Positive for at least one of the islet antibodies

Age

> 40% older than 40
> 20% older than 55
Differences between T1DM and LADA

- Antibody clustering
- T-cell reactivity
- Genetic susceptibility
Monogenic Diabetes
Maturity-Onset Diabetes of Youth

MODY

- Monogenic defects in $\beta$ cell function
- Inherited in an autosomal dominant pattern
- Usually onset is < 25 year of age
- Most children diagnosed with diabetes by age 6 months (neonatal diabetes) have MODY not T1DM
Components of the Comprehensive Diabetes evaluation
Components of the Comprehensive Diabetes Evaluation (1)

Medical history (1)

- Age and characteristics of onset of diabetes (e.g., DKA, asymptomatic laboratory finding)
- Eating patterns, physical activity habits, nutritional status, and weight history; growth and development in children and adolescents
- Diabetes education history
- Review of previous treatment regimens and response to therapy (A1C records)
Components of the Comprehensive Diabetes Evaluation (2)

Medical history (2)
- Current treatment of diabetes, including medications, adherence and barriers thereto, meal plan, physical activity patterns, readiness for behavior change
- Results of glucose monitoring, patient’s use of data
- DKA frequency, severity, cause
- Hypoglycemic episodes
  - Hypoglycemic awareness
  - Any severe hypoglycemia: frequency, cause

Components of the Comprehensive Diabetes Evaluation (3)

Medical history (3)
- History of diabetes-related complications
  - Macrovascular: CHD, cerebrovascular disease, PAD
  - Other: psychosocial problems,* dental disease*
- Microvascular: retinopathy, nephropathy, neuropathy
  - Sensory neuropathy, including history of foot lesions
  - Autonomic neuropathy, including sexual dysfunction and gastroparesis

*See appropriate referrals for these categories.

Components of the Comprehensive Diabetes Evaluation (4)

Physical examination (1)
- Height, weight, BMI
- Blood pressure determination, including orthostatic measurements when indicated
- Fundoscopic examination
- Thyroid palpation
- Skin examination (for acanthosis nigricans and insulin injection sites)

Acanthosis Nigricans
Questions?