New Rules for Diagnosing Hyperglycemia in Pregnancy: Impact on Fetus and Mother

These webinars are made possible by:

Navajo Area Sweet Success Group Associate Programs

Navajo Area Diabetes Program

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Novo Nordisk is changing diabetes
New Rules for Diagnosing Hyperglycemia in Pregnancy Impact on Fetus and Mother

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Maternal Fetal Medicine

UC San Diego
School of Medicine
Outline

• What’s new in the diagnosis of T2DM?
• Why treat GDM?
• Why consensus was needed?
• HAPO Trial
• New Guidelines
• Preliminary UCSD Data
>1/3 of women in the US are Obese

64% are overweight or Obese
Preschool obesity
A new study says 18 percent of preschoolers are obese, with higher percentages among most minorities.

Prevalence of obesity
4-year-olds. 2005

American Indian/Native
Alaskans 31.2%
Hispanics 22.0%
Black non-Hispanic 20.8%,
White non-Hispanic 15.9%
Asian 12.8%

Source: National Center for Education Statistics
USA: Diabetes & Prediabetes - Diagnosed And Undiagnosed

--10.7% Diabetes

+ 19% Prediabetes = approximately 29% of adult US population
2010: Criteria for diagnosis of diabetes

1. A1C 6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

   OR

2. FPG 126 mg/dl. Fasting is defined as no caloric intake for at least 8 h.*

   OR

3. 2-h plasma glucose 200 mg/dl during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

   OR

4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose 200 mg/dl.

*In the absence of unequivocal hyperglycemia, criteria 1–3 should be confirmed by repeat testing.
Prediabetes 2010
Glucose Categories of increased risk for Diabetes

**A1C 5.7–6.4%**

**IFG:** FPG 100 mg/dl to 125 mg/dl

**IGT:** 2-h PG ;75-g OGTT 140 mg/dl to 199 mg/dl

*For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at higher ends of the range*
Diagnostic Criteria in Pregnancy

- Prior to 24 weeks
- Same Criteria
  - Fasting ≥ 126 mg/dL
  - A1C ≥ 6.5%
  - Random plasma glucose of >200mg/dL
    confirmation
Why Treat GDM?
Pederson Hypothesis

FETUS

FETAL HYPERGLYCEMIA

FETAL HYPERINSULINEMIA (cord c-peptide)

MACROSOMIA

MOTHER

PLACENTA

GLUCOSE

INSULIN
Are Our Children Becoming Obese…
Long Term Effects

Nutrition in utero and infancy

- Undernutrition increases risk
- Overfeeding increases risk
- Breastfeeding lowers risk

Risk of fatness as adults

Adult Obesity After Prenatal Diabetes Exposure

BMI was 2.6 kg/m² higher

Dabelea et al, Diabetes, 2000
Childhood Metabolic Syndrome
Effect of Exposure to Maternal GDM

[Bar chart showing prevalence of MS for different groups: LGA/GDM, AGA/GDM, LGA/Con, AGA/Con. LGA/GDM has the highest prevalence marked with an asterisk.]
**FIGURE 2.** Diabetes begets diabetes: the alterations of maternal fuel metabolism lead to altered fetal islet function (hyperinsulinism). This intrauterine event predisposes to, or identifies risk for childhood obesity and adolescent IGT, GDM, and later DM. Reproduced from *Diabetes in Women*, 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2004 with permission.
Can Treatment of GDM Reduce Fetal Obesity?
Why Treat?

The NEW ENGLAND JOURNAL of MEDICINE

Effect of Treatment of Gestational Diabetes Mellitus on Pregnancy Outcomes

Treatment of GDM Reduces Adverse Outcome

<table>
<thead>
<tr>
<th>OUTCOME</th>
<th>ROUTINE CARE (N = 510)</th>
<th>INTERVENTION (N = 490)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Weight</td>
<td>3482 ± 660</td>
<td>3335 ± 551</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>LGA</td>
<td>22%</td>
<td>13%</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Macrosomia</td>
<td>21%</td>
<td>10%</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>18%</td>
<td>12%</td>
<td>0.02</td>
</tr>
<tr>
<td>SGA</td>
<td>7%</td>
<td>7%</td>
<td>ns</td>
</tr>
</tbody>
</table>

20% of intervention group required insulin

Crowther CA, et al. NEJM, 2005
A Multicenter, Randomized Trial of Treatment for Mild Gestational Diabetes

Mark B. Landon, M.D., Catherine Y. Spong, M.D., Elizabeth Thom, Ph.D.,
Marshall W. Carpenter, M.D., Susan M. Ramin, M.D., Brian Casey, M.D.,
Ronald J. Wapner, M.D., Michael W. Varner, M.D., Dwight J. Rouse, M.D.,
John M. Thorp, Jr., M.D., Anthony Sciscione, D.O., Patrick Catalano, M.D.,
Margaret Harper, M.D., George Saade, M.D., Kristine Y. Lain, M.D.,
Yoram Sorokin, M.D., Alan M. Peaceman, M.D., Jorge E. Tolosa, M.D., M.S.C.E.,
and Garland B. Anderson, M.D., for the Eunice Kennedy Shriver National
Institute of Child Health and Human Development Maternal–Fetal
Medicine Units Network*
Why Treat?

12% of patients in treatment group required pharmacotherapy

Landon, et al. NEJM 2009
Was Consensus for Diagnosing GDM Needed?
# Diagnosing GDM in the US

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fasting</strong></td>
<td>90mg/dL</td>
<td>105mg/dL</td>
<td>95mg/dL</td>
<td>95mg/dL</td>
</tr>
<tr>
<td><strong>1-hr</strong></td>
<td>165mg/dL</td>
<td>190mg/dL</td>
<td>180mg/dL</td>
<td>180mg/dL</td>
</tr>
<tr>
<td><strong>2-hr</strong></td>
<td>145mg/dL</td>
<td>165mg/dL</td>
<td>155mg/dL</td>
<td>155mg/dL</td>
</tr>
<tr>
<td><strong>3-hr</strong></td>
<td>125mg/dL</td>
<td>145mg/dL</td>
<td>140mg/dL</td>
<td>140mg/dL</td>
</tr>
</tbody>
</table>
## Diagnosing GDM Outside the US

<table>
<thead>
<tr>
<th>Group</th>
<th>Glucose load</th>
<th>FPG mg/dL</th>
<th>1-hr mg/dL</th>
<th>2-hr mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADIPS</td>
<td>75 gm</td>
<td>100</td>
<td></td>
<td>144</td>
</tr>
<tr>
<td>EASD</td>
<td>75 gm</td>
<td>108</td>
<td></td>
<td>162</td>
</tr>
<tr>
<td>CDA</td>
<td>75 gm</td>
<td>95</td>
<td>190</td>
<td>160</td>
</tr>
<tr>
<td>WHO/NICE</td>
<td>75 gm</td>
<td>126</td>
<td></td>
<td>140</td>
</tr>
</tbody>
</table>
HAPO Trial

• Observational Trial
• Given a 75-gram 2-hour oral glucose tolerance test (OGTT) at about 28 weeks of gestation
• Exclusion criteria
  – Fasting > 105
  – 2 hour > 200
• Routine prenatal care
HAPO Trial

• Primary Outcomes
  – BW>90\textsuperscript{th} %ile
  – Neonatal hypoglycemia
  – Neonatal hyperinsulinemia
    (c peptide>90\textsuperscript{th} %ile)
  – Primary cesarean delivery

• Secondary Outcomes
  – Neonatal fat mass
  – Shoulder dystocia
  – Preterm delivery
  – Pre-eclampsia
  – NICU admission
<table>
<thead>
<tr>
<th>Category</th>
<th>FPG</th>
<th>1-hr PG</th>
<th>2-hr PG</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt; 75</td>
<td>≤ 105</td>
<td>≤ 90</td>
</tr>
<tr>
<td>2</td>
<td>75 – 79</td>
<td>106 - 132</td>
<td>91 – 108</td>
</tr>
<tr>
<td>3</td>
<td>80 – 84</td>
<td>133 – 155</td>
<td>109 – 125</td>
</tr>
<tr>
<td>4</td>
<td>85 – 89</td>
<td>156 – 171</td>
<td>126 – 139</td>
</tr>
<tr>
<td>5</td>
<td>90 – 94</td>
<td>172 – 193</td>
<td>140 – 157</td>
</tr>
<tr>
<td>6</td>
<td>95 – 99</td>
<td>194 – 211</td>
<td>158 - 177</td>
</tr>
<tr>
<td>7</td>
<td>≥ 100</td>
<td>≥ 212</td>
<td>≥ 178</td>
</tr>
</tbody>
</table>
Results of HAPO

- Birth Weight > 90th Percentile
- Primary C-Section
- Clinical Hypoglycemia
- Cord C-Peptide >90th Percentile

Each graph shows the frequency (%) of different glucose categories over time (Fasting, One Hour, Two Hour) for each of the four categories.
Fasting Plasma Glucose and Outcomes
1-Hour Plasma Glucose and Outcomes
2-Hour Plasma Glucose and Outcomes

The graph illustrates the frequency (%) of outcomes exceeding the 90th percentile for different concentrations (mg/dl) of glucose. The outcomes are categorized into different concentration ranges:

- Birthweight
- % Body fat
- Cord C-peptide

The graph shows an increasing trend in frequency (%) as the concentration increases.
From Associations to Diagnostic Criteria: What Is the IADPSG*?

**Affiliated Organizations**

- EASD
- JAPD (Japan)
- ADIPS (Australasia)
- West Coast USA DPSG
- DPSI (India)
- Canadian Special Interest Group for Diabetes and Pregnancy

**Associated Groups**

- European Association of Perinatal Medicine
- Society of Maternal Fetal Medicine
- ADA Pregnancy Council

*International Association of Diabetes in Pregnancy Study Group*
Setting GDM OGTT Cut-Points

**Neonatal Outcomes**

90\(^{th}\) Percentile:
- Birth weight, Body fat, C-peptide insulin
- Odds Ratio 1.75

**75 gram 2 hour GTT**
- Fasting greater than or equal to 92
- 1 hour greater than or equal to 180
- 2 hour greater than or equal to 153
## Diagnosis of GDM in Pregnancy: Threshold Values

<table>
<thead>
<tr>
<th>Glucose Measure</th>
<th>mg/dl</th>
<th>&amp; HAPO values ≥ Threshold*</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG</td>
<td>92</td>
<td>8.3</td>
</tr>
<tr>
<td>1-hr OGTT-PG</td>
<td>180</td>
<td>14.0</td>
</tr>
<tr>
<td>2-hr OGTT-PG</td>
<td>153</td>
<td>16.1</td>
</tr>
</tbody>
</table>

Approximately 1.7% Unblinded → 17.8 % diagnosed with GDM
## Frequencies of Outcomes: Glucose Values < or > Threshold

<table>
<thead>
<tr>
<th>Outcome</th>
<th>% All Values &lt; Threshold</th>
<th>% Any ≥ 92/180/153</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birthweight &gt;90th percentile</td>
<td>8.3</td>
<td>16.2</td>
</tr>
<tr>
<td>Cord C-peptide &gt;90th percentile</td>
<td>6.7</td>
<td>17.5</td>
</tr>
<tr>
<td>% Body fat &gt;90th percentile</td>
<td>8.5</td>
<td>16.6</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>4.5</td>
<td>9.1</td>
</tr>
<tr>
<td>Preterm birth (&lt;37 weeks)</td>
<td>6.4</td>
<td>9.4</td>
</tr>
<tr>
<td>Shoulder dystocia/birth injury</td>
<td>1.3</td>
<td>1.8</td>
</tr>
<tr>
<td>Primary Cesarean section</td>
<td>16.8</td>
<td>24.4</td>
</tr>
</tbody>
</table>
### Frequencies of Outcomes: Comparison of RCT & HAPO

<table>
<thead>
<tr>
<th>Outcome</th>
<th>NICHD RCT</th>
<th>FPG&lt;95</th>
<th>FPG &lt;95</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not treated</td>
<td>Treated (1-hr &gt;180; 2hr &gt;155)</td>
<td>(1-hr &lt;180; 2-hr &lt;155)</td>
</tr>
<tr>
<td>BW &gt;90(^{th}) percentile</td>
<td>14.5</td>
<td>7.1</td>
<td>14.0</td>
</tr>
<tr>
<td>C-peptide &gt;95(^{th}) percentile</td>
<td>22.8</td>
<td>17.7</td>
<td>18.2 (90(^{th}) %)</td>
</tr>
<tr>
<td>NICU admission</td>
<td>11.6</td>
<td>9.0</td>
<td>11.4</td>
</tr>
<tr>
<td>Shoulder Dystocia</td>
<td>4.0</td>
<td>1.5</td>
<td>1.9</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>5.5</td>
<td>2.5</td>
<td>8.3</td>
</tr>
</tbody>
</table>
### Fasting Hyperglycemia

Table of Adjusted Odds Ratios for Associations Between Maternal Fasting Glucose Categories and Primary Outcomes, adapted from Riskin-Mashia, et al; Diabetes Care 2009

<table>
<thead>
<tr>
<th>FAST GLU</th>
<th>Number (% of total)</th>
<th>LGA and/or Macrosomia (% outcome)</th>
<th>LGA and/or Macrosomia (C.I) OR</th>
<th>No. 1st CS (% with outcome)</th>
<th>1st CS OR (C.I)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 &lt;75</td>
<td>1525 (24.9)</td>
<td>120 (7.9)</td>
<td>1.0</td>
<td>182 (12.7)</td>
<td>1.0</td>
</tr>
<tr>
<td>2 75-79</td>
<td>1587 (25.9)</td>
<td>134 (8.4)</td>
<td>1.08 (0.84-1.40)</td>
<td>222 (14.9)</td>
<td>1.21 (0.98-1.5)</td>
</tr>
<tr>
<td>3 80-84</td>
<td>1427 (23.3)</td>
<td>168 (11.8)</td>
<td>1.56 (1.22-2.00)</td>
<td>195 (14.8)</td>
<td>1.22 (0.98-1.52)</td>
</tr>
<tr>
<td>4 85-89</td>
<td>893 (14.6)</td>
<td>100 (11.2)</td>
<td>1.48 (1.12-1.95)</td>
<td>141 (17.0)</td>
<td>1.43 (1.12-1.82)</td>
</tr>
<tr>
<td>5 90-94</td>
<td>415 (6.8)</td>
<td>61 (14.7)</td>
<td>2.02 (1.45-2.80)</td>
<td>58 (15.9)</td>
<td>1.45 (1.04-2.00)</td>
</tr>
<tr>
<td>6 95-99</td>
<td>179 (2.9)</td>
<td>31 (17.3)</td>
<td>2.45 (1.60-3.77)</td>
<td>28 (17.3)</td>
<td>1.56 (1.00-2.42)</td>
</tr>
<tr>
<td>7 100-105</td>
<td>103 (1.7)</td>
<td>20 (19.4)</td>
<td>2.82 (1.67-4.76)</td>
<td>17 (20.0)</td>
<td>1.94 (1.11-3.41)</td>
</tr>
</tbody>
</table>
Summary of IADPSG Recommendations

- **First Prenatal Visit:** Test for overt DM on all or only “high risk” women
  - Fasting plasma glucose
  - HbA1c
  - Random plasma glucose
- **Results not diagnostic of overt diabetes**
  - FPG ≥92 mg/dl (<126 mg/dl) = GDM
  - FPG <92 mg/dl: 75gm OGTT 24 – 28 weeks
- **If one abnormal value on 75g OGTT= GDM**
USA: Diabetes & Prediabetes - Diagnosed And Undiagnosed

• 17-18% GDM

• 29% of adult US population
  – 10.7% Diabetes + 19% Prediabetes

• Rate is consistent with current population trends
**DAPP Modification**

**First Prenatal Visit (<13 wks)**
- Many cases of diabetes or abnormal glucose tolerance are not detected until pregnancy.
- Early detection reduces complications.
  - **Test:** Women who have ANY risk factor:
    - Non-Caucasian
    - BMI ≥ 25 (at risk BMI may be lower in some ethnic groups)
    - History of GDM or pre-diabetes, unexplained stillbirth, malformed infant
    - Previous baby 4000 gm or more (8 lbs 13 oz)
    - 1st degree relative with diabetes mellitus
    - Glucosuria
    - Medications that raise glucose (e.g. steroids, betamimetics, atypical antipsychotics)
    - Polycystic ovarian syndrome, cardiovascular disease, hypertension, hyperlipidemia

**Universal Testing at 24-28 weeks**
- 2011 ADA standard is 75 gm 2h OGTT for all women not previously diagnosed with diabetes @ 24-28 weeks gestation
- Fast 8-10 hours, remain seated during test
- Consider adding to third trimester labs

*If entry to care 13-23 6/7 weeks and risk factors are present, test as soon as possible with a 75 gm 2 hour Oral Glucose Tolerance Test (OGTT)*

---

<table>
<thead>
<tr>
<th>FPG: _______</th>
<th>1 hr: _______</th>
<th>2 hr: _______</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 92 mg/dL</td>
<td>≥ 180 mg/dL</td>
<td>≥ 153 mg/dL</td>
</tr>
</tbody>
</table>

**Add A1c or FPG or Random Glucose to Prenatal labs**
- Date: ________  
  - Result: ________

**A1c ≥ 6.5%**
- or FPG ≥ 126 mg/dL,
- or Random ≥ 200mg/dL

**Diagnose Type 2 Diabetes**

**A1c 5.7 - 6.4%**
- or FPG ≥ 92 mg/dL and < 126 mg/dL

**Treat as Gestational Diabetes Mellitus (GDM)**

**A1c < 5.7% or FPG < 92**

**Test @ 24 – 28 wks with OGTT**

**If any value at or above cut off, treat as GDM**

---

**REFER TO SWEET SUCCESS**

**Date Referred: ________**

**NOTE:** For early diagnosis (prior to 24 weeks gestational age), Sweet Success will obtain A1c at initial visit after referral

*If entry to care 13 - 23 6/7 weeks and risk factors are present, test as soon as possible with a 75 gm 2 hour OGTT*

Modified from CDAPP website
Why Incorporate A1C?

- Measurement now standardized and reliable
- FPG- 12-15% variance
- A1C- 1-9% variance

**A1C 5.7–6.4%**

- Impaired glucose tolerance as defined by ADA
- WHO recommends treatment of impaired glucose tolerance
Any Data on A1C

- 124 women with GDM
- OGTT compared to A1C
- A1C of 6% - identified 87% of GDM patients
- Small trial
- Retrospective

Benefits of New Guidelines

• Diagnosis of overt diabetes
• 75g 2 hour GTT
  — Comparable to rest of the world
• Potential improvement in neonatal outcomes
Concerns Regarding New Guidelines

• Prospective interventional trial is needed
• Cost effectiveness data lacking
  – Increase in potential interventions
  – Utilization of resources
• Long term neonatal data lacking
NIH Consensus Statement

• One Step criteria for diagnosis
  – Operational advantage
  – Consistent, international diagnostic standard across lifespan
  – Standardization of best practices in patient care
  – Comparability for research purposes

• Drawbacks
  – Increase prevalence of GDM
  – Data lacking on improvement of outcomes
  – Concerns about medical interventions
  – Concerns about cost
  – Concern about psychologic impact