Gestational Diabetes: New Rules for Diagnosis: Which to Follow?

Thomas Moore MD

Objectives:
at the conclusion of this session the participant will

• Have learned what’s new in the diagnosis of T2DM
• Be able to outline the benefits of treating GDM
• Summarize the results of the HAPO Trial
• Understand the basis for new Diagnostic Guidelines
• Appreciate the preliminary data obtained at UCSD
1/3 of women in the US are Obese

Number and Percentage of U.S. Population with Diagnosed Diabetes, 1958-2008

US RATES OF GDM, 1989-2004

Getahun et al AJOG 2008;52561-a5
Criteria for Type 2 Diabetes (ADA)

1. A1C > 6.5%.
   OR
2. FPG > 126 mg/dl.
   OR
3. 2-h plasma glucose >200 mg/dl during an 75 g OGTT.
   OR
4. A random plasma glucose >200 mg/dl.

*In the absence of unequivocal hyperglycemia, criteria 1–3 should be confirmed by repeat testing.

‘Prediabetes’ = Those Likely to Develop Type 2 Diabetes Within 5 Years

- A1C 5.7–6.4%
- Impaired Fasting Glucose (IFG) – 100 -- 125 mg/dl
- Impaired Glucose Tolerance (IGT) – 2-h PG on 75-g OGTT = 140 -- 199 mg/dl

ADA Recommendations: Detection and Diagnosis of GDM

- Screen for undiagnosed type 2 diabetes at the first prenatal visit in those with risk factors, using standard diagnostic criteria (B)
- In pregnant women not previously known to have diabetes, screen for GDM at 24–28 weeks’ gestation, using a 75-g OGTT and specific diagnostic cut points (B)
- What to do with Prediabetes?
  - FPG 100-125 mg/dl?
  - HbA1c 5.7 – 6.4%?
**US: Diabetes & Prediabetes**

10.7% Diabetes  
+  
19% Prediabetes  
________________  
almost 30% of adult US population

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**US Childhood Obesity**

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**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  

<table>
<thead>
<tr>
<th>Group</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Indian/</td>
<td>31.7%</td>
</tr>
<tr>
<td>Native Alaskan</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>22.0%</td>
</tr>
<tr>
<td>Black, non-Hispanic</td>
<td>20.8%</td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>15.9%</td>
</tr>
<tr>
<td>Asian</td>
<td>12.2%</td>
</tr>
</tbody>
</table>

SOURCE: National Center for Education Statistics
Are Our Children Becoming Fat Because We Overfeed Them or …

*Because they were overfed in the womb and are 'programmed' for obesity?*

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**Adult Obesity After Prenatal Diabetes Exposure**

- Siblings not exposed to diabetes in utero
- Siblings exposed to diabetes in utero

BMI was 2.6 kg/m² higher

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**Childhood Metabolic Syndrome: Effect of Exposure to Maternal GDM**

- LGA/GDM
- AGA/GDM
- LGA/Con
- AGA/Con

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Pathophysiology of Fetal Obesity with Diabetes

Long Term Effects of Maternal Hyperglycemia
Can Treatment of GDM Reduce Fetal Obesity And Downstream Diabetes?

- Two RCTs

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>

Crowther CA, et al. NEJM, 2005

20% of intervention group required insulin
Mild GDM RCT: Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Treated</th>
<th>Untreated</th>
<th>RR</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birthweight g</td>
<td>3302 +/- 502</td>
<td>3408 +/- 589</td>
<td>0.0005</td>
<td></td>
</tr>
<tr>
<td>Birthweight &gt; 4000g</td>
<td>5.9</td>
<td>14.3</td>
<td>0.41</td>
<td>0.0001</td>
</tr>
<tr>
<td>LGA %</td>
<td>7.1</td>
<td>14.5</td>
<td>0.49</td>
<td>0.0006</td>
</tr>
<tr>
<td>Fetal mass g</td>
<td>427 +/- 198</td>
<td>466 +/- 222</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>Preterm %</td>
<td>9.5</td>
<td>11.6</td>
<td>0.81</td>
<td>0.28</td>
</tr>
<tr>
<td>SGA %</td>
<td>7.5</td>
<td>6.4</td>
<td>1.18</td>
<td>0.49</td>
</tr>
<tr>
<td>NICU Admit %</td>
<td>9</td>
<td>11.6</td>
<td>0.77</td>
<td>0.19</td>
</tr>
<tr>
<td>IV Glucose</td>
<td>5.3</td>
<td>6.8</td>
<td>0.77</td>
<td>0.32</td>
</tr>
<tr>
<td>RDS</td>
<td>1.9</td>
<td>2.9</td>
<td>0.66</td>
<td>0.33</td>
</tr>
</tbody>
</table>

If GDM Treatment is Beneficial, Whom Should We Treat?
Question for Audience:

Are you presently using the
-- Two Step Test?
-- One Step Test?
-- Both?

Diagnosing GDM in the US:
3 Hour 100gm OGTT

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>90mg/dL</td>
<td>105mg/dL</td>
<td>95mg/dL</td>
<td>95mg/dL</td>
</tr>
<tr>
<td>1-hr</td>
<td>165mg/dL</td>
<td>190mg/dL</td>
<td>180mg/dL</td>
<td>180mg/dL</td>
</tr>
<tr>
<td>2-hr</td>
<td>145mg/dL</td>
<td>165mg/dL</td>
<td>155mg/dL</td>
<td>155mg/dL</td>
</tr>
<tr>
<td>3-hr</td>
<td>125mg/dL</td>
<td>145mg/dL</td>
<td>140mg/dL</td>
<td>140mg/dL</td>
</tr>
</tbody>
</table>

2 Abnormal Values = GDM

Diagnosing GDM Outside the US:
2 Hr 75 gm OGTT

<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>144</td>
<td></td>
</tr>
<tr>
<td>EASD</td>
<td>75 gm</td>
<td>108</td>
<td>162</td>
<td></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>
The History of the OGTT in Pregnancy – O’Sullivan and Mahan

- 752 unselected pregnant women recruited on registration at Boston City Hospital in 1956 – 1957 underwent a 100-g 3 hr OGTT.
- These data generated statistical norms (means + SDs).
- A second selected group of 1013 women received the 100-g OGTT in pregnancy and were retested annually in the nonpregnant state for up to 8 years.

Likelihood of Type 2 DM after Gestational Diabetes – O’Sullivan and Mahan

Follow-up results on cohort 2 (predictive performance with dichotomized data)

<table>
<thead>
<tr>
<th>Threshold values</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive (%)</th>
<th>Negative (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean + 3SD</td>
<td>24.1</td>
<td>96.2</td>
<td>59.7</td>
<td>84.6</td>
</tr>
<tr>
<td>Mean + 2SD</td>
<td>61.2</td>
<td>74.2</td>
<td>36.1</td>
<td>89.7</td>
</tr>
<tr>
<td>Mean + 1SD</td>
<td>99.5</td>
<td>33.7</td>
<td>25.7</td>
<td>99.6</td>
</tr>
</tbody>
</table>

What’s Wrong with the Two Step GDM Test?

<table>
<thead>
<tr>
<th>50g Cutoff</th>
<th>Dx%</th>
<th>% OGTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>140 mg/dl</td>
<td>80%</td>
<td>10%</td>
</tr>
<tr>
<td>130 mg/dl</td>
<td>90%</td>
<td>20%</td>
</tr>
</tbody>
</table>
Fetal Growth Dynamics

The metabolic clock is ticking!

9#14oz, cesarean
Hyperglycemia and Adverse Pregnancy Outcomes (HAPO)

- 25,505 pregnant women at 15 centers in nine countries
- 75-g OGTT at 24 - 32 weeks of gestation.
- Data collected from 'non-GDMs' with
  - FPG ≤ 105 and
  - 2-hour PG ≤ 200


Should GDM Diagnostics Identify Downstream Maternal Type 2 Diabetes or Fetal Risk?

- O’Sullivan and Mahan focused on subsequent maternal disease.
- HAPO focused on fetal effects of maternal hyperglycemia
  - 25,505 pregnant women at 15 centers in 9 countries
  - 75-g OGTT at 24 to 32 weeks of gestation.
- Primary outcomes were birth weight above the 90th percentile for gestational age, primary cesarean delivery, clinically diagnosed neonatal hypoglycemia, and cord-blood serum C-peptide level above the 90th percentile.


HAPO Trial Outcomes

- Primary Outcomes
  - BW>90th %ile
  - Neonatal hypoglycemia
  - Neonatal hyperinsulinemia (c peptide>90th %ile)
  - Primary cesarean delivery
- Secondary Outcomes
  - Neonatal fat mass
  - Shoulder dystocia
  - Preterm delivery
  - Pre-eclampsia
  - NICU admission
Fasting Plasma Glucose and Outcomes

Using HAPO Data for Setting GDM OGTT Cut-Points

Neonatal Outcomes

75 gram 2 hour GTT: Any Value:

- Fasting > 92
- 1 hour ≥ 180
- 2 hour ≥ 153

90th Percentile:

- Birth weight
- Body fat
- C-peptide insulin

Odds Ratio 1.75

International Association of Diabetes in Pregnancy Study Groups -- 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
3 IADPSG Recommendations

- Diagnose overt Type 2 diabetes early in pregnancy
- Diagnose Prediabetes early in pregnancy and treat as GDM
- Diagnose GDM at 24-28 weeks using
  - One Step 75g OGTT

Summary of IADPSG Recommendations

- **First Prenatal Visit:**
  - Diagnose Type 2 Diabetes
    - FPG ≥126 mg/dL, HbA1c ≥ 6.5,
  - Diagnose Prediabetes:
    - FPG 92 - 126 mg/dl, HbA1c 5.7 – 6.4
- **24 – 28 weeks: 75g 2 hr OGTT**
  - FPG 92
  - 1 hr 180
  - 2 hr 153
- **If any one abnormal value on 75g OGTT = GDM**

Arguments Against IADPSG Switch

- OGTT has poor reproducibility
- Even with very strict threshold values, only a minority of fetal macrosomia will be identified
- GDM is related to childhood obesity, but mainly in case of maternal obesity
- Overdiagnosis of GDM may result in overtreatment, expense, medical stigma
- Stricter OGTT criteria will result in increasing workload

Visser GHA. AJOG. http://dx.doi.org/10.1016/j.ajog.2012.10.881
Arguments For IADPSG Switch

- Previous OGTT thresholds were set in such a way that about 2.5% of population would classify as GDM, irrespective of perinatal outcome
- Striking recent increase in obesity and type 2 diabetes in general population may well correspond to GDM incidence of about 20%
- Treatment of GDM improves perinatal outcome
- Diagnosis is cost-effective

NicHD GDM Consensus 2012: Evidence Report

- Evidence supports association of maternal glucose with macrosomia and CS using either 75 g or 100 g OGTT. However clear thresholds for increased risk were not found.
- Treatment of GDM results in less preeclampsia and macrosomia.
- Current evidence does not show that GDM treatment affects neonatal hypoglycemia or future metabolic outcomes.
- There is little evidence of short-term harm from treating GDM other than an increased demand for services.

NicHD GDM Consensus 2012: Panel Report

- The two-step approach is largely restricted to the United States. There would be value in a consistent, international diagnostic standard across one’s lifespan.
- However, the one-step approach, as proposed by the IADPSG, is anticipated to increase the frequency of the diagnosis of GDM by twofold to threefold, to a prevalence of approximately 15% to 20%.
NICHD GDM Consensus 2012: Panel Report (2)

- One Step will generate
  - additional direct and indirect healthcare costs, labeling of newly GDM women, may increase CS and NICU admissions.
  - Increased costs, life disruptions, and psychosocial burdens.
- Available studies do not provide clear evidence that the One Step is cost-effective in comparison with the current two-step.
- Therefore, the Two Step is affirmed (pending new data).

UCSD Experience with IADPSG and California Sweet Success Guidelines
2 Step vs IADPSG Screening Results

- Traditional screening January - June 2011
- IADPSG screening June - December 2011
- 120 patients diagnosed with GDM
- GDM diagnosed in 3.8% by 2 step criteria (January - June 2011)
- GDM diagnosed in 8% by new IADPSG criteria (July - December 2011)
- 2.5% diagnosed with T2DM (A1c ≥6.5% or FPG ≥126mg/dL)

UCSD IADPSG Diagnoses of GDM

- Data from July 2011 - December 2011

| First Visit |
|-----------------|----------|--------|----------|----------|
| A1C N=23 |
| FPG N=9 |
| Both A1C + FPG N=11 |
| 2 hour GTT N=20 |
| Traditional 2 Step N=57 |
| n=43 |
| A1GDM 9 3 4 11 33 |
| A2GDM 14 6 7 9 24 |
| Birthweight 3045±862 3648±524 2981±776 3284±366 3313±476 |
| Ponderal Index 2.5±0.35 2.62±0.31 2.49±0.33 2.48±0.32 2.56±0.36 |

UCSD IADPSG GDM Diagnosis in First Trimester

- Total of 43 patients
- The median GA at medication start for all first trimester diagnoses was 17.2 wks (9.3-33wks)
- 23/43 (53%) with A1C alone
  - The median GA at medication start was 20.3 wks (9.3-33 wks).
  - 7/23 (30%) of the A1C only group started medication prior to 20 wks (median GA 18.3 wks)
New ACOG GDM Guideline 2013

ACOG GDM 2013: Early Screening.
For GDM, T2DM or Both?
- Early Screen
  - Prior GDM
  - Impaired glucose tolerance or impaired fasting glucose
  - Obesity (BMI > 30)
- Does not specify: GCT/3hrOGTT or FPG/A1c. Both?
- If negative, do GDM 2-step testing at 24-28 weeks
Question for Audience:

Are you presently doing First Trimester GDM Screening Y/N?

ACOG GDM 2013 Affirms 2 Step
Which GCT Value: 130/135/140 mg/dl?

• Cites Esakoff et al AJOG (2005) 193, 1040–4
• “140 mg/dl has lower false-positive rates and improved positive predictive values”
• “130 and 135 mg/dl have only ‘marginal’ improvements in sensitivity”
• In absence of clear data, recommends use of 135 or 140 mg/dl “consistently” in each practice.

Question for Audience:

If you are using 2 Step, what GCT cutoff?
130 mg/dl
135 mg/dl
140 mg/dl
ACOG GDM 2013: GCT Thresholds

ACOG GDM 2013
Continue the 3hr OGTT

Postpartum Testing of GDM
Future Directions

• 1 Step or 2 Step? Choose for your organization.
• Future data needed:
  - Cost-effectiveness data
  - Follow-up of IADPSG mothers to determine risk of later development of diabetes
  - Follow-up of offspring to assess long term risks related to prenatal GDM
• Optimize glucose control!
• Use GDM as an opportunity to change life trajectory!