

Screening for gestational diabetes revisited

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Gestational Diabetes Mellitus

- Significance and consequences of GDM
- Traditional diagnostic criteria
- Insights from recent studies
- Screening for GDM updated

Gestational Diabetes Mellitus

- Significance and consequences of GDM

Gestational diabetes

- Defined as “any degree of glucose intolerance with onset or first recognition during pregnancy”
- Important because it impacts maternal and child health care both during and after pregnancy

Endocrinology of Pregnancy

- The placenta produces larger quantities of hormones than any other human organ:
 - Human placental lactogen
 - Estrogen / progesterone
- The majority of its products are released into the maternal circulation to induce changes on the fetuses' behalf.

Glucose Metabolism in Pregnancy

- Fetal growth is dependent upon maternal glucose
- Carbohydrates from maternal diet
- Stored glycogen converted to glucose
- High levels of glucose transported by diffusion to the fetus
- Fetal production of insulin

Glucose Metabolism in Pregnancy

- First Half of Pregnancy (Anabolic)
 - Pancreatic beta-cell hyperplasia causes hyperinsulinemia
 - Increased uptake and storage of glucose
- Second Half of Pregnancy (Catabolic)
 - Placental hormones block glucose receptors and cause insulin resistance
 - Increased lipolysis
 - Increased gluconeogenesis
 - Decreased glycogenesis
 - Increased glucose and amino acids for the fetus

Gestational Diabetes

- Defined by Statistical Criteria
 - 3-hour 100 gram oral glucose tolerance test
 - Abnormal defined as 2 or more values at, or above, two standard deviations above the mean
- Originally described to identify a group of women at increased risk of type 2 diabetes
- Later identified as a group at increased risk of pregnancy complications (Pedersen Hypothesis)
- The debate about the break point between 'normal' and 'abnormal' continues to this day.



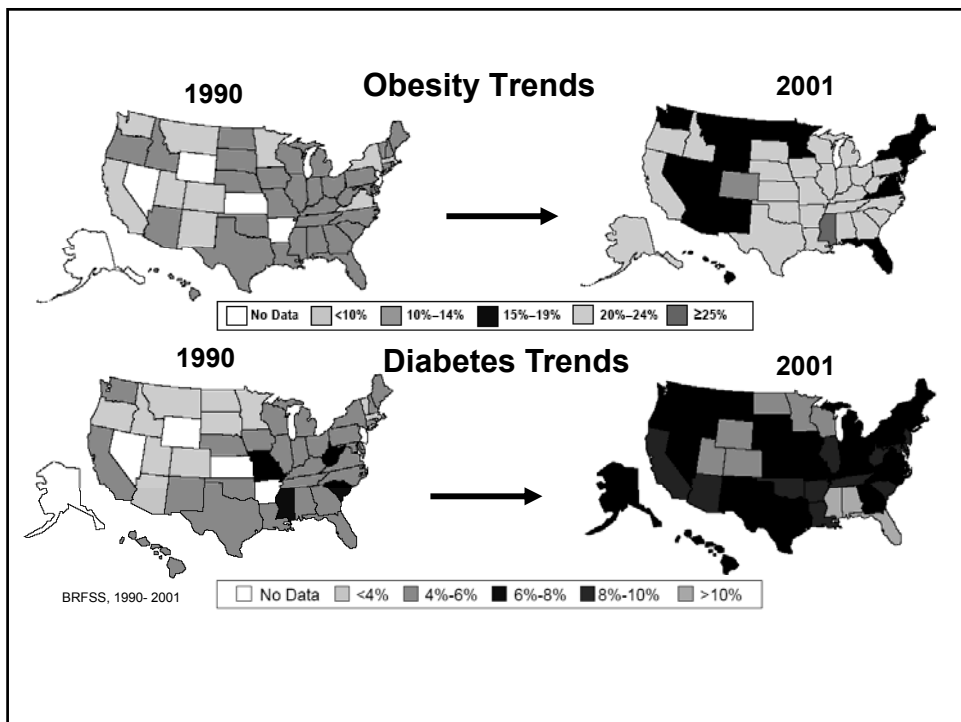
Maternal hyperglycemia
↓
Fetal hyperglycemia
↓
Fetal hyperinsulinemia
↓



Pederson Hypothesis
(1952)

Gestational diabetes

- Underlying risk factors include increased maternal age, obesity, h/o GDM in prior pregnancy, h/o large babies



Gestational Diabetes

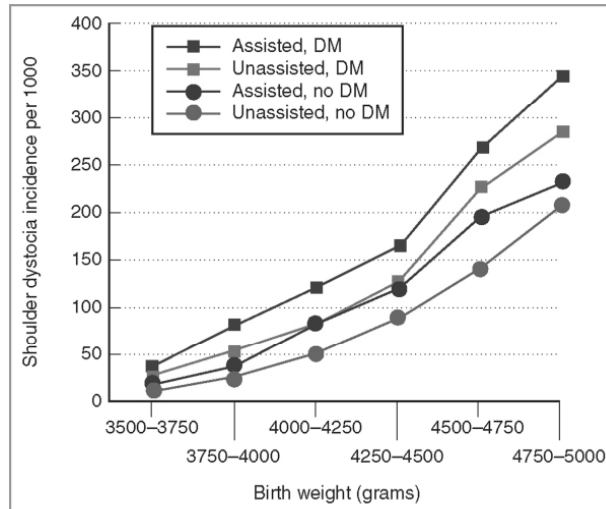
Maternal Risks

- Excessive weight gain
- Preeclampsia
- Cesarean section
- Future gestational diabetes
- Subsequent type 2 diabetes and heart disease

Risks to Offspring

- ⊕ Macrosomia
- ⊕ Birth trauma
- ⊕ Hypoglycemia
- ⊕ Delayed lung maturation
- ⊕ Hypocalcemia
- ⊕ Polycythemia
- ⊕ Stillbirth
- ⊕ Childhood disease

Neonatal Morbidity - Shoulder Dystocia



Nesbitt TS et al *AJOG* 1998

Gestational Diabetes Mellitus

- Traditional diagnostic criteria

Diagnostic criteria for gestational diabetes

- Chosen to identify women at high risk of diabetes after pregnancy
- Derived from criteria used for non-pregnant individuals
- Not designed to identify pregnancies with increased risk for adverse perinatal outcomes

Recommendations for screening for GDM

- Depended on who you asked!!
 - ADA
 - ACOG
 - WHO
 - 4th International Workshop-Conference on GDM
 - National Diabetes Data Group
 - United States Preventive Services Task Force
 - 5th International Workshop-Conference on GDM

Screening for GDM

- First step: Early identification of risk factors
- Second step: One hour 50 g glucose screen
- Third step: Three hour 100 g OGTT for diagnosis

Risk Factors for GDM: Assess at First Prenatal Visit

- **Overweight before pregnancy (BMI > 25)**
- **1st degree relative with diabetes**
- **Previous glucose intolerance/ GDM**
- **Previous macrosomia or large for gestational age baby**
- PCOS
- Age > 25 yrs
- Members of certain ethnic groups
- Multiparous women (13%)
- *Left column are **MAJOR RISK factors***

Screening for GDM

- Risk assessment at first visit, with no screening for low risk
 - Low-risk ethnicity (Caucasian, European)
 - Age < 25
 - BMI \leq 25
 - No known diabetes in first degree relative
 - No h/o glucose intolerance
 - No h/o obstetric complications usually associated with GDM

4th International Workshop-
Conference on Gestational
Diabetes Mellitus, ADA, ACOG

50–G oral glucose tolerance screen for GDM

7.8 mmol/l cutoff -- 80% sensitivity

7.2 mmol/l cutoff -- 90% sensitivity

Alternatively, patients with high risk factors can go directly to diagnostic testing instead of initial screening

ADA and WHO Criteria for the Diagnosis of Gestational Diabetes Mellitus

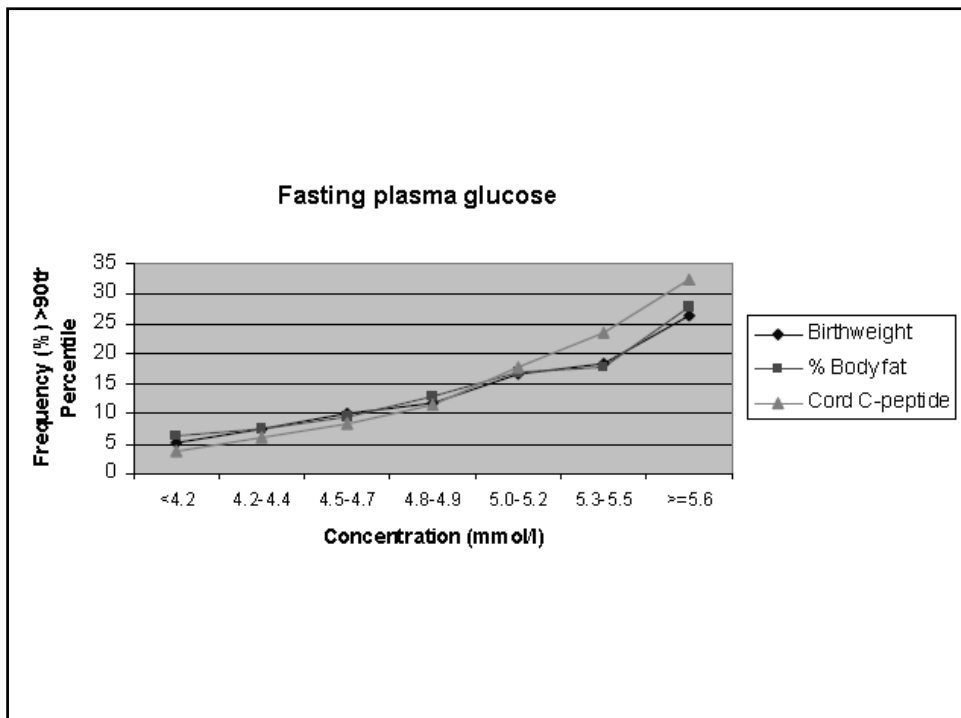
	ADA 100-g	ADA 75-g	WHO 75-g
Fasting (mmol/l)	5.3	5.3	7.0
1-hour (mmol/l)	10.0	10.0	----
2-hour (mmol/l)	8.6	8.6	7.8
3-hour (mmol/l)	7.8	----	----
Two or more values must be met or exceeded for dx of GDM with 100 g OGTT			

Gestational Diabetes Mellitus

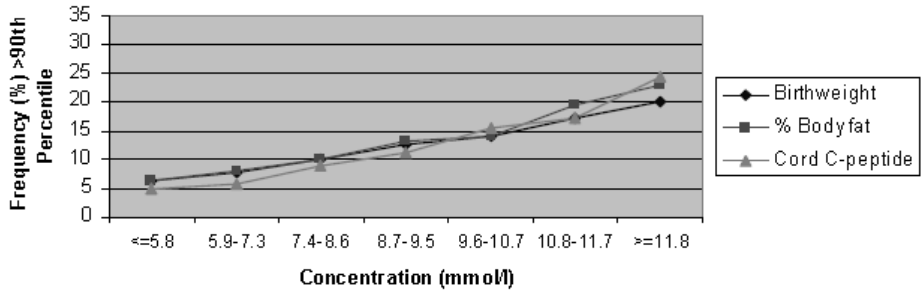
- Insights from recent studies

Hyperglycemia and Adverse Pregnancy Outcomes (HAPO). NEJM. May, 2008.

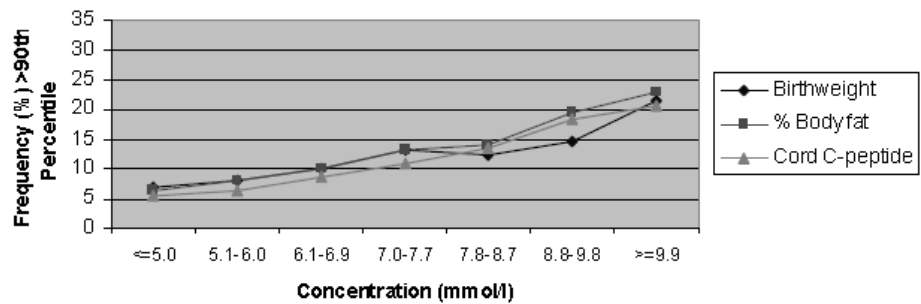
- Hypothesis: maternal hyperglycemia less severe than overt DM will still increase risk for adverse pregnancy outcomes
- 25,505 pregnant women at 15 centers in 9 countries underwent 75-g oral glucose-tolerance testing at 24-32 weeks gestation



1 hour plasma glucose



2 hour plasma glucose



Outcome	FPG, 1-hr and 2-Hr OGTT values all < threshold	FPG and/or 1-hr and/or 2-hr OGTT values > threshold
Birthweight > 90 th percentile	8.3%	16.2%**
Cord C-peptide > 90 th percentile	6.7%	17.5%**
Percent body fat > 90 th percentile	8.5%	16.6%**
Preeclampsia	4.5%	9.1%**
Preterm delivery (< 37 weeks)	6.4%	9.4%**
Primary cesarean section	16.8%	24.4%**
Shoulder dystocia and/or birth injury	1.3%	1.8%*
Clinical neonatal hypoglycemia	1.9%	2.7%*
Hyperbilirubinemia	8.0%	10.0%**
Intensive neonatal care	7.8%	9.1%*

*Threshold values: FPG \geq 5.1 mmol/l (92 mg/dl), 1-hr PG \geq 10.0 mmol/l (180 mg/dl), 2-hr \geq 8.5 mmol/l (153 mg/dl)
 *Difference between groups significant at p < 0.01
 **Difference between groups significant at p < 0.001

Hyperglycemia and Adverse Pregnancy Outcomes (HAPO). NEJM, May, 2008.

Conclusions

- With increasing maternal glucose levels, the frequency of each primary outcome increased, although less so for clinical neonatal hypoglycemia than for the others
- Secondary outcomes of preeclampsia, shoulder dystocia or birth injury, premature delivery, NICU admit, and hyperbilirubinemia also showed significant positive associations with maternal glycemia

HAPO Conclusion

- Strong, continuous associations of maternal glucose levels below those diagnostic of GDM were seen with birthweight and increased cord-blood C-peptide levels.
- The current criteria for diagnosing and treating hyperglycemia during pregnancy needs to be re-evaluated.

Gestational Diabetes Mellitus

- Screening for GDM updated

International Association of Diabetes and Pregnancy Study Groups' Recommendations

- First prenatal visit
 - Measure FPG, A1C, or random glucose on all or only high-risk women
 - If results indicate overt diabetes , treat and f/u as for preexisting diabetes
 - If results are not diagnostic of overt diabetes and FPG \geq 5.1mmol/l but $<$ 7.0mmol/l, diagnose as GDM; if FPG $<$ 5.1mmol/l, test for GDM at 24-28 weeks

*International Association of Diabetes
and Pregnancy Study Groups, 2009*

Derivation of HAPO-based glucose thresholds for GDM

- Average glucose values at which odds for birthweight, cord C-peptide and %body fat $>$ 90th centile reached 1.75 times the estimated odds of these outcomes at mean glucose values, based on fully adjusted logistic regression models

International Association of Diabetes and Pregnancy Study Groups' Recommendations

Booking visit - to diagnose overt diabetes (preexisting) in pregnancy

Measure of glycemia	Threshold
Fasting glucose	≥ 7.0 mmol/l
HbA1C	≥ 48 mmol/mol (6.5%)
Random glucose	≥ 11.1 mmol/l

International Association of Diabetes and Pregnancy Study Groups, 2009

International Association of Diabetes and Pregnancy Study Groups' Recommendations

- First prenatal visit
 - Measure FPG, A1C, or random glucose on all or only high-risk women
 - If results indicate overt diabetes, treat and f/u as for preexisting diabetes
 - If results are not diagnostic of overt diabetes and FPG ≥ 5.1 mmol/l but < 7.0 mmol/l, diagnose as GDM; if FPG < 5.1 mmol/l, test for GDM at 24-28 weeks
- 24-28 weeks
 - 2-hr 75-g OGTT after overnight fast on all women not previously found to have overt diabetes or GDM
 - Overt diabetes if FPG ≥ 7.1 mmol/l
 - GDM if one or more values equals or exceeds thresholds
 - Normal if all values on OGTT less than thresholds

International Association of Diabetes and Pregnancy Study Groups, 2009

International Association of Diabetes and Pregnancy Study Groups' Recommendations

24 – 28 weeks : Diagnosis of GDM (75-g OGTT)

Glucose measure	Glucose threshold
FPG	5.1 mmol/l
1-hr plasma glucose	10.0 mmol/l
2-hr plasma glucose	8.5mmol/l

*One or more of these values must be met or exceeded for diagnosis of GDM

International Association of Diabetes and Pregnancy Study Groups, 2009

International Association of Diabetes and Pregnancy Study Groups' Recommendations

24 – 28 weeks : Diagnosis of GDM (75-g OGTT)

Glucose measure	Cumulative % GDM
FPG	8.3
1-hr plasma glucose	14.0
2-hr plasma glucose	16.1

*One or more of these values must be met or exceeded for diagnosis of GDM

International Association of Diabetes and Pregnancy Study Groups, 2009

Screening for GDM - remaining questions

- Cost effectiveness of different strategies in different healthcare settings
- Development of simpler strategies that do not require OGTT
- Optimal management including glycemic targets in pregnancy
- Optimal follow-up post-pregnancy