Gestational Diabetes

Brenda Dawley, MD
Associate Professor, Department of Obstetrics and Gynecology
Marshall University, Joan C Edwards School of Medicine

Laura Mullarky, RN CDE
Diabetes Nurse Specialist, Cabell Huntington Hospital Perinatal Center

Sponsored by
West Virginia DHHR, Office of Maternal, Child and Family Health, Diabetic Work Group and
The West Virginia Perinatal Partnership CAMC Health Education & Research Institute

Objectives

PARTICIPANTS WILL BE ABLE TO:

- 1. discuss screening methods to diagnose gestational diabetes
- 2. understand the physiology of gestational diabetes and its effect on the fetus and neonate
- 3. describe the medical management options for gestational diabetes
- 4. counsel patients regarding life style changes for improved outcomes

Disclosure

- It is the policy of the CAMC Health Education and Research Institute that any faculty (speaker) who makes a presentation at a program designated for AMA Physician's Recognition Award (PRA) Category I or II credit must disclose any financial interest or other relationship (i.e. grants, research support, consultant, honoraria) that faculty member has with the manufacturer(s) of any commercial product(s) that may be discussed in the educational presentation.
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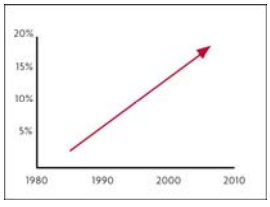
Gestational Diabetes Update

- Definitions and Physiology
- Diagnostic Tests
- Patient Management

The Diabetes Epidemic

- The majority of older Americans are now diabetic or pre-diabetic.
- The incidence of gestational diabetes has risen from 2.5% to 18.5% or more.



Endocrinology of Pregnancy

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

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

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

Pedersen Hypothesis (1952)

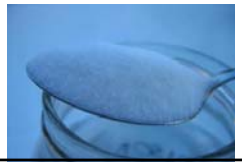
- Maternal hyperglycemia →
- Fetal hyperglycemia →
- Fetal hyperinsulinemia →
- Excess fetal fat

Infants of Diabetic Mothers

17 pound baby born to Brazilian diabetic mother Courtesy: MSNBC

Potential risks

- Macrosomia
- Brachial plexus injury
- Fracture with delivery
- Fetal hypoglycemia
- Fetal hyperbilirubinemia
- Fetal hypocalcemia
- Childhood obesity
- Neuropsychological outcomes
- Development of diabetes
- Apnea and bradycardia
- Perinatal mortality
- 3rd/4th degree lacerations
- Instrument deliveries
- Cesarean delivery
- Preeclampsia
- Future diabetes mellitus



Congenital Anomalies

- **Cardiac (most common): transposition of great vessels, VSD, ASD**
- **Central nervous system: spina bifida, Anencephaly, hydrocephalus**
- **Skeletal: cleft lip/palate**
- **Genitourinary tract: Caudal regression/Anal atresia, Renal agenesis, Duplex ureters, Cystic Kidney**
- **Situs inversus**

Who Has GDM?: ADA Definition

- Insulin resistance/ glucose intolerance first diagnosed during pregnancy

- 14% will remain diabetic after pregnancy
- 50% will ultimately become adult diabetics
- 84% will prove to be diabetic in future pregnancies

Who Has GDM?: Testing Protocols

- No consensus on what test is best, but…
- Two main strategies are in common use:
  - Non-fasting one hour test
  - Fasting two hour test
- When to test is also important

When to Test (IADPSG/HAPO/ACOG)

- With Risk Factors
  - Before Pregnancy
  - Early Pregnancy
- Everyone Not Yet Diagnosed
  - 24-28 weeks
- Gestational Diabetics: Test again post partum

Risk Factors for GDM- Early Test?

1. Obesity and overweight
2. Prior large infant (>4 kg)
3. Family history of diabetes
4. Past history of diabetes in a previous pregnancy
5. History of adverse pregnancy outcome
6. Certain ethnic groups
7. Advanced maternal age

One Hour Screening Test (ACOG)

- Measurement of plasma glucose 1 hour after 50g of glucose.
  - >140 mg/dl identifies **80%** of women with GDM
  - >130 mg/dl identifies **90%** of women with GDM.
- Women with elevated values require a 100g diagnostic glucose tolerance test ("3 hr test")

Three Hour GTT for Elevated Screen

- Three days unrestricted diet
- Eight hour fast
- Fasting serum glucose
- 100 g glucose beverage
- One, two and three hour serum tests

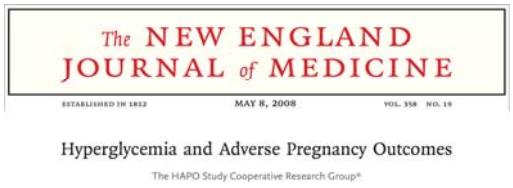
Three Hour GTT for Elevated Screen

Timing of measurement	National Diabetes Data Group (1979)	Carpenter and Coustan (CC) 1982
Fasting	105 mg/dl	95 mg/dl
1 hour	190 mg/dl	180 mg/dl
2 hour	165 mg/dl	155 mg/dl
3 hour	145 mg/dl	140 mg/dl

Problems with the ACOG test

- Not outcome based
- Not clear what to do with borderline cases
- Delays are possible
- A better test is available!

The Two Hour Test: Outcome Based


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 8, 2008 VOL. 358 NO. 19

Hyperglycemia and Adverse Pregnancy Outcomes

The HAPO Study Cooperative Research Group*

HAPO
(Hyperglycemia and Adverse Pregnancy Outcomes*)

Followed > 23,000 women after a 2-hour 75 gram GTT to determine whether there were glucose value thresholds that separated normal outcomes from complicated outcomes.

Women with FBS > 105 or 2-hr glucoses > 200 were unblinded.

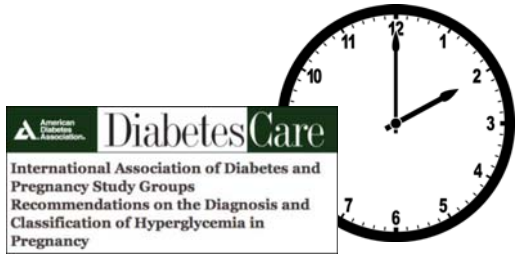
Followed for BW > 90th percentile, primary cesarean, neonatal hypoglycemia, cord-blood C-peptide > 90th percentile.

*NEJM 2008;358:1991-2002

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 need to be re-evaluated.

IADPSG* Has Adopted the 2hr Test



*International Association of Diabetes and Pregnancy Study Groups

IADPSG Thresholds: 92/180/153

Glucose measure	Glucose concentration threshold* mmol/l	mg/dl	Above threshold (%) Cumulative
FPG	5.1	92	8.3
1-h plasma glucose	10.0	180	14.0
2-h plasma glucose	8.5	153	16.1†

To diagnose overt diabetes in pregnancy

Measure of glycemia	Consensus threshold
FPG‡	≥7.0 mmol/l (126 mg/dl)
A1C‡	≥6.5% (DCCT/UKPDS standardized)
Random plasma glucose	≥11.1 mmol/l (200 mg/dl) + confirmation§

Only one elevated value is necessary to make a diagnosis of GDM

Post Partum GTT: Many Missed

- A recent West Virginia survey of post-partum gestational diabetics found that 54% denied having a Glucose Tolerance Test (GTT) recommended at/after their six week post partum visit.

54%

- Research suggests that about 15% of these tests would have been positive for continuing diabetes.

15%

Once a diagnosis is made

- Classify the severity of the problem
- Assess the knowledge and motivation of the patient and her family
  - Both patient and family attend class
- Assemble the care team
  - Medicine
  - Nursing
  - Nutrition
  - Family

Once a diagnosis is made

- Prepare a written plan with goals
  - Meal Plan
  - Monitoring Schedule
    - Blood sugars
    - Office Visits/Phone Calls: Individualize
    - Testing: Twice Weekly, Start Early
  - What to do if…
- Good Idea: Have patient sign the plan!

ADA Classification

- **Type 1 diabetes,** formerly referred to as insulin-dependent or juvenile-onset diabetes.
- **Type 2 diabetes,** formerly referred to as non–insulin-dependent or adult-onset diabetes
- **(GDM)** Gestational diabetes mellitus

American Diabetes Association.
Cure • Care • Commitment®

White's Classification

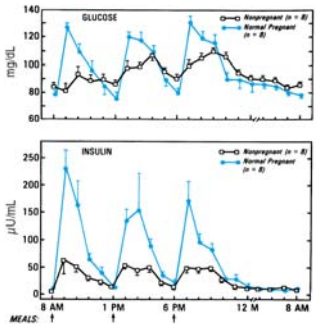
Class	Onset	Fasting Plasma Glucose	2-hour Postprandial Glucose	Therapy
A_1	Gestational	< 105 mg/dL	< 120 mg/dL	Diet
A_2	Gestational	> 105 mg/dL	> 120 mg/dL	Insulin

Class	Age of Onset (yr)	Duration (yr)	Vascular Disease	Therapy
B	Over 20	< 10	None	Insulin
C	10 to 19	10 to 19	None	Insulin
D	Before 10	> 20	Benign retinopathy	Insulin
F	Any	Any	Nephropathy	Insulin
R	Any	Any	Proliferative retinopathy	Insulin
H	Any	Any	Heart	Insulin

Dr. Priscilla White
(1900-1989)

Pathophysiology

- Normal pregnancy is characterized by:
  - Mild fasting hypoglycemia
  - Postprandial hyperglycemia
  - Hyperinsulinemia



Management: Glycemic Control

- Tight control greatly reduces macrosomia.
- Glycosylated Hemoglobin A1C (Hgb A1C) level should be less than or equal to 6%
  - Goal: Normal Hgb A1c level for at least 3 months prior to conception
- A Hgb A1C concentration near 10% is associated with miscarriage and 20-25% fetal anomaly rate.

What is Control?

- Blood glucose goals during pregnancy
  - Fasting < 95mg/dL
  - 2-hr postprandial am < 120mg/dL
  - 2 am < 120mg/dL and >60mg/dl
- Abnormal postprandial glucose measurements are more predictive of adverse outcomes than pre-prandial measurements

Why control blood sugar?

Fasting blood sugar	Macrosomia
>105 mg/dl	28.6 %
95-105	10%
<95 mg/dl	3%

Management Plan for GDM

- Nutrition
- Medications
- Lifestyle
- Testing
- Motivation and Follc up

Nutrition

- About 30kcal/kg/day
  - Modify to control weight gain
- Becomes 1800-2400 kcal/day
  - 300 at breakfast
  - 500 at lunch
  - 700 at dinner
  - (200 for each of three snacks)

Nutrition: Caloric Balance

- 40-50% from complex, high-fiber carbohydrates
- 20% from protein
- 30-40% from fats

Nutrition: Carb Counting

- Can be easier to learn
- Works well with "Portion Plate"
- Still emphasizes high-fiber carbs

Management: Insulin

- Insulin requirements increase rapidly, especially from 28 to 32 weeks of gestation.
- Expect (units/kilo/day)
  - 1st trimester: 0.75
  - 2nd trimester: 1.0
  - 3rd trimester: 1.25

Management: Insulin

- JCAHO no longer allows sliding scale insulin
- But you can give a coverage rule at home
  - One unit for each 10 mg/dl over 100 (pre-meal)

Insulin Analogue: Lispro (Humalog)

- Rapid-acting insulin analog (lispro) is Cat. B
  - Theoretical concerns about teratogenesis, antibody formation, growth-promoting properties
  - Majority of evidence shows that it does not cross placenta and has no adverse maternal or fetal effects
  - Often dosed as 1unit/10 carbs

Long Acting: Levamir

- Long-acting insulin
  - Can be dosed daily
  - Usually twice a day in pregnancy
- Advantage over NPH
  - Probably fewer highs and lows generally
  - Longer acting, fewer 2 AM lows especially
- Initiation Guidelines
  - When >20% of fasting are elevated
  - Usually 20 units AM and PM

Insulin pumps

- The effectiveness of continuous, subcutaneous insulin infusion in pregnancy is well established.
- Can allow for improvement in pregnancy outcomes for difficult-to-control diabetics.

Oral Hypoglycemic Agents

- Sulfonylureas (Glyburide)
  - Augment insulin release
  - 2nd generation (Glyburide)
    - Low transplacental transfer
- Biguanides (Metformin)
  - Increases insulin sensitivity
  - Crosses placenta

Oral Hypoglycemic Agents

Comparison of glyburide & Insulin in women with GDM

- 404 women with GDM
- randomly assigned between 11 & 33 weeks to receive glyburide or insulin
- primary end point: achievement of the desired level of glycemic control
- Secondary end points: maternal and neonatal complications

Langer O, Conway DL, Berkus MD, Xenakis EM-J, Gonzales O. A comparison of gly buride and insulin in women with gestational diabetes mellitus. N Engl J Med 2000;343:1134-1138.

Oral Hypoglycemic Agents

Comparison of glyburide & Insulin in women with GDM

no significant differences in % of infants who had

- Macrosomia
- Lung complications
- Hypoglycemia
- Admitted to a neonatal intensive care unit
- Fetal anomalies

Oral Hypoglycemic Agents

GDM: Therapeutic strategies

Metformin

- decreases hepatic glucose output
- improving peripheral glucose uptake, thus reducing insulin resistance
- may be a more logical alternative to insulin for women with GDM who are unable to cope with the increasing insulin resistance of pregnancy

Oral Hypoglycemic Agents

The Metformin in Gestational Diabetes (MiG) trial

- Prospective randomized multicenter trial
- Testing the hypothesis that metformin compared with insulin, is associated with:
  - similar perinatal outcomes,
  - improved markers of insulin sensitivity in the mother and baby
  - improved treatment acceptability

A Trial in Progress: Gestational Diabetes: Treatment with metformin compared with insulin (the Metformin in Gestational Diabetes (MiG) trial)
Janet A Rowan. Diabetes Care. Alexandria: Jul 2007. Vol. 30 pg. S214, 6 pgs

Confounding Factors

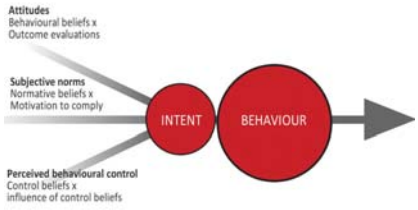
- Large number of subjects needed
- 450 infants undergoing cesarean delivery to prevent one permanent brachial plexus injury
- Lowered cesarean delivery threshold: resulting morbidity and costs outweigh benefits?

Improving Outcomes

- Theories
- Strategies
- Pearls

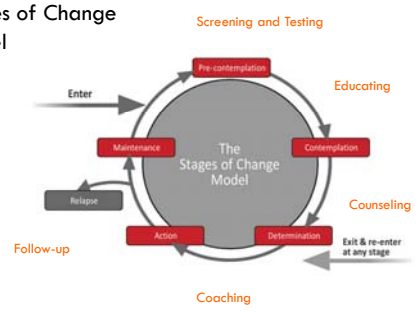
Adult Behavior Change Models

- Theory of Planned Behavior



Adult Behavior Change Models

- Stages of Change Model



Problem Patients

- Dunwana Lurn
  - Lack of Knowledge
- Cleopatra
  - Denial
- Carol Cut Corners
  - Unstable Lifestyle
- Ima Splitter
  - Doctor "X" Says

Clinical Pearls

- Tag the chart
- Catch them in ultrasound
- Involve their mom
- Be tenacious
- Expect the best and never give up

Conclusions

- Gestational diabetes is reaching epidemic levels
- Screening is essential in all pregnant women, particularly those from ethnicities with increased risk
- Tight glycemic targets are required for optimal maternal and fetal outcome
- Patient education is essential to meet targets
- Long term follow up of the mother and baby is essential

Thank you for participating!

Diabetes in Pregnancy Webinar

- Sponsored by:
  - WV Department of Human Resources, Office of Maternal, Child, and Family Health
- Lecture notes courtesy of:
  - Ryan Stone, MD, Assistant Professor, Department of Obstetrics and Gynecology, Joan C Edwards School of Medicine, Marshall University, Huntington, WV
  - Brenda Dawley, MD, FACOG, Associate Professor, Department of Obstetrics and Gynecology, Joan C Edwards School of Medicine, Marshall University, Huntington, WV
  - Laura Mullarky, RN CDE, Perinatal Center, Cabell Huntington Hospital, Huntington, WV
  - Allan S. Chamberlain, MD, FACOG, United Health Professionals, Barboursville, WV
  - Shauna Lively, RN, EdD, CLS, WV Perinatal Partnership Outreach Education Coordinator
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