Management of Diabetes in Pregnancy:
An Update for the Busy Clinician

Saturday, November 09, 2013

7.25 AMA PRA Category 1 Credits™
Program Schedule

8:00 – 8:15 a.m. Welcome & Introduction • Epidemiology and Scope of the Problem  
- Dr. Sean Blackwell

8:15 – 8:45 What Every Obstetrician Should Know About a Diabetic Diet  
- Dr. Lara Friel

8:45 – 9:15 Screening and Diagnosis of Gestational Diabetes  
- Dr. Adi Abramovici

9:15 – 9:45 Glycemic Control During Pregnancy: What Are Our Targets?  
- Dr. Clara Ward

9:45 – 10:15 Question and Answer Session

10:00 – 10:30 Break

10:30 – 11:00 When and What Medications to Use for DM in Pregnancy: Insulin, Glyburide, Metformin, etc.  
- Dr. Sean Blackwell

11:00 – 11:30 Management of Chronic Hypertension, Renal Disease and Other Co-Morbidities in the Diabetic Gravida  
- Dr. Baha Sibai

11:30 – Noon Fetal Imaging and Antenatal Testing for the Diabetic Gravida  
- Dr. Eleazer Soto

Noon – 12:30 Question and Answer Session

12:30 – 1:15 Lunch

1:15 – 1:45 Timing and Mode of Delivery for the Diabetic Gravida  
- Dr. Sean Blackwell

1:45 – 2:15 Intrapartum and Postpartum Management of Diabetes  
- Dr. Janice Whitty

2:15 – 2:45 Hyperglycemia, Hypoglycemia: Management of Diabetic Emergencies  
- Dr. Baha Sibai

2:45 – 3:15 Question and Answer Session

3:15 – 3:30 Break

3:30 – 4:00 Fetal, Neonatal and Childhood Consequences of Diabetes  
- Dr. Hector Mendez-Figueroa

4:00 – 4:30 Interactive Clinical Case Presentations with Audience Participation  
- Dr. Baha Sibai

4:30 p.m. Wrap up and Conclusion
Diabetes in Pregnancy: Epidemiology & Scope of the Problems
Scope of the Problem

Prevalence

- Total: 25.8 million children and adults in the United States—8.3% of the population—have diabetes.
  - Diagnosed: 18.8 million people
  - Undiagnosed: 7.0 million people
  - Pre diabetes: 79 million people
  - New Cases: 1.9 million new cases of diabetes were diagnosed in people aged 20 years and older in 2010.


Scope of the Problem

Race and Ethnicity

- For aged 20 years or older:
  - 7.1% of non-Hispanic whites
  - 8.4% of Asian Americans
  - 12.6% of non-Hispanic blacks
  - 11.8% of Hispanics
- Among Hispanics rates were:
  - 7.6% for Cubans
  - 13.3% for Mexican Americans
  - 13.8% for Puerto Ricans


Scope of the Problem

Type 1 vs. Type 2

- Shift in ratio of pre-gestational DM type
  - Previously 3:1 (Type 1: Type 2)
  - Paradigm change Ratio 1:5-10 (Type 1: Type 2)

What Every Obstetrician Should Know About a Diabetic Diet

Lara Friel, M.D.
Assistant Professor, Division of Maternal-Fetal Medicine
What Every Obstetrician Should Know About a Diabetic Diet

Lara A. Friel, M.D., Ph.D.
Assistant Professor
Division of Maternal Fetal Medicine
November 9, 2013

Disclosure

- No relevant financial or nonfinancial relationships to disclose.

Objectives

1) Describe the obstacles our Houston population faces in adhering to a diabetic diet
2) Discuss ADA diet/MyPlate.gov
3) Learn how to maximize diabetes education with individualization
4) Review exercise in pregnancy/diabetes management
Obstacles

1) Poor diet and physical inactivity are the most important factors contributing to an epidemic of obesity affecting people in all segments of our society.

2) Food insecurity.

3) Food/calorie overabundance.

4) Carbohydrate counting, utilization of exchange lists, and glycemic indexing can be complicated for much of the population.

1) Poor Diet


Top Sources of Calories Among Americans 2 Years and Older

1) Grain-based desserts
   Cake, cookies, pie, rolls, sweet rolls, pastries, and donuts

2) Yeast breads
   White bread and rolls, mixed-grain bread, flavored bread, whole-wheat bread, and bagels

3) Chicken and chicken mixed dishes
   Fried and baked chicken parts, chicken strips/patties, stir-fries, casseroles, sandwiches, salads, and other chicken mixed dishes

4) Soda/energy/sports drinks
   Sodas, energy drinks, sports drinks, and sweetened bottled water including vitamin water

5) Pizza

1) Poor Diet


Dietary Guidelines for Americans 2010
U.S. Department of Agriculture
U.S. Department of Health and Human Services
www.dietaryguidelines.gov

• Texas has a household food insecurity rate that is significantly higher than the national average (along with six other states). 18.5% 2009-2011

2) Food Insecurity: Texas

• Texas has a household food insecurity rate that is significantly higher than the national average (along with six other states). 18.5% 2009-2011

• Nearly one in five Texans, 4.6 million people (18.5%), lives in poverty. (2.6% higher than the national average)


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2) Food Insecurity: SE Texas

- 94% are not homeless
- 49% of households have at least one working adult
- 18% of clients are Caucasian, 39% are African-American, and 41% are Hispanic
- 62% are making choices between paying utility bills and food
- 50% are making choices between paying mortgage/rent and food

Houston Food Bank, Hunger Study 2010 (performed every 4 years)

Carbohydrates are Inexpensive


3) Food/Calorie Overabundance

- Texans eat out 20 percent more than residents of any other state
  - Average of 3.8 times per week compared to 3.1 times per week nationally
- No city eats out more than Houston
  - Residents patronize restaurants an average of 4.1 times per week

2012 America's Top Restaurants report from Zagat Survey LLC
2012 Texas Restaurants Survey
4) Exchange List

- 1/2 cup of canned or frozen fruit
- 1 small piece of fresh fruit (4 oz.)
- 1 slice of bread (1 oz.) or 1 (6 inch) tortilla
- 1/2 cup of oatmeal
- 1/3 cup of pasta or rice
- 4-6 crackers
- 1/2 English muffin or hamburger bun
- 1/2 cup of black beans or starchy vegetable
- 1/4 of a large baked potato (3 oz.)
- 2/3 cup of plain fat-free yogurt or sweetened with sugar substitutes
- 2 small cookies
- 2 inch square brownie or cake without frosting
- 1/2 cup oficio free yogurt or sweetened with sugar substitutes
- 1 Tbsp syrup, jam, jelly, sugar or honey
- 2 Tbsp light syrup
- 6 chicken nuggets
- 1/2 cup of casseroles
- 1 cup of soup
- 1/4 serving of a medium French fry

4) Glycemic Index

- Ranking of carbohydrates on a scale from 0 to 100 according to the extent to which they raise blood sugar levels after eating.

- High GI foods are rapidly digested and absorbed and result in marked fluctuations in blood sugar levels.

- Low-GI foods, are slowly digested and absorbed, produce gradual rises in blood sugar and insulin levels.

4) Glycemic Index

- GI represents the type of carbohydrate in a food but says nothing about the amount of carbohydrate which should be eaten

- Ripeness and storage time

- Processing

- Cooking method

- Variety of a food item
Choose MyPlate.gov

• Endorsed by:
  - The American Diabetes Association
  - The Academy of Nutrition and Dietetics
  - California Diabetes and Pregnancy Program Sweet Success

• Presented at the 6th Annual Collaborative Diabetes Education Conference for Healthcare Professionals in 2012

Create your Plate Method (1)

• Using your dinner plate, put a line down the middle of the plate.
• Then on one side, cut it again so you will have 3 sections on your plate.
• 9-Inch plate
2. Fill the largest section with non-starchy vegetables such as:
• spinach, carrots, lettuce, greens, cabbage
• green beans, broccoli, cauliflower, tomatoes,
• vegetable juice, salsa, onion, cucumber, beans, okra,
• mushrooms, peppers, kumquat.

3. Now in one of the small sections, put starchy foods such as:
• whole grain breads, such as whole wheat or rye
• whole grain, high-fiber cereal
• cooked beans such as pinto beans or black-eyed peas
• potatoes, green peas, corn, lima beans, sweet potatoes, winter squash
• low-fat crackers and snack chips, pretzels and fat-free popcorn.

4. On the other small section, put your protein such as:
• chicken or turkey without the skin
• fish such as tuna, salmon, cod or catfish
• other seafood such as shrimp, clams, oysters, crab or mussels
• lean cuts of beef and pork such as sirloin or pork loin
• tofu, eggs, low-fat cheese.
5. Add an 8 oz. glass of non-fat or low-fat milk.
   • If you don’t drink milk, you can add another small serving of carb such as a 8 oz. container of light yogurt or a small roll.

6. Add a piece of fruit or a 1/2 cup fruit salad and you have your meal planned.
   • Examples are fresh, frozen, or canned in juice or frozen in light syrup or fresh fruit.
Breakfast

- Insulin resistance is usually greater in the morning.
- Breakfast carbohydrate load may need to be restricted to 15-30 grams.
- Fruit juices, fruits, milk, ready-to-eat or instant cereals, bagels, and croissants are usually excluded.
- Individual tolerance determined by self blood glucose monitoring.

Website: American Diabetes Association.

Meal Measure

Shopdiabetes.org

Breakfast

Eat 15g carbohydrates from the Grains group
Include:
- 1-2 servings Protein
- Unlimited servings of non-starchy Vegetables

Do not eat Fruit, yogurt or drink milk.

Example of a breakfast:
One egg omelet with cheese & vegetables and one slice toast
### Fruit: Carbs

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
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<tr>
<td></td>
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<td>1 Cup Carbs (g)</td>
<td>1 Cup Carbs (g)</td>
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<tr>
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<td>Strawberries</td>
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<td>Pear</td>
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<tr>
<td></td>
<td>11.1</td>
<td>16.3</td>
<td>20.5</td>
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<tr>
<td></td>
<td>Watermelon</td>
<td>Apple</td>
<td>Beet</td>
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<td>17.3</td>
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<td></td>
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### Snacks

Eat 15g-30g carbohydrates from Fruit, Grains, or Dairy group

- Include:
  - At least 1 serving Protein with every snack
  - Unlimited servings of non-starchy Vegetables
- Examples of snacks:
  - 1 small tortilla + 1 ounce cheese
  - 2 rice cakes + 2 tablespoons nut butter
  - 1/2 banana + 24 almonds

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### Sample Daytime Snacks

- ½ toasted English muffin with 1 Tbsp natural style peanut butter
- 1 quesadilla (1 small tortilla and 1 ounce cheese)
- 1 cup melon with ½ cup cottage cheese
- 1 small apple (cut into slices) with 1 Tbsp natural-style peanut butter
- 2 Tbsp sunflower seeds and 2 Tbsp raisins
- ½ turkey or ham sandwich
- 6 saltine crackers with 1 ounce tuna
Sample Bedtime Snacks

- 2/3 cup rice with 1 ounce meat, chicken or fish
- 1 small tortilla with 1 ounce meat and ½ cup beans
- 1 ham or turkey sandwich
- 1 cup sugar-free yogurt and ½ peanut butter sandwich
- 1 cup milk and ½ toasted English Muffin with melted cheese and sliced tomatoes
- 1 cup milk with a mini sandwich (1 ounce dinner roll and 1 ounce sandwich meat or cheese)

Website: American Diabetes Association.

Individualize the Plan!

- Patient-centered care is defined as an approach to providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions

- In order to maximize our efforts
  - Address cultural issues
  - Address personal health beliefs

Committee on Quality of Health Care in America: Institute of Medicine, 2001.

Tortilla: Size

<table>
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<tr>
<th>Size</th>
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<th>8-inch</th>
<th>10-inch</th>
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Fatsecret.com/calories-nutrition

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**Tortilla: Type**

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<th>Type</th>
<th>Corn</th>
<th>White flour</th>
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**Rice: Type**

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<th>Brown</th>
<th>Sticky</th>
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<td>169</td>
</tr>
<tr>
<td>Fat (g)</td>
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<td>1.74</td>
<td>0.33</td>
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<tr>
<td>Carbs (g)</td>
<td>53.4</td>
<td>44.4</td>
<td>36.7</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>4.4</td>
<td>5.0</td>
<td>3.5</td>
</tr>
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</table>

**Lifestyle Intervention**

- **Nutrition Therapy** + **Regular Exercise**

- The cornerstone of management for T2DM

- At least 150 minutes/week of moderate-intensity aerobic physical activity

Exercise in Pregnancy

- ACOG recommends that pregnant women engage in 30 minutes or more of moderate exercise on most, if not all, days of the week
  - Both aerobic and strength conditioning exercises are encouraged in pregnant women without complications
  - Sedentary women, start with 15 minutes of continuous exercise 3 times per week, gradually increasing to 30 minutes per day (for a total of 150 minutes per week)

ACOG Committee Opinion, Number 267, January 2002 (Reaffirmed in 2009).

Exercise in Pregnancy

- Exercise should include a 5-10 minute warm-up and a cool-down period
- Moderate intensity
  - Talk test
  - One can talk, but not sing, during the activity

ACOG Committee Opinion, Number 267, January 2002 (Reaffirmed in 2009).

Exercise

- Avoid high impact or excessively jarring exercises and contact sports
- Minimize the risk of loss of balance/falling and abdominal trauma
- Heavy weightlifting, or similar activities that require straining, are to be discouraged.

ACOG Committee Opinion, Number 267, January 2002 (Reaffirmed in 2009).

Exercise

- Walking
- Treadmill walking
- Low impact aerobics
- Step aerobics (until uterus blocks vision of step)
- Water aerobics
- Swimming
- Stepping Machine (including elliptical)
- Bicycling (only in early pregnancy)
- Stationary bicycling
- Dancing
- Yoga
- Light weight training
- General gardening

ACOG Committee Opinion, Number 267, January 2002 (Reaffirmed in 2009).

Lifestyle Intervention Overview

- Eat 3 meals and 3 snacks, 2-3 hours apart
- Bedtime snack so that no more than 10 hours pass before breakfast
- Plenty of fluids (caffeine-free, sugar-free).
- Walk 10-15 minutes after each meal


Clinical Recommendations: Diabetic Diet

1) Know your patient’s obstacles in adhering to a diabetic diet
   - Addressing cultural issues and personal health beliefs will help to maximize your efforts

2) Use MyPlate when discussing/reviewing the diabetic diet

3) Exercise is an important adjunct in diabetes management
Screening and Diagnosis of Gestational Diabetes

Adi Abramovici, M.D.
Assistant Professor, Division of Maternal-Fetal Medicine
Gestational Diabetes Screening and Diagnosis: The Whom, When and How

Adi Abramovici, M.D.
Division of Maternal Fetal Medicine
University of Texas Health Science Center at Houston

Disclosure Statement
I do not have relevant financial relationships with commercial interests related to the content of this presentation.

Objectives
- Discuss how to screen and diagnose Gestational Diabetes Mellitus (GDM)
- Recognize common challenges when screening/diagnosing GDM
### Why Screen?
- Prevalence 6-7% in the United States
  - 240,000 of 4 Million annual births
- Lifetime risk of Type 2 DM: 50%
- Increased Risk:
  - Preeclampsia
  - Fetal macrosomia
  - Neonatal hypoglycemia

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### Who Is At Risk?
- Family Hx
- Obesity
- Age >25 years
- Previous delivery >9 pounds
- Hx impaired glucose tolerance
- Hispanic/African American

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### Who Is At Risk?
- Unexplained perinatal loss/malformed infant
- Maternal birth weight >9 pounds
- Glycosuria at the first prenatal visit
- Polycystic ovary syndrome
- Current use of glucocorticoids
- Essential hypertension
- Metabolic syndrome
**Whom Should Be Screened?**

- In the United States, universal screening appears to be the most practical approach
- Up to 20 percent of women diagnosed with GDM have no risk factors
- ACOG recommends *Universal Screening*

**When to Screen?**

- ACOG recommends:
  - High Risk: First Prenatal Visit
  - Universal screening 24-28 weeks

**Early Screening?**

- Prior GDM
- Known impaired glucose tolerance
- Obesity BMI >30
How to Screen?

• There is no worldwide standard for screening and diagnosis of diabetes during pregnancy.

• In the United States, the most common approach is: 2-step approach

2-Step Approach

• Step 1:
  - Give 50 gram oral glucose load
  - Glucose:
    \[ \geq 130 \text{ mg/dL (per Carpenter/Coustan)} \]
    \[ \geq 135 \text{ mg/dL or } \geq 140 \text{ mg/dL (per ACOG)} \]

• Step 2:
  - Administration of a full glucose tolerance test

Which Cutoff is Best?

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<th>Threshold</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tr>
<td>130</td>
<td>88-99%</td>
<td>66-77%</td>
</tr>
<tr>
<td>135</td>
<td>80-90%</td>
<td>67-80%</td>
</tr>
<tr>
<td>140</td>
<td>70-88%</td>
<td>69-89%</td>
</tr>
</tbody>
</table>
100 gram 3-hour GTT

- Recommended by ACOG/2013 NIH Consensus Conference
- 2 Elevated values = positive test
- Carpenter/Coustan vs. National Diabetes Data Group thresholds
- Consider eliminating if 1-Hour >190-200ng/dL

2 diagnostic criteria for 3-hour GTT

<table>
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<tr>
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<th>Carpenter/Coustan</th>
<th>NDDG</th>
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<tr>
<td>Fasting</td>
<td>95</td>
<td>105</td>
</tr>
<tr>
<td>One hour</td>
<td>180</td>
<td>190</td>
</tr>
<tr>
<td>Two hours</td>
<td>155</td>
<td>165</td>
</tr>
<tr>
<td>Three hours</td>
<td>140</td>
<td>145</td>
</tr>
</tbody>
</table>

1-Step Approach

- 75 gram two-hour oral GTT
- Administered at 24 to 28 weeks of gestation
- Omits the screening 50 gram glucose
- Not Endorsed by ACOG
75-gram GTT

- HAPO Study

- Adverse outcomes
  - Macrosomia
  - Cesarean delivery
  - Neonatal hypoglycemia
  - Preeclampsia

The 2013 NIH Consensus Conference recommended against adoption of the one step approach and criteria because it would increase the prevalence of GDM, leading to more frequent prenatal visits, more fetal and maternal surveillance, and more interventions, including induction of labor, without clear demonstration of improvements in the most clinically important health and patient-centered outcomes.

Challenging Scenarios

- Early screening? 2-Step vs. Fasting vs. HgA1C

- Early abnormal 1-hour, normal 3-hour?

- Counseling regarding diet/fasting prior to screening?

- Special considerations
  - Bariatric patients
  - Inability to tolerate glucose
SUMMARY AND RECOMMENDATIONS

• Universal screening
• Screening 24-28 weeks using a 2-step approach
• Cutoffs:
  ➢ 1 Hour: 135 mg/dL
  ➢ 3 Hour: 95/180/155/140 mg/dL
• High Risk Women:
  ➢ Screen 1st Visit
  ➢ If negative: Repeat 24-28 weeks

Questions?

“You’ll have to eat that donut outdoors. Nobody wants to inhale secondhand carb!”
Glycemic Control During Pregnancy: What Are Our Targets?

Clara Ward, M.D.
Assistant Professor, Division of Maternal-Fetal Medicine
Glycemic Control During Pregnancy: What are our targets?

Clara Ward, MD
Assistant Professor
Division of Maternal Fetal Medicine
Department of Obstetrics, Gynecology, and Reproductive Sciences

Objectives

- How do we assess glycemic control at presentation?
- How do we assess glycemic control throughout gestation?
- Why does it matter?
- What should our targets be?

Objectives

- HbA1c
  - Background
  - Definitions
  - Targets
  - Significance
  - Caveats
- Glycemic Targets
  - What numbers
  - When to check
  - Which values matter
  - What is good control
  - Special circumstances
Hemoglobin A1c

- Represents mean glucose concentration over prior 8-12 weeks
  - Weighted average
    - More emphasis on last 30 days
  - Marker of disease control
    - HbA1c of 8% → mean serum glucose 180
      - Each 1% → 30 mg/dL

ADAG Study 2008. Diabetes Care; 31:1-6

Hemoglobin A1c

- Normal: ≤5.6%
- Pre-diabetes: 5.7-6.4%
- Overt diabetes: ≥6.5%
- Goal non-pregnant: <7.0%
  - Diabetes Complications and Control Trial (DCCT)
  - United Kingdom Prospective Diabetes Study (UKPDS)
  - Goal pregnant/pre-conceptional: <6.0%

Hemoglobin A1c

Hemoglobin A1c

- Correlated with adverse pregnancy outcomes
  - Spontaneous abortion
  - Congenital anomalies
  - Intrauterine fetal demise
  - Preterm labor
  - Macrosomia
  - Shoulder dystocia
  - Preeclampsia
  - Maternal complications of diabetes

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Fig. 1 Relationship between HbA1c levels at conception and congenital malformations Ylinen et al. (13)


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Periconceptional Glycemic Control

- Fasting <120
- Preprandial <140
- Postprandial <140
- HbA1c <6%


Hemoglobin A1c: Caveats

- Unreliable in pregnancy
- Changes in RBC physiology
- Does not reflect short term variations
- Decreased in pregnancy
- False sense of glycemic control
- Decreased clearance in pregnancy
- Unable to accurately assess effect of therapy
- Questionable correlation with actual glucose values
- Varying laboratory ranges of normal

ADIPS 2005.
NICE 2008.

Hemoglobin A1c

- Risk of perinatal complications decreases with decrease in HbA1c on a population level
- However, HbA1c cannot be used to assess risk of adverse perinatal outcomes in individual pregnancy
- Correlates with other manifestations of poor control

Hemoglobin A1c

Who and when should we test?

- GDM
  - Low yield/not recommended
- Occult Type 2 DM
  - Early identification of glucose intolerance
- Pre-gestational
  - PNC intake
- Repeat measurement
  - Noncompliant

Hemoglobin A1c

- Greatest benefit is periconceptional
  - Assess risk of congenital malformations
  - Shape approach to counseling
  - Assess need for admission during organogenesis
- Preconception care and pregnancy planning reduces morbidity
- Define pre-gestational insulin resistance, associated risks, and impact on future health

Glucose Monitoring

- All pre-gestational and gestational diabetics during pregnancy
- Minimum 4 times daily
  - Fasting
  - 1 or 2 hours after meal
- Logs with DIETARY INFORMATION
Glucose Monitoring

Weekly Compared With Daily Blood Glucose Monitoring in Women With Diet-Treated Gestational Diabetes

J. Suck Hawkins, MD, Brian M. Cecry, MD, Julie Y. Lu, MD, Krista Mee, MD, Donald D. Martin, MD, and Kenneth J. Lawton, MD


The New England Journal of Medicine

Postprandial Versus Preprandial Blood Glucose Monitoring in Women With Gestational Diabetes Mellitus Requiring Insulin Therapy

Margaret S. Yeh, MD, Ceclia A. Heier, MD, Mare A. Hargreave, MD, Thomas A. Jones, MD, Jeanne L. Tofigh, MD, Jean M. Lee, MD, and Andrew T. Davis, MD

Glucose Monitoring

One or two hours postprandial glucose measurements: Are they the same?

Ted S. Mier, MD, Susan D. McEvoy, MD, and Gary L. Hands, RN, IMPT, and Daniel J. Schlosser, MD

Philadelphia, Pa

Differences: This study evaluated differences in glucose levels measured after 1 hour by 1.2 mmol/L/l of those measured after 2 hours by 1.5 mmol/L/l postprandially in women with gestational diabetes mellitus (2004)
Glucose Monitoring

• Differential measurement?
• Postprandial peak at 90 minutes after all meals
  — Ben-Haroush et al. 2004. AJOG 191: 576e81
• No difference in neonatal or maternal outcomes

Glycemic Targets

• Fasting
  • Goal: ≤95
• Preprandial
  • Goal: <100
• Postprandial
  • Goal: <140 (1 hour) vs. <120 (2 hours)


• T1DM
  • Mean BG <100, 100-150, >150
  • 3.8%, 16%, and 24% risk of perinatal loss, respectively
  • GDM and T2DM (Pima)
  • Direct relationship between OGTT and perinatal mortality
Glycemic Targets

- GDM have more perinatal loss than non-GDM
  - O'Sullivan et al 1973. AJOG 1: 901-4
- Perinatal loss most prevalent in those patients with LGA
- Postprandial BG <140 decreases risk by 75%
- Mean BG <115 reduces risk of perinatal mortality

Glycemic Targets

- Mean BG <115 reduces risk of perinatal mortality

Glycemic Targets

- Postprandial BG <140 decreases risk by 75%

Glycemic Targets

- Mean BG <115 reduces risk of perinatal mortality
Glucose Monitoring: Which targets are most important?

• Gestational vs. Pre-gestational
• Fasting vs. Postprandial
• Initiation vs. Term

BOTTOM LINE:
They are all important!

Glucose Monitoring: Surveillance

• Abnormal GTT (or PNC intake for pregestational)
  • 1 week of dietary logs and SMBG
  • Nutritional counseling/diabetic education
• Initial assessment of control
  • If >50% of values above target range
    • Reassess in 1 week
    • Possibility of nutritional modifications
    • If mild elevations ~15 mg/dl above target
      • Encourage ambulation after meals/before SMBG
• Intensive surveillance
  • Noncompliant, late to/lapse of care
• Self-titration

Assessing Control

• Weekly review of logs/medication changes
  • Phone
  • Fax
  • Email
• Noncompliance
  • Weekly appointments
  • Admission
• Rewards
  • Decrease frequency of fingersticks after 35 weeks

November 09, 2013
Assessing “Good” Control

• Goal is <50% of blood glucose measurements above the target range
  • Are you eating in the middle of the night?
  • When did you really check your sugar/take your insulin?
  • Can you walk for 15 minutes after meals?
  • So you had tortillas, cake, ice cream, soda, and gummi worms at your kid’s party?

Assessing “Good” Control

• “My what good control you have”
  • Calorie and carbohydrate restriction
  • Failure to snack
  • Failure to fake better
    • All glucose values end in 5 or 0

Glucose Monitoring:
Special Circumstances

• GDMA1
  • Reduced frequency if excellent control >35 weeks
• Pregestational Diabetes
  • Preprandial monitoring
  • Nocturnal Hypoglycemia
    • 2 AM check
• Alternative Schedules
Is tighter control better?

- Strict 60-90 mg/dL vs. Moderate 80-116 mg/dL
- Risks
  - Hypoglycemia (<60 mg/dL)
  - Transient exacerbation of retinopathy
- Caveats
  - What kind of diabetic
  - Rebound hyperglycemia
  - Low morale
- No significant clinical benefit

Middleton 2012, Cochrane Review

Are we on target?

Patient Frequency By Level Of Glycemia

Langer and Conway 2000, JMFM 9: 35-41

Patient Materials

- [http://www.lillydiabetes.com/Pages/downloadable-materials.aspx](http://www.lillydiabetes.com/Pages/downloadable-materials.aspx)
- Meal planning and carbohydrate guide
- Log books
- Diabetes spinner: carbohydrate estimation
- [http://www.diabetescare.net/handouts.asp](http://www.diabetescare.net/handouts.asp)
- UCSF--comprehensive
Recommendations: HbA1c

- Goal HbA1c <6% prior to conception
- Pregestational DM: Check HbA1c at PNC intake
- Early positive GTT: Check HbA1c at diagnosis
- Gestational DM: Don’t check HbA1c
- Serial/Routine measurement of HbA1c not recommended

Recommendations: Monitoring

- Logs: glucose and diet
- Fingerstick glucose at every PNC visit
- SMBG 4 times daily
  - Fasting: goal <95
  - Postprandial: goal <120 (2 hours) or <140 (1 hour)
- Pregestational DM
  - 2AM or preprandial checks as needed

Recommendations: Surveillance

- Abnormal GTT (or PNC intake for pregestational)
  - 1 week of dietary logs and SMBG
  - Nutritional counseling/diabetic education
  - Initial assessment of control in 1 week
    - If >50% of values above target range
      - Possibility of nutritional modifications
      - If mild elevations ~15 mg/dL above target
        - Encourage ambulation after meals/before SMBG
      - Consider admission if <10 weeks
    - Intensive surveillance
      - Noncompliant, late to/lapse of care
Recommendations:
Surveillance

- Glycemic control is a continuum
- Partnership
- Care of the pregnancy complicated by diabetes begins preconceptionally
When and What Medications to Use for DM in Pregnancy: Insulin, Glyburide, Metformin, etc.

Sean Blackwell, M.D.
Chair, Department of Obstetrics, Gynecology and Reproductive Sciences
What are medication options for the Diabetic Gravida?

Sean C. Blackwell, M.D.
Professor and Chair, Department of Obstetrics, Gynecology and Reproductive Sciences
Director, Larry C. Gildrop M.D. Center for Perinatal and Women’s Health Research
Assistant Dean for Healthcare Quality in Perinatal Medicine and Women’s Health
University of Texas Medical School at Houston (UTHealth) Medical School
Sean.Blackwell@uth.tmc.edu

Objectives

• To discuss insulin type and dosing options for women with Type 1 and Type 2 DM.

• To evaluate criteria, risks, and challenges for use of oral hypoglycemic medications for women with T2 and GDM during pregnancy.

Case

• Ms. Jones is G 4 P 3 here for 1st prenatal care visit-referred from family practice physician who confirmed pregnancy. She has history of T2 diabetes but not on treatment. She is 12 weeks gestation and has Hb A1C = 9.0%
Type 2 DM

• Despite increased use of oral hypoglycemics, most women still receive insulin

• Starting dose = 0.7 – 1.0 units/kg/day

• Thus is weight = 70 kg = 50-70 total units per day

• Key point = this is an approximation to start, much biological variation

Insulin preparations

![Insulin Preparations Diagram]

<table>
<thead>
<tr>
<th>Insulin Preparation</th>
<th>Onset of Action</th>
<th>Peak</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lente Human (NPH)</td>
<td>1-2 hours</td>
<td>12-24 hours</td>
<td>24-72 hours</td>
</tr>
<tr>
<td>Insulin Regular (RI)</td>
<td>30-60 minutes</td>
<td>2-3 hours</td>
<td>6-12 hours</td>
</tr>
<tr>
<td>Humulin Regular (RI)</td>
<td>2-4 hours</td>
<td>4-8 hours</td>
<td>12-24 hours</td>
</tr>
<tr>
<td>Humulin N BiP (RI)</td>
<td>30 minutes</td>
<td>1 hour</td>
<td>12-24 hours</td>
</tr>
<tr>
<td>Humulin Lente (RI)</td>
<td>1-2 hours</td>
<td>4-6 hours</td>
<td>24-72 hours</td>
</tr>
<tr>
<td>Humulin (RI)</td>
<td>30 minutes</td>
<td>2-3 hours</td>
<td>24-72 hours</td>
</tr>
<tr>
<td>Humulin N BiP (RI)</td>
<td>2-3 hours</td>
<td>24-72 hours</td>
<td></td>
</tr>
<tr>
<td>Humulin Lente (RI)</td>
<td>1-2 hours</td>
<td>24-72 hours</td>
<td></td>
</tr>
</tbody>
</table>

Premixed Insulin

<table>
<thead>
<tr>
<th>Insulin Preparation</th>
<th>Onset of Action</th>
<th>Peak</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novolin 30/70H</td>
<td>2-3 hours</td>
<td>2-4 hours</td>
<td>12-24 hours</td>
</tr>
<tr>
<td>Novolin 70/30H</td>
<td>30 minutes</td>
<td>2-3 hours</td>
<td>12-24 hours</td>
</tr>
<tr>
<td>Humulin 30/70, song 70/30, Humulin 50/50</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Key point: this is an approximation to start, much biological variation.
Regimen Options

- Long acting + rapid acting**
  - Glarganine (daily)
  - Humolog (with meals)

- Intermediate acting + rapid
  - NPH (twice daily)
  - Humolog (with meals)
Regimen Options

Management Pearls

- If doing well pre-pregnancy, don’t change schedule
- Don’t change from Rapid Acting to Regular
- Don’t give Regular at lunchtime
- May need to change from long acting to intermediate acting
  - “Flat profile” in pregnancy may be undesirable when variations in basal insulin are likely

Management Pearls

- Ask/listen to patient for input on changes
- Keep it simple, make changes based on patterns
- Try to change one insulin and one dose at a time
- Avoid hypoglycemia
- When control is poor, it is often the diet
- DM compliance is proportional to how complex/difficult/burdensome the health provider makes insulin therapy
Case

- Ms. Jones is G 4 P 3 here for 1st prenatal care visit-referred from family practice physician who confirmed pregnancy. She has history of T2 diabetes but not on treatment. She is 12 weeks gestation and has Hb A1C = 9.0%

Treatment options for DM?

Glyburide

- Second-generation sulfonylurea that binds to pancreatic cell receptors to increase insulin secretion as well as increasing peripheral insulin
- Brand names: Micronase, DiaBeta, Glynase
- Onset of action = 30 minutes
- Time to peak response = 2-3 hours
- Maximum daily dose = 20 mg (some recommendations allow up to 30 mg/day)

Glyburide and GDM

- Langer et al. (NEJM)
  - RCT insulin vs. glyburide
  - Sample size = 404
  - Similar improvements glycemia, LGA, macrosomia
  - 4% “failure rate” glyburide

- Subsequent studies suggest failure rates 15-20%
  - Risk factors failure = morbid obesity and fasting values > 110-115 mg/dL
Glyburide vs. Metformin

- Two RCT’s in GDM
  - Glyburide vs. Metformin
  - Combined sample size > 900 subjects
  - No difference major perinatal outcomes

- However, 35-46% of women on metformin required insulin
- No safety issues noted metformin or glyburide

Role Oral Hypoglycemics

- Glyburide for GDM
  - Choose optimal candidates
  - Due to compliance issues may tolerate “risk of failure” and supplement insulin prn

- Extrapolated for T2DM
  - No large, high quality trials
  - Unknown risks/benefits

Management Pearls

- If a women is “stable” on metformin or glyburide and becomes pregnancy, reasonable to continue

- Recognize “higher” failure rate with T2DM and unknown risks/benefits
  - Imperfect control and need for supplemental insulin may be better than no control
  - If have to add multiple dose insulin with oral agents, may be better to convert
Management of Chronic Hypertension, Renal Disease and Other Co-Morbidities in the Diabetic Gravida

Baha Sibai, M.D.
Professor, Division of Maternal-Fetal Medicine
Management of Chronic Hypertension, Renal Disease and other co-morbidities in Diabetic Pregnancy

Baha M. Sibai, MD
Professor
Director, Maternal Fetal Medicine Fellowship
Department of Obstetrics, Gynecology & Reproductive Sciences

Management of CHTN and medical co-morbidities in diabetic Pregnancy

Learning Objectives

1. To discuss the impact of preexisting medical conditions on pregnancy outcome in DM.
2. To discuss the effects of pregnancy on preexisting medical conditions in association with DM
3. To describe a step-wise management plan for management of diabetic pregnancy in association with medical co-morbidities

White Classification for DM

<table>
<thead>
<tr>
<th>Class</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Onset ≥20 yr or duration &lt; 10yr</td>
</tr>
<tr>
<td>C</td>
<td>Onset 10-19 yr or duration 10-19yr (no vascular disease)</td>
</tr>
<tr>
<td>D</td>
<td>Onset &lt;10 or duration ≥20 yr or retinopathy or HTN only</td>
</tr>
<tr>
<td>F</td>
<td>Nephropathy (≥500mg proteinuria at &lt; 20 wk)</td>
</tr>
<tr>
<td>H</td>
<td>Arteriosclerotic heart disease : ischemia, MI</td>
</tr>
<tr>
<td>R</td>
<td>Proliferative retinopathy</td>
</tr>
<tr>
<td>T</td>
<td>History of renal transplant</td>
</tr>
</tbody>
</table>
End Organ Damage in DM

Target-Organ Damage in DM

• Heart
  – Ischemia /MI
  – Angina: stable or unstable
  – Heart failure / LV hypertrophy

• Nephropathy
  – Incipient: micro-albuminuria
  – Overt: 0.3-3.0 g / 24 hr
  – Severe: >3 g /24 hr
  – ESRD: CR >2.3 mg/dl

• Retinopathy
  – Non-proliferative
  – Proliferative

• Neuropathy
  – Gastroparesis / peripheral

Management of Co-morbidities in Diabetic Pregnancy

• Evaluation prior to conception/first visit
  – Glucose control (Hgb A1C)
  – Presence of HTN, BP control
  – Nephropathy
  – Retinopathy
  – Hyperlipidemia
  – Myocardial ischemia
  – Renal transplant, dialysis

• Current medications / response to RX
  – Insulin, antihypertensives, cardiac drugs
  – Other: Statins, thyroid medications

• Outcome in previous pregnancies
  – Preeclampsia, PTD, FGR, Perinatal death
  – Maternal complications

November 09, 2013
Factors Associated with Adverse Pregnancy Outcome in DM

- Pre-eclampsia
- Pyelonephritis
- Polyhydramnios
- Poor Compliance
  - Poor Management:
    - Poor control of glucose
    - Poor control of BP
    - Poor response to complications

CHTN in pregestational DM

- Most common co-morbidity (10-40%):
  - Advanced age in type 2
  - Obesity in type 2
  - Increases rate of adverse outcome
- BP and proteinuria will increase in pregnancy:
  - Frequent adjustment of BP medications
  - More than one drug may be needed
  - DX of preeclampsia is difficult
    - Development of new onset SXs
    - Onset of Pulmonary edema
    - Change in platelets/ liver enzymes

Pregnancy outcome in CHTN, DM & combined

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control n=522,377</th>
<th>Chronic HTN n=5560</th>
<th>DM n=3718</th>
<th>Both n=433</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUFD</td>
<td>0.3</td>
<td>0.8</td>
<td>0.8</td>
<td>2.2</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>2.7</td>
<td>28.7</td>
<td>9.5</td>
<td>31.7</td>
</tr>
<tr>
<td>SGA</td>
<td>10.1</td>
<td>18.3</td>
<td>9.7</td>
<td>18.2</td>
</tr>
<tr>
<td>LGA</td>
<td>2.2</td>
<td>2.6</td>
<td>8.1</td>
<td>6.0</td>
</tr>
<tr>
<td>Shoulder dystocia</td>
<td>1.1</td>
<td>1.0</td>
<td>2.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Placental abruptio</td>
<td>0.8</td>
<td>2.0</td>
<td>1.4</td>
<td>1.9</td>
</tr>
</tbody>
</table>
Chronic HTN, DM, or Combined Pregnancy Outcomes

Preeclampsia in DM ± vascular disease

Target BP of 130/80 mm Hg in DM

- Reduces macro & micro-vascular complications
  - Retinopathy
  - Nephropathy
  - Ischemic heart disease
- In microalbuminuria, it reduces
  - Preeclampsia
  - PTD
**Antihypertensive Drugs to Use in Pregnancy**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual dose (mg)</th>
<th>Maximum dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>200 x 2/d</td>
<td>2400</td>
</tr>
<tr>
<td>Chlorothiazide</td>
<td>12.5-25/d</td>
<td>25</td>
</tr>
<tr>
<td>Nifedipine (LA)</td>
<td>10-30/d</td>
<td>120</td>
</tr>
<tr>
<td>Nicardipine (SR)</td>
<td>60-120/d</td>
<td>240</td>
</tr>
<tr>
<td>Metoprolol (XL)</td>
<td>50-100/d</td>
<td>200</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>10-25 x 4/d</td>
<td>300</td>
</tr>
<tr>
<td>Furosemide</td>
<td>20 x 2/d</td>
<td>80</td>
</tr>
<tr>
<td>Carvedilol</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**ACE Inhibitors / ARBs in Pregnancy**

Usually safe prior to 16 wks

- Fetal Anomalies (? 1st Trimester)
- FGR
- Oligohydranmios
- Fetal deformations
- Neonatal renal dysfunction
- Neonatal renal failure

**Diabetic Retinopathy in Pregnancy**

Dx and Management

- Non-proliferative
  - Mild: microaneurysms + dot hemorrhages
  - Severe: cotton-wool spots, edema
- Proliferative
  - New blood vessels in retina
  - Vitreous hemorrhage, retinal detachment
- Retinal digital imaging
  - First visit and 28 wk
  - 16-20 wk if abnormal
  - If proliferative / macular edema: monthly
- Laser Photocoagulation
  - Proliferative & macular edema
Diabetic Nephropathy

- Incipient: albumin 30-300mg/24 hr
- Overt:
  - Protein > 300 mg/24hr at ≤ 13 wks
  - Protein 300-500 mg/24hr at < 20 wks
- Prevalence of 5-10%
  - Due to increased Type 2
- With or without HTN
  - Various stages of renal function
  - With or without retinopathy

Renal Function changes in Diabetic Nephropathy

- GFR: limited change, ↑ in 33%
- Proteinuria
  - 24/46 (58%) ↑ > 1g/24 from 1st → 3rd T
  - 25/46 (56%) > 3g/24h
- Mild renal dysfunction (Cr <1.4; protein <3g/24h)*
  - Minimal impact on long-term function
- Moderate-severe nephropathy (Cr >1.4)*
  - ESRD /dialysis during or after pregnancy
  - 45% accelerated, irreversible decline in function

* Outcomes influenced by glycemic control, HTN, preeclampsia

Pregnancy in Diabetic Nephropathy

Factors associated with poor outcome

- Cr ≥1.4 mg/dl (124 µmol/L)
- Proteinuria > 3g/24h
- Hgb < 8g/dl
- Chronic HTN > 5 yrs
- Left ventricular dysfunction by ECHO
- Ischemic changes on ECG
- Unstable angina in pregnancy
- Poor compliance with insulin/antihypertensives
Management of Diabetic Nephropathy

**Maternal**

- **Glycemic Control**
  - Hg A1c at 1st visit
  - Self BG monitoring
  - Multiple insulin injections/pump

- **Hypertension Control**
  - Goal of 130/80 mm Hg
  - CCB /Beta blockers
  - Diuretics

- **Monthly CBC, CMP starting at 24 wks**

- **Massive edema, proteinuria, ↓ albumin**
  - Furosemide + albumin
  - Lovenox prophylaxis

---

**Pregnancy outcomes in Diabetic Nephropathy (%)**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Kitzmiller n=26</th>
<th>Bagg n=24</th>
<th>Carr n=43</th>
<th>Reece n=31</th>
<th>Gordon n=45</th>
<th>Khoury N=60</th>
<th>Rosenn n=61</th>
<th>Sibai n=58</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-ecclampsia</td>
<td>15</td>
<td>33</td>
<td>35</td>
<td>35</td>
<td>53</td>
<td>40</td>
<td>51</td>
<td>36</td>
</tr>
<tr>
<td>PTB &lt;35 wk</td>
<td>31 *</td>
<td>46</td>
<td>21 **</td>
<td>23 *</td>
<td>16 *</td>
<td>15 **</td>
<td>25 *</td>
<td>36</td>
</tr>
<tr>
<td>IUGR</td>
<td>21</td>
<td>--</td>
<td>19</td>
<td>19</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Perinatal Survival</td>
<td>89</td>
<td>100</td>
<td>91</td>
<td>94</td>
<td>100</td>
<td>95</td>
<td>94</td>
<td>98</td>
</tr>
</tbody>
</table>

*PTB <34 wk
**PTB <32 wk

---

**Neonatal outcome in presence or absence of proteinuria**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Proteinuria Present (n=86)</th>
<th>Proteinuria Absent (n=376)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Delivery at &lt;37 wk.</td>
<td>50</td>
<td>58</td>
</tr>
<tr>
<td>Delivery at &lt;35 wk.</td>
<td>25</td>
<td>29</td>
</tr>
<tr>
<td>Birth weight &lt;10th%</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Birth weight &gt;90th%</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Birth weight &gt;4000g</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>NICU</td>
<td>56</td>
<td>70</td>
</tr>
<tr>
<td>Perinatal Death</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

---
Management of Diabetic Nephropathy
Fetal testing, timing of delivery

- Serial U/S for growth, AFI
- UA Doppler if FGR
- NST / BPP at 28 wks
  - Repeat 1-2x/wk as needed
  - Immediate if acute change
- Delivery at 34-37 wks or earlier
  - Obstetric complications
  - Medical complications

Diabetic coronary heart disease in Pregnancy

- Ischemia / MI
  - Hyperlipidemia
  - Young, Type 1
- Heart failure/ LV hypertrophy
  - Type 2
  - Old and high parity
  - Obese
  - Hypertensive
  - Family HX
- Maternal death: 8/24 (33%)
  - Ischemia/MI prior preg (0/11)
  - MI in pregnancy: 8/13 (62%)
- Existence of non-cardiac organ damage
  - Renal
  - Retinal
  - Hyperlipidemia
  - Hypertension

Diabetic Heart Disease in Pregnancy
Evaluation & Counseling

- Prior to pregnancy/ 1st visit
  - ECG, ECHO, stress test
  - Nuclear medicine cardiac imaging
  - Cardiac Cath, Angiography
  - Medications
  - Stent
  - Defibrillator
- Counseling
  - Recent MI, unstable angina: Avoid pregnancy
  - MI or unstable angina < 20 wk: Discuss options
  - Discuss complications
  - Need for prolonged hospitalization
Diabetic heart disease in Pregnancy

Management & Delivery

- **Management**
  - Stable angina:
    - Beta-blockers
    - LDA
    - Nitrates
  - Unstable angina:
    - Stent
    - Coronary bypass surgery
  - Myocardial infarction:
    - Morphine
    - Heparin/ TPA/ Aspirin
    - IV nitro,
    - Coronary bypass
    - Admit to CCU
    - Heart failure
    - Dyshrhythmia

- **Delivery**
  - Hemodynamic stable
  - Induction at term
  - Myocardial infarction
    - Delay for at least 2 weeks
    - Invasive monitoring
    - ? C/S or operative delivery
  - Close postpartum monitoring

Diabetes with hyperlipidemia / atherosclerosis

Effects of Pravastatin

- **Antithrombotic action**
  - Interferes with coagulation cascade
    - Downregulation of TF
    - Upregulation of thrombodulin
    - Reduce thrombin/ factor Va generation
  - Inhibits platelet activation
    - Downregulation of cyclooxygenase1
    - Upregulation of NO synthase

- **Cholesterol lowering action: plaque stabilization**

Diabetic patients with co-morbidites

Maternal – Fetal Management

- **Liberal Hospitalization**
  - Evaluation & RX of complications
- **Frequent prenatal visits**
- **Aggressive control of BS / BP**
- **Monitor organ function (serial)**
- **U/S for fetal growth**
  - 28 wks & every 3 wks
- **NST / BPP at 28 wks**
- **Delivery at ≤ 37 wks**
**Diabetic patients with co-morbidities**

**Recommendations**

- Pregestational diabetics should be evaluated for TOD
- Good pregnancy outcome is achieved by:
  - Tight BP and glucose control
  - Compliance with medications and visits
  - Management of target organ damage
  - Proper M-F surveillance
  - Timely delivery at a tertiary center
- In women with HTN, the goal BP is < 130/80 mmHg
- Women with ESRD / CAD should be counseled against pregnancy
- Diabetics with comorbidities require multidisciplinary management
Fetal Imaging and Antenatal Testing for the Diabetic Gravida

Eleazer Soto, M.D.
Assistant Professor, Division of Maternal-Fetal Medicine
Fetal Imaging and Antenatal Testing for Pregnant Women with Diabetes

Eleazar Soto M.D
Assistant Professor
Division of Maternal Fetal-Medicine
University of Texas Health Science Center at Houston
(UTHealth Medical School)

Congenital anomalies in Diabetic patients

• Most important cause of perinatal death in pregnancies complicated by type 1 and type 2 Diabetes Mellitus
• Congenital anomalies accounts for 30-50% of all perinatal mortality.

Congenital anomalies in Diabetic patients

• There are no specific abnormalities associated with increasing maternal hyperglycemia
• The degree of maternal hyperglycemia appears to have a greater influence on the number of organ systems rather than on the specificity of the organ involved
Frequency of Congenital Anomalies in Infants of Diabetic Mothers

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mills et al.</td>
<td>25/279</td>
<td>9.0</td>
</tr>
<tr>
<td>Greene et al.</td>
<td>35/451</td>
<td>7.7</td>
</tr>
<tr>
<td>Steel and Duncan et al.</td>
<td>12/239</td>
<td>7.8</td>
</tr>
<tr>
<td>Fuhrmann et al.</td>
<td>22/292</td>
<td>7.5</td>
</tr>
<tr>
<td>Simpson et al.</td>
<td>9/106</td>
<td>8.5</td>
</tr>
<tr>
<td>Albert et al.</td>
<td>29/289</td>
<td>10</td>
</tr>
</tbody>
</table>

Congenital anomalies in Diabetic patients

- The prevalence of major congenital anomalies:
  - 46 per 1000 births in women with diabetes
  - 48/1000 births for type 1 diabetes (4.8%)
  - 43/1000 births for type 2 diabetes (4.3%)
- Rate of anomalies in the general population (1-2%)
- 6-30% may have multiple anomalies in pregestational Diabetes Mellitus

Interesting Fact:

- Rate of anomalies reported in New Zealand;
  - Type 1: 5.9% / Type 2: 4.4%
  - Gestational Diabetes 1.4%
- Women with Gestational Diabetes were then reclassified after postnatal glucose tolerance
  - The congenital abnormality rate for those women later reclassified as having unrecognized type 2 diabetes was 4.6%, whereas in the remaining women with gestational diabetes, the rate had fallen to 0.9%.
**Hemoglobin A₁c in Diabetic Pregnancy**

R. D. G. Leslie  
D. A. Pyke  
P. N. John  
J. M. White

Departments of Diabetes and Haematology, King’s College Hospital, London SE5 9RJ

**Medical Intelligence**

Elevated Maternal Hemoglobin A₁c in Early Pregnancy and Major Congenital Anomalies in Infants of Diabetic Mothers

Edith Meller, M.D., John W. Harb, M.D., John P. Casanev, M.D., Peter J. Due, M.D., Raw K. Graham, Ph.D., John D. Sutherland, M.D., and John J. Ketley, M.D.

May 28, 1981; 304(22):1331–3

Hb A₁c above 8.5 had 22.4% anomalies

**The risk of major or minor congenital anomaly according to peri-conceptional hemoglobin A₁c**

![Graph showing the risk of congenital anomalies with increasing HbA1c levels.](image)

**Combined frequency of major congenital anomaly and spontaneous abortion according to the HbA1c during the first trimester of pregnancy**

![Graph showing the combined frequency of major congenital anomalies and spontaneous abortions.](image)


Diabetes Teratogenesis

- Genetic HLA subtypes
- Somatomedin inhibition
- Ketone body excess
- Hyperglycemia
- Free oxygen radical excess

Multifactorial

Complete AV canal defect
Ventricular septal defect (VSD)

Type II DM at 20 weeks with

The ventricular septum and free walls appear thicker than usual

Cranial Signs of Neural Tube Defect
Neural Tube Defect

Anencephaly


### Caudal regression


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### CONGENITAL MALFORMATIONS IN INFANTS OF DIABETIC MOTHERS

<table>
<thead>
<tr>
<th>System</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Transposition of the great vessels, ventricular septal defect, atrial septal defect, tetralogy of Fallot, coarctation, single umbilical artery, hypoplastic left ventricle, cardiomegaly</td>
</tr>
<tr>
<td>Central nervous</td>
<td>Anencephaly, open neural tube defects, holoprosencephaly, absent corpus callosum, Arnold-Chiari anomaly, schizencephaly, microcephaly, macrocephaly, agenesis of olfactory tracts, hydrocephaly</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>pyloric stenosis, duodenal atresia, microcolon, anorectal atresia, omphalo-enteric cyst/fistula, hernias</td>
</tr>
<tr>
<td>Urogenital</td>
<td>Renal agenesis, renal cysts, hydronephrosis, duplication of ureter, ureterocoele, uterine agenesis, micropenis, hypospadias, cryptorchidism, hypoplastic testes, ambiguous genitalia</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Caudal dysgenesis, craniosynostosis, costovertebral anomalies, limb reduction, club foot, contractures, polysyndactyly</td>
</tr>
<tr>
<td>Other</td>
<td>Cleft palate</td>
</tr>
</tbody>
</table>

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### CONGENITAL MALFORMATIONS IN INFANTS OF DIABETIC MOTHERS

<table>
<thead>
<tr>
<th>System</th>
<th>Incidence per 1000 births</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>2 to 34 per 1000 births</td>
</tr>
<tr>
<td>Central nervous</td>
<td>5 per 1000 births</td>
</tr>
<tr>
<td>Urogenital</td>
<td>2 to 32 per 1000 births</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>1 to 5 per 1000 births</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>2 to 20 per 1000 births</td>
</tr>
</tbody>
</table>
Late developing anomalies

Duodenal atresia

Echogenic Kidneys
Nuchal translucency: 11–13+6 weeks scan

Reference range of fetal NT with CRL

99th centile is about 3.5 mm throughout gestational range
First trimester and diabetes

- Increasing nuchal thickness confers greater risk of all major types of CHD, even among euploid fetuses
- At least 25-50% of fetuses with CHD have increased nuchal translucency
- Nuchal translucency appears to predict the presence of congenital heart disease better than most traditional risk factors

Hyett J et al. BMJ. 1999;318(7176):81

When should we attempt to screen for anomalies and do an anatomical survey?

- First trimester nuchal thickness measurement: 11-13 6/7 weeks
- BMI <30: 18-22 weeks
- BMI >30: >20-22 weeks

Routine ultrasound screening in diabetic pregnancies

S. E. WONG*, F. Y. CHAN*, B. B. CINCOFFTA, J. J. N. OATES* and H. D. MCBRIDE*  
*Department of Internal Medicine; †Department of Obstetrics and Gynaecology, Princess Alexandra Hospital, Brisbane, Queensland, Australia

- 12169 low-risk pregnant women and 130 women with pre-existing diabetes
- 8% of anomalies in Diabetes group vs 1.4% in low risk group
- Detection rate of congenital anomalies for diabetic women was significantly lower than that for the general population within the same institution (30% vs. 73%)
Majority of women who had repeat ultrasound scans still had unsatisfactory image quality.

Importance of the antenatal detection of major congenital anomalies:

- Allows discussion of the options of termination of pregnancy,
- In selected cases, fetal surgery.
- Preparation for optimal management at and following delivery.

Should all women with gestational diabetes need fetal echocardiography?
Should all women with pregestational diabetes need fetal echocardiography?

- Increased nuchal translucency in the first trimester
- Suspected cardiac anomaly during a comprehensive fetal anatomic survey ultrasound
- When the cardiac views are restricted by increased body fat and confirmation of normal cardiac structure cannot be made.
- Four chamber with LVOT and RVOT may be cost-effective

Fetal growth and Diabetes

- 4,000 to 4,500 g
- birth weight above the 90th percentile for population and sex-specific growth curves
Diabetes, growth abnormalities and ultrasound

- Macrosomia affects up to 50% of all diabetic pregnancies.
  - Shoulder dystocia – Erb’s palsy
  - Cesarean section
- Range of error of ultrasound is about 15%
- Accuracy of estimated fetal weight is worse in women with diabetes and for macrosomic babies
- No difference in the proportion of women with type 1 or type 2 diabetes with antenatal evidence of macrosomia

How often should we do fetal growth assessments?

- Starting at 28 weeks
- Then around 32-34, and 37-38 wks
Antepartum Fetal Surveillance

- The goal of antepartum fetal testing is to prevent fetal death
- Several techniques, NST, BPP, modified BPP, and Umbilical artery Doppler
- Each method has been independently found to be predictive of fetal compromise in high risk pregnancy groups. However, whether the tests are equally predictive in pregnancies with diabetes is questionable

Antepartum Fetal Surveillance

- Stillbirth and perinatal mortality rates per 1000 births compared with the general population were 26.8 and 31.8 versus 5.7 and 8.5.
- Stillbirths have been observed most often after the 36th week of pregnancy in patients with vascular disease, poor glycemic control, hydramnios, fetal macrosomia, or preeclampsia
Stillbirth rates in women with and without Gestational Diabetes

BPP and diabetes

• A normal test result, is usually thought to be reassuring of fetal well-being
• Limitations

What are the limitations of BPP in diabetic pregnancies?
Polyhydramnios is often associated with Diabetes (poorly controlled)

Rise in maternal glucose levels is known to stimulate fetal breathing movements

Umbilical artery
- Conflicting results regarding UA artery RI and PI and maternal glycemia
- No association between umbilical artery resistance and HbA1c levels
- If diabetic vasculopathy is present, placental function may be affected, thereby increasing the risk for fetal growth restriction
Gestational Diabetes and antenatal testing

- Women with gestational diabetes and diet control (well controlled A1) do not require antenatal testing
- Women with gestational diabetes poorly controlled with diet that requires therapy (i.e. insulin or glyburide) require antenatal testing.

When to start

- 34 weeks of gestation (10 point BPP)
- Testing can be started earlier if any co-morbidity is present (i.e. IUGR, CHTN)

How often

- Clinical judgment
- Once or twice weekly

ACOG

The following recommendations are based on limited or inconsistent scientific evidence (Level II):  
- Women with high-risk factors for stillbirth should undergo biweekly fetal surveillance using the NST, CST, BPP, or modified BPP.  
- Initiating testing at 32-34 weeks of gestation is appropriate for most women who are at increased risk of stillbirth, although in pregnancies with multiple or particularly worrisome high-risk conditions, testing may be initiated as early as 26-28 weeks of gestation.  
- When the clinical condition that has prompted testing persists, a reassuring test should be repeated periodically (either weekly or depending on the test used) and the need for more frequent testing discussed. If high risk conditions persist or clear with therapy, repeat testing may be performed twice weekly until delivery. Any significant deterioration in the maternal medical status or any episode of adverse maternal or fetal outcome requires fetal reevaluation, regardless of the amount of time that has elapsed since the last test.
Summary

- Congenital anomalies is the first cause of perinatal death and morbidity among women with diabetes mellitus
- The rate of fetal anomalies is 4-5%
- Hemoglobin A1C may be of values for counseling and screening patients during the first trimester
- Cardiovascular and CNS anomalies are the most common anomalies
- Nuchal Translucency measurement between 11-13 6/7 weeks is recommended to assess the risk of Cardiovascular disease.
Summary

- Comprehensive anatomy survey 18-22 weeks
- Selective Fetal echocardiogram
- Growth scan every 4 weeks starting at 28 weeks
- Weekly antenatal testing after 34 weeks
  - 10 point BPP (NST and BPP)
  - Earlier if additional complications or indications are present

Thank you

Table 23.1 Congenital malformations in infants of diabetic mothers

<table>
<thead>
<tr>
<th>Organ system</th>
<th>Common</th>
<th>Rare, occasional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>Corrected transposition</td>
<td>Tetralogy of Fallot</td>
</tr>
<tr>
<td></td>
<td>Ventricular septal defect</td>
<td>Hypoplastic left heart</td>
</tr>
<tr>
<td></td>
<td>Conductive</td>
<td>Truncus arteriosus</td>
</tr>
<tr>
<td></td>
<td>Atrial septal defect</td>
<td>Dextrocardia right ventricle</td>
</tr>
<tr>
<td></td>
<td>Cardiomegaly</td>
<td>Pulmonary stenosis</td>
</tr>
<tr>
<td></td>
<td>Anomalous venous return</td>
<td></td>
</tr>
<tr>
<td>Skeletal</td>
<td>Sacral agenesis</td>
<td>Polydactyly</td>
</tr>
<tr>
<td></td>
<td>Vertebral and rib anomalies</td>
<td>Syndactyly</td>
</tr>
<tr>
<td></td>
<td>Limb reduction defects</td>
<td>Cleft foot</td>
</tr>
<tr>
<td>CNS</td>
<td>Anencephaly</td>
<td>Occipital encephalocele</td>
</tr>
<tr>
<td></td>
<td>Neural tube defects</td>
<td>Holoprosencephaly</td>
</tr>
<tr>
<td></td>
<td>Microcephaly</td>
<td>Septo-optic dysplasia</td>
</tr>
<tr>
<td></td>
<td>Hydrocephaly</td>
<td></td>
</tr>
</tbody>
</table>
Umbilical artery and DM

- UA PI is higher in Diabetic pregnancies than uncomplicated pregnancies.
- No association between umbilical artery resistance and HbA1c levels
- Conflicting results regarding UA artery RI and PI and maternal glycemia
- If diabetic vasculopathy is present, placental function may be affected, thereby increasing the risk for fetal growth restriction
Lemon and Banana (spina bifida)

- Frontal bone scalloping
- Seen in 1% normal fetuses
- Abnormal anterior curvature cerebellar hemispheres
- False-positive extremely rare

Late developing anomalies

- Some anomalies do not become manifest until late in pregnancy:
  - Duodenal atresia. The stomach may not increase in size and the duodenum may not dilate until well after 20 weeks.
  - Infantile polycystic kidney disease, where the kidneys may not become enlarged or ‘echogenic’ in appearance until after the 20th week

Why BPP is controversial in diabetic pregnancies?

- A rise in maternal glucose levels is known to stimulate fetal breathing movements, contributing to a positive score for one of the components of the BPP.
- Maternal diabetes is often associated with increased amniotic fluid, again a positive score in the BPP.
- Two of the five tests of fetal well-being are influenced positively simply by having diabetes in pregnancy

Timing and Mode of Delivery for the Diabetic Gravida

Sean Blackwell, M.D.
Chair, Department of Obstetrics, Gynecology and Reproductive Sciences
Timing and Mode of Delivery for the Diabetic Gravida

Sean C. Blackwell, M.D.
Professor and Chair, Department of Obstetrics, Gynecology and Reproductive Sciences
Director, Larry C. Gibraltor M.D. Center for Perinatal and Women's Health Research
Assistant Dean for Healthcare Quality in Perinatal Medicine and Women's Health
University of Texas Medical School at Houston (UTHealth) Medical School
Sean.blackwell@uth.tmc.edu

Objectives

• To discuss the rationale for medically-indicated delivery < 39 wks for women with DM in pregnancy.
• To review the risks and benefits of medically indicated delivery < 39 wks for women with DM in pregnancy.
• To review the risks and indications for cesarean delivery in women with DM in pregnancy.

Why Timed Delivery?

• Women with pre-gestational DM
  – Effort for “tight” glycemic control
  – Multiple visits, tests, imaging
  – Achieve 37 wks

• Getting to term GESTATION is “VICTORY” for many DM women
Why Timed Delivery?

- Balancing the risks of:

  Neonatal M&M (delivery 37-38 wks)
  Vs.
  Continued Pregnancy (delivery >= 39 wks)

Potential maternal and newborn consequences of early term birth

Potential maternal and fetal consequences of continued pregnancy

- Maternal Morbidity & Mortality
  (preeclampsia, poor glycemic control)
- Fetal Morbidity & Mortality
  (Stillbirth, uteroplacental insufficiency, shoulder dystocia)

- Neonatal Morbidity & Mortality
  (Immaturity related)
- Maternal Morbidity & Mortality
  (Prolonged/failed induction, Cesarean delivery)

Gestational Age

37 wks  38 wks  39 wks

Timing of Elective Repeat Cesarean Delivery at Term and Neonatal Outcomes

Respiratory Morbidity in Late Preterm Births

The Consortium on Tocolysis


http://jama.ama-assn.org/content/304/4/415.full.pdf+html
Timing of Indicated Late Preterm and Early Term Birth Workshop

Co-sponsored by
- Eunice Kennedy Shriver National Institute of Child Health and Human Development and
- Society for Maternal Fetal Medicine
February 7-8, 2011
San Francisco, CA
ACOG committee opinion no. 560: Medically indicated late-preterm and early-term deliveries.

- The neonatal risks of late preterm (34 0/7-36 6/7 weeks of gestation) and early-term (37 0/7-38 6/7 weeks of gestation) births are well established.
- However, there are a number of maternal, fetal, and placental complications in which either a late-preterm or early-term delivery is warranted.
- The timing of delivery in such cases must balance the maternal and newborn risks of late-preterm and early-term delivery with the risks of further continuation of pregnancy. Decisions regarding timing of delivery must be individualized.
- Amniocentesis for the determination of fetal lung maturity in well-dated pregnancies generally should not be used to guide the timing of delivery.

NICHD Work Shop

- Pre-gestational
  - Well controlled, compliant, no co-morbidity 39–40 wks
  - Co-morbidity, including FGR, follow particular condition
  - With preexisting vascular disease, consider 37-39 wks
  - Poorly controlled even after optimization, including hospitalization, consider < 39 wks

- Gestational
  - Well controlled on lifestyle changes, deliver 39-40 wks
  - Poorly controlled or non-compliant deliver 37 wks, individualize before 37 wk (consider intensive control)
  - Co-morbidity, including FGR, follow particular condition

Bottom Line: Timing

Pregestational DM + medication requiring GDM

- Medically indicated < 39 wks
  - Co morbidities (HTN, renal Dz)
  - IUGR
  - Poorly controlled even after optimization

- No data comparing 37 vs 38 wks for medically-indicated timed delivery
- Limited value amniocentesis for FLM
Bottom Line: Timing

“39 week Rule”

- Delivery prior to 39 weeks in this woman whose pregnancy is complicated diabetes is medically indicated.
- As the maternal fetal medicine physician caring/consulting in this case I recommend timed delivery at 38 wks.

Mode of Delivery: Diabetes

Centers report 50-75% CD for pre-gestational DM

<table>
<thead>
<tr>
<th>Table 2: Selected Clinical Factors and Outcomes of Women with Diabetes Mellitus Based on White’s Classification System</th>
</tr>
</thead>
<tbody>
<tr>
<td>--------------</td>
</tr>
<tr>
<td>Preterm birth (CD wks %)</td>
</tr>
<tr>
<td>Induced (%)</td>
</tr>
<tr>
<td>Cesarean delivery (%)</td>
</tr>
<tr>
<td>Birth weight &gt; 4000 g (%)</td>
</tr>
<tr>
<td>Need for neonatal resuscitation (%)</td>
</tr>
</tbody>
</table>

White's Classification of Diabetes in Pregnancy in the 21st Century: Is It Still Valid?

Why is CD rate so high?

- High labor induction rates
  - Term and PTB
- Prior cesarean and low TOLAC
- Increasing obesity and morbid obesity
- Multiple co-morbidities
- Risk SD with suspected macrosomia
Shoulder dystocia and BW

TABLE 2. Rate of Shoulder Dystocia Related to Birth Weight and Diabetic Status

<table>
<thead>
<tr>
<th>Birth Weight (g)</th>
<th>Women Without Diabetes (%)</th>
<th>Women with Diabetes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4,000</td>
<td>0.1–1.1</td>
<td>0.6–3.7</td>
</tr>
<tr>
<td>4,000–4,449</td>
<td>1.1–10.0</td>
<td>4.9–23.1</td>
</tr>
<tr>
<td>&gt;4,500</td>
<td>4.1–22.6</td>
<td>20.0–50.0</td>
</tr>
</tbody>
</table>

ACOG Shoulder dystocia PB 1997

Suspected macrosomia

- Planned cesarean delivery to prevent shoulder dystocia may be considered for suspected fetal macrosomia with EFW > 4,500 grams
  - Implication GDM and pre-gestational DM

- Key issues:
  - Literature states clinical and U/S EFW similar accuracy
  - EFW error up to 20% if EFW > 4000 grams
  - Labor induction doesn’t decrease SD risk
  - Informed consent

Bottom Line: Cesarean

- GDM
  - 30-40 % overall CD rate
- Pre-gestational DM
  - 50-60 % overall CD rate

- High % with prior CD and low TOLAC rate
- Of women without prior CD, very high induction rates (40-50%)
- High % obesity (60-75% with BMI > 30 kg/m²)
Intrapartum and Postpartum Management of Diabetes

Janice Whitty, M.D.
Professor, Division of Maternal-Fetal Medicine
Intrapartum and Postpartum Management of Diabetes

Janice E. Whitty, MD
Professor, Maternal-Fetal Medicine
Department of Obstetrics, Gynecology & Reproductive Sciences
The University of Texas Health Science Center at Houston
Department Safety Officer
Medical Director, Labor & Delivery – Lyndon B. Johnson Hospital

Disclosure Statement

I do not have relevant financial relationships with commercial interests related to the content of this presentation.

Learning Objectives

Examine guidelines and recommendations for intrapartum and postpartum management of women with gestational and pre-gestational diabetes.
Gestational Diabetes & Type II DM Co-Morbidities
- Obese
- CHTN
- Preeclampsia
- Utero-placental insufficiency
- Intrapartum Hemorrhage
- Infection
- Thromboembolic disease
- Failed regional anesthesia, intubation

On Admission
- CBC, BMP, T&S
- Anesthesia consult
- EFW/EFM
- Consider fetal macrosomia and shoulder dystocia
- TED Hose, SCDs
- Strict I&O
- NPO
- IV access

Key Therapeutic Goal:
Avoid Maternal Hyperglycemia!
Reduced:
- Fetal Acidemia
- Neonatal hypoglycemia
Avoid hypoglycemia as well
Intrapartum Fetal Acidemia

- Fetus
  - ↑ Glucose
  - ↑ Insulin
  - ↑ Metabolic Rate
  - ↑ Oxygen Consumption
  - ↓ Arterial Oxygen
  - ↑ Fetal Acidemia

Intrapartum Fetal Hypoxemia

- Hyperglycemia
- Ketoacidosis
- Preeclampsia
- Maternal Vasculopathy
- All can reduce placental blood flow

Neonatal Hypoglycemia

- > 50% of macrosomic newborns
- Glucose < 35-40 mg/dl in first 15 hrs. of life
- Rapid drop in glucose after cord clamping
- Maternal glucose control last half of gestation
- Maternal glycemic control during L&D
- ↑ Cord free insulin and C-peptide
- Exaggerated pancreatic response to glucose loading
Obese Newborn

Potential Role of Fetal Exposure to Maternal Type II Diabetes

Intrapartum

Maternal Glucose Targets:
- 70-110 mg/dl (3.9-6.1 mmol/L)
- Type I, Type 2 and GDM
- Obtained from observational data primary involving outcome in Type 1 DM
- Glucose levels >180 mg/dl will result in neonatal hypoglycemia.

ACOG 2005
Garber Endocrine Practice 2004
Intrapartum

Gestational Diabetes Diet Controlled (GDMA1)
- Rarely require insulin in labor
- Measure glucose on admission
- Start glucose infusion D5LR@125 ml/hr
- Check glucose every 4 hours
- If glucose >120 mg/dl start insulin infusion

Planed Cesarean IDDM
- Give PM insulin or PO meds
- Decrease dose of PM long acting insulin
- NPO after 12 MN
- Start IV Dextrose @ 125 ml/hr.
- If CS delayed give 1/3 of AM intermediate insulin or cover with sliding scale
- Monitor glucose intra op and cover
- Monitor glucose q2h post op

IDDM/GDM A2 Intrapartum Glucose Management
- Bedtime usual dose of intermediate-acting insulin or agent
- Hold AM insulin dose
- Begin intravenous infusion of normal saline
- Check glucose hourly
- Active labor or glucose < 70 mg/dL
- Start 5% Dextrose 100–150 cc/hr. (2.5 mg/kg/min) to achieve a glucose level of 100 mg/dL.
- Start Regular insulin IV @ 1.25 U/h if glucose levels exceed 100 mg/dL.

## Titrate Insulin Infusion

<table>
<thead>
<tr>
<th>Plasma/Capillary Glucose (mg/dL)</th>
<th>Infusion Rate (U/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;80</td>
<td>Insulin off</td>
</tr>
<tr>
<td>80-100</td>
<td>0.5</td>
</tr>
<tr>
<td>101-140</td>
<td>1.0</td>
</tr>
<tr>
<td>141-180</td>
<td>1.5</td>
</tr>
<tr>
<td>181-220</td>
<td>2.0*</td>
</tr>
<tr>
<td>&gt;220</td>
<td>2.5*</td>
</tr>
</tbody>
</table>

## Intrapartum Glucose Management

### Protocol 2: Recommended for women with type 1 diabetes

<table>
<thead>
<tr>
<th>Plasma/Capillary Glucose (mg/dL)</th>
<th>Infusion Rate (U/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;70 (&lt;3.9)</td>
<td>0.0</td>
</tr>
<tr>
<td>71-90 (3.9-5.6)</td>
<td>0.5</td>
</tr>
<tr>
<td>91-110 (5.1-6.1)</td>
<td>1.0</td>
</tr>
<tr>
<td>111-130 (6.2-7.2)</td>
<td>2.0</td>
</tr>
<tr>
<td>131-150 (7.3-8.3)</td>
<td>3.0</td>
</tr>
<tr>
<td>151-170 (8.4-9.4)</td>
<td>4.0</td>
</tr>
<tr>
<td>171-190 (9.5-10.6)</td>
<td>5.0</td>
</tr>
<tr>
<td>&gt;190 (&gt;10.6)</td>
<td>Check Ketones</td>
</tr>
</tbody>
</table>

### Protocol 3

- CBS <130 mg/dL (7.2 mmol/L)
  - 3 percent decrease Lactated Ringers at 125 mL/hour
- CBS >130 mg/dL (7.2 mmol/L)
  - Lactated Ringers at 125 mL/hour
  - Check Ketones

---

## Post Partum Pre-gestational

- Insulin Requirements risk for hypoglycemia
- Monitor glucose every 2-4 hr.
- Diabetic diet
- Insulin 1/2 - 1/3 end of pregnancy dose
- Type 2 may not need insulin for 24-48 hrs
- Encourage breastfeeding
- Need 500 additional Kcal (CHO 100 g, protein 20 g)
Postpartum GDM

- Most will not need hypoglycemic therapy
- Check FBS
- FBS < 126 d/c home on regular diet
- If FBS ≥ 126 DM - refer for therapy
- Encourage breastfeeding, exercise and weight loss (tip NIH App LactMed for drugs in BF)
- Counsel re risk of overt DM, need for f/u
- 2 hr. GTT at 6 weeks
Risk of DM after GDM

- Up to 30% will have DM or impaired GT
- Sevenfold lifetime risk of DM
- FH, race and obesity increase the risk
- LGA children of women with GDM have increased risk of DM and 50% have evidence of the metabolic syndrome
- Obesity is increased in children of GDM

Diagnostic Criteria for Diabetes Mellitus, Impaired Fasting Glucose, and Impaired Glucose Tolerance.

<table>
<thead>
<tr>
<th>TEST</th>
<th>DIABETES</th>
<th>IMPAIRED FASTING GLUCOSE</th>
<th>IMPAIRED GLUCOSE TOLERANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting glucose ≥ 126</td>
<td>Not applicable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75-g 2-h oral glucose tolerance test</td>
<td>Fasting glucose ≥ 100-125</td>
<td></td>
<td></td>
</tr>
<tr>
<td>or</td>
<td>Fasting glucose ≥ 126</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-h glucose ≥ 200</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Gestational Diabetes Postpartum Follow-up

- Consider referral for management: weight loss and physical activity counseling as needed
- Consult maternal-fetal medicine and obstetrician: impaired fasting glucose and IGT
- Medical nutrition therapy: yearly assessment of glycemic status
- Assess glycemic status: every 3 years
- Weight loss and physical activity counseling as needed
Contraception IDDM

- Barrier preferred
- IUD no increased infection
- Combined low dose OC may increase TE and MI restrict use to those without vascular or other risk factors
- Depo-Provera (DMPA) deterioration in CHO metabolism, TG & HDL, TC and LDL unchanged
- Progestin only preferred

Kjos 1990

Contraception GDM

- Prospective randomized study
- 230 women recent H/O GDM
- Randomized to low dose combined vs. progestin only
- No significant difference in progression to DM
- OC no adverse effect on TC, LDL, HDL or TG

Summary

- Tight glucose in the control last half of pregnancy and Intrapartum may prevent fetal acidemia and neonatal hypoglycemia
- Women who require insulin or oral hypoglycemic therapy should be managed with glucose and insulin drips in labor
- Glucose should be 70 – 110 mg/dl
- Women who have GDM type 1 rarely need insulin in labor
Summary

• All DM women should have EFW in labor
• If EFW > 4500 gm. consider Cesarean
• Need for insulin decreases in active labor
• Need for glucose increases in active labor
• Consider DVT prophylaxis in labor/OR/PP
• Postpartum glucose decreases significantly
• Decrease insulin 1/3 - 1/2
• GDM usually don’t need insulin postpartum

Summary

• All diabetic women should breast feed
• Encourage diet, exercise and weight loss
• GDM women are at risk for overt DM & recurrent GDM
• GDM need 2 hr. GTT 6-12 wks. PP
• If DM refer for therapy, counseling
• It Glucose intolerant- counseling, exercise weight loss, possible pharmacologic RX

Summary

• Barrier contraception is safer but all methods can be used if no contraindication
• Diabetes in pregnancy ↑risk of childhood obesity, metabolic syndrome and DM
• Improved maternal care may be a factor in improving family and community health
Hyperglycemia, Hypoglycemia: Management of Diabetic Emergencies

Baha Sibai, M.D.
Professor, Division of Maternal-Fetal Medicine
Diabetic Ketoacidosis in Pregnancy

Baha M. Sibai, MD
Professor
Director, Maternal Fetal Medicine Fellowship
Department of Obstetrics, Gynecology & Reproductive Sciences

DKA in Pregnancy

Learning Objectives

• Discuss causes and pathophysiology of DKA in pregnancy

• Discuss the diagnosis and goal directed management of DKA in pregnancy

• Review the preventive strategies to prevent DKA in pregnancy

DKA in Pregnancy

Incidence and Pregnancy Outcomes

• 0.5-3% of all diabetic pregnancies

• Maternal mortality is < 1%

• Fetal mortality is 9-36%

November 09, 2013
How pregnancy predisposes to DKA
- State of accelerated starvation
- Insulin resistance
  - HPL
  - Prolactin
  - Cortisol
- Progesterone effects
- Respiratory changes
- Beta hCG

DKA in Pregnancy
Precipitating Factors
- Cessation of insulin therapy during pregnancy (40%)
- Previously undiagnosed diabetes mellitus (30%)
- Infection (20%)
- Emesis
- Insulin pump failure
- Beta-sympathomimetic drugs
- Corticosteroids
- Poor management
Dehydration
Ketosis
Acidosis (metabolic)

Common symptoms and signs of diabetetic ketoacidosis in pregnancy

Symptoms
• Polyuria.
• Polydipsia.
• Nausea.
• Vomiting.
• Abdominal pain.
• Weakness.
• Weight loss.

Signs
• Hyperpnea.
• Ketotic breath.
• Tachycardia.
• Hypotension.
• Dry mucous membranes.
• Dizziness.
• Coma.

Laboratory Findings

- Plasma glucose (usually > 250 mg/dL)*
- Arterial pH < 7.30
- Anion gap > 12 mEq/L
- Elevated base deficit
- Positive serum/urine ketones: specially 3β-hydroxybutyrate (most abundant)**
- Falsey normal potassium level might be present.
- Low serum bicarbonate (often less than 15 mEq/L)
  Elevated serum EUN and creatinine due to dehydration and possible renal failure

* DKA in pregnancy can present with much lower glucose levels.
** Shams MA et al. Met J 2002, only detect acetacetate.

Management of DKA in Pregnancy

- Medical/Obstetric ICU
- Vital signs Q 15 min
- Large bore IV or central line
- ABG, glucose, electrolytes, ketones (q 1-2 hr)
- Urine analysis, culture, other infection
- Oxygen at 6 L/min
- Continuous pulse oximetry
- Contractions & FHR (≥ 24 wks)
- Bedside flow sheet
  - Intake - output
  - Results of blood tests
  - Medications
DKA in Pregnancy

**Pitfalls of Treatment/ Complications**

- Cerebral edema
- Hyperchloremic acidosis
- Hypoglycemia
- ARDS
- Pulmonary edema
- Arrythmias
DKA in Pregnancy
Fetal Monitoring and Timing of Delivery

- Fetal monitoring if > 24 wk
- FHR abnormalities in the acute phase
- No intervention on fetal behalf unless the mother’s condition is stable enough

Reversible Fetal Hypoxia-acidosis in DKA*

- Metabolic acidosis
  - Increased maternal Hgb affinity to O₂
  - Less oxygen to fetus
  - Fetus unable to exchange acids
- Reduced tissue perfusion
  - Reduced UPBF
- Hyperglycemia
  - Fetal hyperglycemia, ↑ insulin
  - Increased oxygen requirements

* Usually last 6 hrs before correction
FHR tracing during DKA
After correction of hyperglycemia and acidosis

FHR tracing/timing of Delivery in DKA
Emergency C/S, Apgar scores 2, 3, 5, pH = 6.85

Transient Changes in Fetal Testing in DKA

- Fetal heart rate
  - Tachycardia
  - Absent accelerations
  - Poor variability
  - Late decelerations

- Abnormal biophysical profile
- Doppler (redistribution of blood flow)
  - Increased umbilical artery PI
  - Reduced middle cerebral artery PI
Hypoglycemia in Pregnancy

Baha M. Sibai, MD
Professor
Director, Maternal Fetal Medicine Fellowship
Department of Obstetrics, Gynecology & Reproductive Sciences

GA at Onset of Severe Hypoglycemia in Pregnancy

Frequency of Severe Hypoglycemia/ Patient
**Risk factors for Severe Hypoglycemia during Pregnancy**

- Severe hypoglycemia the year preceding pregnancy
- Self-estimated impaired hypoglycemia awareness
- A long duration of diabetes
- A lower HbA1c in early pregnancy
- Fluctuating glucose values (≤ 60 mg or ≥ 180 mg/dl)
- Excessive supplementary insulin between meals

**Causes of Severe Hypoglycemia**

- Many hypos, 3%
- Physical activity, 2%
- Vomiting, 2%
- Postprandial meal, 10%
- Insufficient carbohydrate intake, 13%
- Excessive supplementary insulin, 14%
- Unknown, 56%

**Insulin Requirements during Pregnancy**

- Triple dose
- Double dose
- Normal Insulin

Weeks:
- Conception
- 5
- 10
- 15
- 20
- 25
- 30
- 35
- Delivery

November 09, 2013
Signs & Symptoms of Hypoglycemia

<table>
<thead>
<tr>
<th>Sxs due to counter regulatory hormones</th>
<th>Sxs with severe hypoglycemia:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachycardia</td>
<td>Confusion</td>
</tr>
<tr>
<td>Chills</td>
<td>Seizures</td>
</tr>
<tr>
<td>Sweating</td>
<td>Coma</td>
</tr>
<tr>
<td>Pallor</td>
<td>Death</td>
</tr>
</tbody>
</table>

Low Blood Sugar during Sleep

- **Symptoms:**
  - Sleep walking
  - Tossing and turning in bed
  - Morning headaches
  - Bad dreams
  - Night sweats
  - Rebounding high morning blood sugars
- **Treatment:**
  - Test blood sugar at 2-4 am

Treatment of Hypoglycemia

- 4 ounces-1/2 cup of juice
  - **Not** orange juice
- Other choices:
  - 4 ounces non-diet soft drink
  - 6 Sweet Tarts or Jelly Beans
  - 8 Lifesavers
  - 4 Starbursts
  - 1 small box of raisins
  - 3-4 glucose tablets with 8 oz of water
Rule of 15 for hypoglycemia

- Blood sugar < 50-60 mg/dL:
  - Take 15 g of carbohydrate
  - Retest BS in 15 minutes
  - Blood sugar should rise at least 15 mg/dl
  - If still < 50 mg/dL, repeat treatment
- Always carry proper snacks with you in case meals or snacks are delayed.

Who Treats Severe Hypoglycemia

- Partner, 75%
- Family, 5%
- Friend/coworker, 4%
- None, 1%
- Ambulance/hospital staff, 15%

Preventative Measures to Reduce Risk of Severe Hypoglycemia

- Identify those at high-risk
  - Women with self-estimated impaired hypoglycemia awareness
  - History of severe hypoglycemia the year preceding pregnancy
- Reduce insulin dose by 10% at 8-16 weeks
- Precautious use of supplementary insulin in early pregnancy
- Carry oral glucose solutions
- Use of rapid- and long-acting insulin analogues?
- Avoid pre-bedtime glucose below 70 mg/dl
- Frequent glucose monitoring including 2 and 4 AM
- Prescribe glucagon pen for use at home by partner
- Use insulin pump therapy combined with real-time continuous glucose monitoring.
Diabetic Patients with Co-morbidities

Recommendations

- Type 1 DM with preterm labor and/or preeclampsia
- Terb increases BS values, M-F tachycardia
  - Avoid its use for PTL
  - Consider Magnesium instead
- Steroids for FLM increase BS values
  - More frequent BS monitoring
  - Adjust dose of insulin
- Protracted N/V are signs of DKA
  - Monitor BS, electrolytes, anion gap
  - Fetal tachycardia + minimal variability: Early acidosis
  - Repetitive late decelerations misdiagnosed as abruptio placentae
- Immediate C/S could lead to adverse M-F outcome
Fetal, Neonatal and Childhood Consequences of Diabetes

Hector Mendez-Figueroa, M.D.
Assistant Professor, Division of Maternal-Fetal Medicine
Fetal, Neonatal, and Childhood Consequences of Diabetes

Hector Mendez-Figueroa, M.D.
Assistant Professor
Department of Obstetrics, Gynecology And Reproductive Sciences
UT Health Sciences in Houston

Disclosure Statement

I do not have relevant financial relationships with commercial interests related to the content of this presentation.

Learning Objectives

1. Discuss the fetal consequences associated with diabetes in pregnancy
2. Examine the impact of diabetes in pregnancy on neonatal health
3. Discuss the long term consequences related to fetal programming and the risk of childhood obesity in women with gestation and pre-gestational diabetes.
CONSEQUENCES OF DM

- Neonatal
- Fetal
- Childhood
- GDM
- Pre-Gestational DM

CLINICAL SCENARIO

27 y/o G2P1 at 28 4/7 weeks has an abnormal 3-hour GTT and has just heard for the first time that she has gestational diabetes in pregnancy. She comes to the office very anxious and worried. Her major concern is:

HOW IS THIS GOING TO AFFECT MY BABY?
Fetal effects - GDM

• Association with congenital anomalies is not clear

• Risk congenital anomalies may be associated with Obesity and elevated FPG
  – OR 2.8 increase in anomalies with GDM + obesity

• Risk of stillbirth – 9.3 per 1,000 births compares to 3.6 per 1,000 births in controls
  – “There is no consensus on the risk of demise in well – controlled GDM” – ACOG practice bulletin

CEMACH, 2005

Fetal effects - GDM

Several studies shown a continuous positive relationship b/w ↑ glucose levels and the incidence of macrosomia.

HAPO Study, NEJM 2008

Fetal effects - GDM

Pooled estimates from both RCTs and cohort studies show significantly higher incidence of BW >4,000 g and >4,500 g among GDM pregnancies

Lapolla, Diabetic Med 2008
Morikawa, Diabetes Res 2010
CLINICAL SCENARIO

37 y/o G1 with a five-year history of type 2 diabetes mellitus treated with oral hypoglycemic presents at 9 weeks for her prenatal intake appointment. She knows that diabetes can adversely affect her pregnancy and is very concerned about it. Her major concern is:

HOW IS THIS GOING TO AFFECT MY BABY?

FETAL EFFECTS – PRE-GESTATIONAL DM

Congenital abnormalities 6-12% all DM pregnancies
Anomalies 6x more likely in infants DM mothers

- HbA1C < 7% - risk not significantly greater
- HbA1C > 9.5% rate of anomalies 20-25%

Guerin et al, Diabetes Care 2007
**FETAL EFFECTS – PRE-GESTATIONAL DM**

- 4.2-fold increase in neural tube defects
- 3.4-fold increase in congenital heart disease
- Disordered fetal growth
  - Intrauterine growth restriction seen in long-standing DM with macrovascular disease
  - Fetal overgrowth is far more common

Farrell et al, Diabet Med 2002

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**FETAL EFFECTS – PRE-GESTATIONAL DM**

- Cardiovascular
  - ASD
  - VSD
  - HLHS
  - TOF
  - Truncus
- Skeletal
  - Sacral agenesis
- Central Nervous system
  - Anencephaly
  - Encephalocele
  - Meningomyelocele
  - Holoprosencephaly
- Genitourinary
  - Renal agenesis
  - Polycystic kidneys

Molsted-Pedersen et al, Lancet 1964

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**CONSEQUENCES OF DIABETES IN PREGNANCY**

- Fetal
- Neonatal
- Childhood
NEONATAL EFFECTS

BIRTH WEIGHT - TREATMENT

Treatment is associated mean difference BW of -120.81g
[-163.40, -78.23 95% CI ]

NIH Evidence report, 2012

NEONATAL EFFECTS

HYPERBILIRUBINEMIA

INCIDENCE

- Treatment has not shown to decrease the incidence (MFMU)
- Treatment benefit was only seen cohort (n=1665) OR 0.26 [0.18- 0.37]

Langer et al, 2005
Chico et al, 2005

NEONATAL EFFECTS

Hypoglycemia

- Studies use different cutoffs, biochemical vs. clinical
- All 3 prospective studies did show increased incidence with DM

- Does treatment in GDM decrease the incidence?

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bonomo et al</td>
<td>1997</td>
<td>300</td>
<td>0.83</td>
<td>0.26-2.67</td>
</tr>
<tr>
<td>Crowther et al</td>
<td>2005</td>
<td>1030</td>
<td>1.34</td>
<td>0.82-2.18</td>
</tr>
<tr>
<td>Garner et al</td>
<td>1997</td>
<td>299</td>
<td>1.63</td>
<td>0.85-3.13</td>
</tr>
<tr>
<td>Landon et al</td>
<td>2005</td>
<td>738</td>
<td>1.18</td>
<td>0.92-1.52</td>
</tr>
</tbody>
</table>
NEONATAL EFFECTS

• Fetal Birth trauma:
  - Increased incidence in retrospective trials.
  - Only 3 prospective studies, none showing any significant difference
  - Inconsistency: 2 RCTs showed no difference and the 1 cohort study showed a difference in favor of the treated group. (n=389, OR 0.02; 95% CI 0.00 - 0.11)

• Clavicular fracture/ Brachial plexus injury
  - No prospective study showing increased incidence on DM
  - Treatment decreased incidence in one cohort study but not RCT (n=389 vs. n=1,000)
  Berggren et al. AJOG 2011

Perinatal Mortality

• 12 studies evaluating neonatal mortality
• No studies demonstrated a significant difference between groups
• Pooled results - GDM 20/1732 (1.2%) vs. 219/26015 (0.8%)

Treatment in GDM
  - 3 RCT to date included n=2,287
  - Only one trial (ACHOIS) reported any cases perinatal death
  - No significant differences found b/w groups for the 3 RCTs
  Crowther, NEJM 2005
  Landon, NEJM 2005

Shoulder dystocia:
  - No GDM vs. GDM: 6 pooled RCT OR - 2.86 (95% CI 1.81-4.51)

Crowther, NEJM 2005
Landon, NEJM 2005
NEONATAL EFFECTS

Admission to NICU

- Rate of admissions to NICU depend on several factors
- Practitioners are more likely to admit infants of diabetic mothers
- 3 RCTs and 1 prospective cohort study showed no significant differences with treatment

![Graph showing rates of admission to NICU]

- Crowthers et al
- Landon et al
- Bonomo et al

NEONATAL EFFECTS

- Respiratory complications
  - RDS seen in approximately 6-8% of pregnancies
  - 2 RCT showed no significant difference b/w groups
  - One cohort (n=1665) showed benefit with treatment: OR 0.16 [95% CI 0.10-0.26]

CONSEQUENCES OF DIABETES IN PREGNANCY

- Fetal
- Neonatal
- Childhood
Childhood effects

Childhood Obesity

• **Pregnancies complicated by DM**
  - Trend increase in childhood obesity at age 5-7 years
  - True for weight, BMI at 85th and 95th percentile (p < 0.01)
  - Offspring GDM – 61% higher odds of being overweight age 7
  - In a nationwide survey: at age 9-14 17.1% at risk for overweight and 9.7% were overweight
  - GDM pregnancy: odds 1.4 (1.1-2.0) for overweight adolescent

  Hiller et al., Diabetes care 2005
  Baptiste et al., Matern Child, 2012

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Childhood effects

Childhood Obesity

• **Seen across the entire range of increasing maternal glucose screen values in GDM**

• **Treated vs. No treated GDM**
  - BMI >95th at 7 to 11 year follow-up, no significant difference b/w groups RR 1.58 (95% CI, 0.66 to 3.79)
  - BMI >85th found no difference between groups (RR 1.19; 95% CI, 0.78 to 1.82, n = 199)

  Hiller et al., Diabetes care 2005

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Childhood effects

**DOES IT PREDISPOSE TO DM?**

• **Type 2 DM/Impaired glucose tolerance**
  - Retrospective data has shown increased risk
  - Infants diabetic mothers 3-5x increase in risk early adulthood
  - One small study follow-up RCT GDM with 7-11 year follow-up
  - Type 2 DM: No significant difference in incidence among the offspring OR 1.88 [95% CI 0.08 - 44.76]
  - IGT: No significant difference in incidence among the offspring OR 5.63 [95% CI 0.31 - 101.32]

  Malcolm et al., Diabetic Med 2006
  Lindsay et al, Diabetes care 2000

---
**Childhood effects**

**Metabolic syndrome**

- **Components:** obesity, hypertension, dyslipidemia, and glucose intolerance
  - Cohort followed 6-11 years compared LGA control vs. LGA DM mothers
  - LGA DM mothers were at significant risk of developing MS in childhood, having 2 or 3 components
  - Also had higher incidence of insulin resistance
  - May be due to maternal obesity???

Boney et al., Pediatrics 2005

**CONCLUSIONS**

1. Fetal effects of GDM appear to be limited to fetal overgrowth, pre-gestational DM is associated with increased risk congenital anomalies
2. Neonatal effects are common for both, some can be reduced with appropriate therapy
3. Very limited data on childhood impact from DM during pregnancy – more studies are required

**QUESTIONS?**
Thank you for attending the Management of Diabetes in Pregnancy: An Update for the Busy Clinician educational event!

CONTACT INFORMATION

UTHealth Maternal-Fetal Center
832.325.7133

Children’s Memorial Hermann Patient Transfer Line
713.704.2577

childrens.memorialhermann.org