Management of Diabetes Mellitus in Pregnancy

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Diabetes Mellitus

- ~17 million Americans have DM
- ~10.2% women >age 20 have DM
- GDM complicates ~7% of all pregnancies
  - > 90% of diabetes in pregnancy
- Pregestational DM complicates ~1-2% of all pregnancies
Diabetes Mellitus

- Anticipated epidemic
- ~30% of children/youth are overweight/obese
- >60% of population is obese/morbidly obese in some states
- Undiagnosed DM is a major health hazard:
  - FBS > 126 mg/dL
  - 2 hour postprandial BS > 200 mg/dL on 75 g GTT
  - Random (“casual”) BS of > 200 mg/dL
  - HgbA1c > 6.5%*

* = New ADA diagnostic criteria 2010

Diabetes in Pregnancy

- appropriate management has resulted in a significant decrease in the perinatal mortality rate (PNMR)
- PNMR decreased from 10-12% to 2-5%
- Attributable risk ~2 x background risk
  - However, studies flawed & old
  - Include undiagnosed type II DM
  - Only recently confirmed in RCT (2005, 2007)
Diabetes in Pregnancy

Centers around two main principles

1) Normalization of glucose values
2) Antenatal surveillance to ensure fetal well-being

Types of DM

1) Type I – autoimmune, β-cell destruction; prone to ketosis; formerly “juvenile onset” or “IDDM”
2) Type II – lifestyle dependent, ethnic predisposition, obesity, age; formerly “adult onset”
3) “Type III” – GDM, pre-diabetes, insulin resistance, carbohydrate intolerance
### Classification of Diabetes Mellitus

1) Gestational Diabetes Mellitus without fasting hyperglycemia (usually no insulin)

2) Gestational Diabetes Mellitus with fasting hyperglycemia (usually insulin)

3) Overt (pre-gestational) Diabetes Mellitus without vascular disease

4) Overt (pre-gestational) Diabetes Mellitus with vascular disease

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### Classification of Diabetes Mellitus

*Modified Priscilla White Classification*

<table>
<thead>
<tr>
<th>Class</th>
<th>Diabetes onset age</th>
<th>Duration</th>
<th>Vascular Disease</th>
<th>Insulin</th>
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<td>0</td>
</tr>
<tr>
<td>A2</td>
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<td>H</td>
<td>Any</td>
<td>Any</td>
<td>+</td>
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</tbody>
</table>
Gestational Diabetes

- Defined as glucose intolerance first diagnosed in pregnancy
- Characterized by:
  - Carbohydrate intolerance & Insulin resistance
  - Defective beta cell compensation
    - The B cell defect
      - Glucokinase mutation
      - Loss of B cell mass
      - Blunted response to normal glucose fluctuations

Gestational Diabetes - clinical significance

1) Increase in lifetime risk of developing diabetes (Type 2)
2) Increase in both perinatal & long term health risks in offspring
   - Obstetric complications
     - Preeclampsia
     - Polyhydramnios
   - Postnatal complications
     - Macroscopia (birth trauma, shoulder dystocia, operative delivery)
     - Neonatal hypoglycemia
     - Hyperbilirubinemia
     - RDS
     - Polycythemia, hyperviscosity
     - Hypertrophic & congestive cardiomyopathy
**Screening for Gestational Diabetes**

**OLD**

Screen all Pregnant Women for GDM between 24-28 weeks

- Screen with random 50 g 1 hour oral glucose load
  - Glucose < 130-140 mg/dl
    - No GDM
  - Glucose > 130-140 mg/dl
    - Proceed with 100 g 3 hour OGTT
      - FBS < 95 (105)
        - 1 hr < 180 (190)
        - 2 hr < 155 (165)
        - 3 hr < 140 (145)
          - 2 or more abnormal values
            - GDM

**Current**

Screen all Pregnant Women for GDM at prenatal intake visit

- Screen with random 50 g 1 hour oral glucose load
  - Glucose < 130-140 mg/dl
    - No GDM
  - Glucose > 130-140 mg/dl
    - Proceed with 100 g 3 hour OGTT
      - FBS < 95
        - 1 hr < 180
        - 2 hr < 155
        - 3 hr < 140
          - 2 or more abnormal values
            - GDM
          - Glucose < 130-140 mg/dl
            - Repeat 100 g 3 hour OGTT at 24-28 weeks
Screening for Gestational Diabetes Current

How to administer 1 hr 50g glucose challenge:
• Fasting? – NO!
• Ensure correct glucola amount/drink is given

How to administer 3 hr 100g OGTT:
• Fasting? – YES! (at least 8 hours)
• No smoking, eating, exercise (walking) during test
• Unrestricted diet 3 days before (do not give to people on ADA diet!)

Do not administer to people on oral hypoglycemic medication!
Do not administer tests after gastric bypass surgery!

Screening for Gestational Diabetes Current

Screen all Pregnant Women for GDM at prenatal intake visit

Screen with random 50 g 1 hour oral glucose load

Glucose 185-199 mg/dl → Proceed with 100 g 3 hour OGTT

FBS < 105 mg/dl

Glucose >200 mg/dl → GDM

FBS > 105 mg/dl
Screening for (Gestational) Diabetes
What does ACOG say?

- ACOG Practice Bulletin #30, 2001, reaffirmed 2010
- ACOG Committee Opinion # 504, September 2011
- No universal recommendation for the ideal approach to screening for GDM
- CONTINUE with two step approach of screening and diagnosis:
  - Patient history, risk factors, 50g 1hr glucose challenge at 24-28 weeks for screening
  - 100g 3hr OGTT for diagnosis

Screening for Gestational Diabetes
HAPO and WHO

- HAPO = Hyperglycemia and Adverse Pregnancy Outcomes study, new recommendations for universal screening 2 hr 75 gOGTT
  - Large, multicenter observational study
  - Demonstrated clear relationship of maternal hyperglycemia, LGA infants, cord blood C-peptide, neonatal hypoglycemia, cesarean delivery
  - Recommend one step approach

- International Association of the Diabetes in Pregnancy Study Group (IADPSG) follows recommendations of HAPO
- WHO has recommended 2 hr 75 g OGTT since the 1970’s
Screening for Gestational Diabetes
HAPO and WHO

- Adoption of HAPO/IADPSG recommendations would increase number of GDM in the US to ~18% of all pregnancies (>20% in the KP population)
- Two recent randomized trials demonstrated benefit in treatment of mild GDM -> reduction of neonatal morbidity
  - Crowther et al, 2005 (AUS)
  - Landon et al, 2007 (MFMU)
- BUT: no evidence that universal adoption of new IADPSG guidelines leads to clinically significant improvements
- Would lead to significant increase in health care cost

Screening for (Gestational) Diabetes
New???

Screen all Pregnant Women for diabetes at prenatal intake visit

- HgbA1c > 5.7 – 6.4 % OR FBS > 92 mg/dL and < 126 mg/dL
  - Screen with FBS OR Random BS OR Hemoglobin A1c
  - 75 g 2 hour OGTT at 24-28 weeks
  - FBS < 92 mg/dL 1 hr < 180 mg/dL 2 hr < 153 mg/dL
  - DM

- HgbA1c > 6.5 % OR FBS > 126 mg/dL OR Random BS > 200 mg/dL
  - GDM
  - 1 or more abnormal values
Screening for Gestational Diabetes

BOTTOM LINE

- CONTINUE two step approach to screening and diagnosis
- Two KP population adjustments:
  1) Begin screening at PNV
  2) Add HgbA1c to screen for undiagnosed diabetes

NIH is planning Consensus Development Conference to determine optimal screening for the US population. Until then – status quo!

Management of GDM

- Other controversies:
  - If positive screening cut off lowered from 140 mg/dL to 130 mg/dL, number of women requiring glucose tolerance testing increased from 14% to 23%
  - Test sensitivity increases from 80 to 90% using 130 mg/dL cut off; both ADA and ACOG allow both screening cut offs.

- Fasting glucose impairment alone:
  - Increases risk for fetal macrosomia
  - No clear guidelines regarding need for, or type of recommended treatment
  - Do NOT use code for GDM in these patients!
Management of GDM

ONE abnormal value on 3 hour OGTT:

OPTIONS:
1) Do Nothing
2) Repeat 3 hour OGTT
3) ADA diet, no glucometer

Impact of intervention? – Unknown
One abnormal value DOES increase risk for macrosomic infants, however, only minimally; no threshold will identify ALL patients at risk

Management of GDM

Goal of GDM Management
ACHIEVE NORMOGLYCEMIA

Normoglycemia (outside of pregnancy) is defined as a:

- FBS < 100 mg/dl
- 1 hour postprandial < 140 mg/dl
- 2 hour postprandial < 120 mg/dl
Management of GDM

Management centers around glycemic control

Glycemic control can usually be achieved by:

1) Diet
   • Carbohydrate restriction
2) Exercise
   • 20 min once to twice daily
3) Medical therapy
   • Insulin (NPH, Regular) or oral hypoglycemics

Management of GDM

Nutritional management is the cornerstone of management for women with GDM
Management of GDM

Diet
- should provide necessary nutrients for both mom and fetus
- should result in normoglycemia
- should result in appropriate weight gain
  - < 90% IBW: 28-40 lbs weight gain
  - IBW: 25-30 lbs weight gain
  - > 120% IBW: 15-20 lbs weight gain
- should prevent ketosis
  - check CHO, calories and fasting duration

Management of GDM

Diet - There is no standard ADA diet!!
- Calories should be calculated as:
  - 25-35 kcal/Kg (IBW)/day
- Composition of diet
  - 40-45%-CHO*
  - 20-25%- protein
  - 35-40%- fat
  * CHO restriction due to CHO intolerance during pregnancy (GDM definition)

Mild to moderate caloric restriction in obese women (BMI >30) by –30-33% can be achieved without ketosis and may improve pregnancy outcomes. Don't over-restrict!
**Management of GDM**

**Diet**

The diet should be divided into 3 meals and 3 snacks/daily

- **Breakfast** - 10-15% of calories
- **AM Snack** - 5-10% of calories
- **Lunch** - 20-30% of calories
- **PM Snack** - 5-10% of calories
- **Dinner** - 30-40% of calories
- **HS Snack** - 5-10% of calories

**Management of GDM**

**Diet**

1) The diet must be validated with home blood glucose monitoring
2) The diet works if euglycemia is achieved
3) Maintenance of accurate food and blood sugar records is important and necessary
4) Exercise should be used concurrently
Management of class A1 GDM

**After Diagnosis:**
- Refer to nutritional counseling, DM team
- Issue glucometer, check FBS, one hour PP BS after every meal
- BS review every 2 weeks
- US for EFW at 36-38 weeks
- Delivery 39-41 weeks if well controlled
- Delivery <40 weeks if HTN, prior stillbirth, poor compliance etc
- If EFW > 4500g consider cesarean section
- 75 g 2 hour OGTT or FBS 6-12 weeks postpartum

**Management of class A1 GDM TIMELINE**

<table>
<thead>
<tr>
<th>Timing</th>
<th>Tests</th>
<th>12 weeks</th>
<th>18 weeks</th>
<th>28 weeks</th>
<th>28-30 weeks</th>
<th>36-38 weeks</th>
<th>40 weeks</th>
<th>40-41 weeks</th>
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<td>Initial Exam</td>
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<td>U/S for EFW</td>
<td>Antepartum fetal heart rate testing</td>
<td>Delivery</td>
</tr>
</tbody>
</table>
Management of GDM

Glucose Monitoring

Target Plasma Glucose Levels in Pregnancy

- FBS – 60-90 mg/dl
- Preprandial – 60-105 mg/dl
- 1 hour postprandial - < 140 mg/dl
- 2 hours postprandial - < 120 mg/dl
- 2 am – 6 am - >60 mg/dl
Management of GDM

Home Glucose monitoring should:
• Include FBS and postprandial values
• Be performed daily until euglycemia achieved
• Monitoring frequency can be decreased if euglycemia is achieved and the patient is compliant

Management of GDM

Factors than affect glucose levels:
• Stress (trauma, infection, etc)
• Time of day (glucose values are increased in the am secondary to increased cortisol and growth hormone levels)
• Exercise
• Amount of CHO in diet
Management of GDM

Exercise
• Facilitates glucose utilization by
  • Increased insulin binding to its receptors
  • Increased insulin affinity for its receptors
• Decreases insulin resistance
• Impacts hepatic glucose output
• Effects become apparent after 2-4 weeks of training

Management of GDM

Exercise
• Certain types of exercise in pregnancy have been suggested to cause fetal distress, uterine contractions, IUGR
• This may be secondary to increased uterine activity associated with lower body exercise
• Need to focus on upper body or whole body cardiovascular training
• Recommend exercise frequency: once to twice daily, at least 10-20 minutes each time
Management of GDM

- Goal in management of class A1 GDM patients is:
  - reduce macrosomia
- If mean FBS > 95-105 mg/dl > 1 week on an appropriate ADA diet OR
- If mean 1hr postprandial exceeds > 140 mg/dl, or 2 hr postprandial > 120 mg/dl > 1 week on an appropriate ADA diet
  - medical therapy should be started
- Approximately 15-20% of all GDM patients will require insulin or other medical intervention

Management of GDM

<table>
<thead>
<tr>
<th>Insulin Type</th>
<th>Insulin Action Onset</th>
<th>Peak Action Duration</th>
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</thead>
<tbody>
<tr>
<td>Humalog</td>
<td>5 min</td>
<td>1 hr 4 hrs</td>
</tr>
<tr>
<td>Regular</td>
<td>30 min</td>
<td>2-4 hrs 6-8 hrs</td>
</tr>
<tr>
<td>Lente</td>
<td>1-3 hrs</td>
<td>7-15 hrs 18-22 hrs</td>
</tr>
<tr>
<td>NPH</td>
<td>1-2 hrs</td>
<td>4-12 hrs 18-24 hrs</td>
</tr>
<tr>
<td>Ultralente</td>
<td>4-6 hrs</td>
<td>9-20 hrs 24-28 hrs</td>
</tr>
<tr>
<td>Glargine</td>
<td>1 hr</td>
<td>no peak 24 hours</td>
</tr>
</tbody>
</table>
Beginning Insulin Therapy

- If mainly postprandial hyperglycemia, use ~ 20-30 units NPH in am
- If FBS is elevated, use ~10-20 units NPH at bedtime
  - If post breakfast elevated, add 5-10 units Regular to am insulin dose
  - If post dinner glucose elevated, add 5-10 units Regular before dinner
  - Rarely, elevated post lunch gluoses may require additional Regular dose before lunch

Management of GDM & DM

Beginning Insulin Therapy

- 1st Trimester – 0.5-0.7 units/Kg/24hr
- 2nd Trimester – 0.8 units/Kg/24hr
- 3rd Trimester – 0.9-1.0 units/Kg/24hr
  - Divide total doses into: 2/3 in am and 1/3 in pm
  - Split am dose into: 2/3 NPH and 1/3 Regular
  - Split pm dose into ½ NPH and ½ Regular
    - Pm dose divided into regular before dinner and NPH at bedtime

Helpful dose calculator: www.perinatology.com
Beginning Insulin Therapy

- If stable and compliant, begin outpatient therapy in conjunction with diabetes team
  - High insulin resistance requires higher doses
- If unstable or non-compliant, admit patient to hospital – place on IV insulin drip with SQ boluses before each meal
  - Calculate 24 hour insulin requirements and then divide doses into am/pm and NPH and regular

Management of GDM & DM

- Calculation of insulin need based on food intake ("carb counting")
  - 1.5 units regular/10 gm CHO at breakfast
  - 1.0 units regular/10 gm CHO at lunch/dinner
- If postprandial hyperglycemia persists, uses sliding scale based on pre-prandial glucose to determine pre-meal insulin requirements
  - < 70: X - 2 units regular
  - 70-100: X
  - 100-140: X + 2 units regular
  - > 140: X + 4 units regular

X = previously calculated dose
Oral hypoglycemic agents in pregnancy

- Langer in NEJM in October 2000
- Randomized controlled trial comparing Glyburide with traditional insulin in 404 women with GDM
  - All patients placed on 25-35 kcal/kg, CHO restricted diet (40-45%)
  - Insulin was started at 0.7 units/kg, divided into 3 SQ injections and increased weekly as necessary
  - The starting dose for Glyburide was 2.5 mg each am and increased 2.5 – 5.0 mg each week (maximum 20 mg)

Glyburide versus Insulin

<table>
<thead>
<tr>
<th>Variable</th>
<th>Glyburide</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA at diagnosis</td>
<td>24±7</td>
<td>25±7</td>
</tr>
<tr>
<td>GA at delivery</td>
<td>38.7±1.6</td>
<td>38.5±2.1</td>
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<tr>
<td>Results of OGTT</td>
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<tr>
<td>FBS</td>
<td>97±14</td>
<td>98±16</td>
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<tr>
<td>1 hr</td>
<td>197±31</td>
<td>201±30</td>
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<tr>
<td>2 hr</td>
<td>174±31</td>
<td>174±29</td>
</tr>
<tr>
<td>3 hr</td>
<td>140±37</td>
<td>134±37</td>
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<tr>
<td>Dose of insulin</td>
<td>---</td>
<td>85±48</td>
</tr>
<tr>
<td>Dose of Glyburide</td>
<td>9±6</td>
<td>---</td>
</tr>
<tr>
<td>Weight gain</td>
<td>21±17</td>
<td>21±15</td>
</tr>
</tbody>
</table>

Langer et al. NEngl J Med 2000;343:1134-8
**Oral hypoglycemic agents in pregnancy**

**Glyburide versus Insulin**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Glyburide</th>
<th>Insulin</th>
<th>P value</th>
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<tbody>
<tr>
<td>FBS</td>
<td>104±25</td>
<td>108±26</td>
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<tr>
<td>Preprandial</td>
<td>104±20</td>
<td>107±23</td>
<td>0.16</td>
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<tr>
<td>Postprandial</td>
<td>114±19</td>
<td>116±22</td>
<td>0.69</td>
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<tr>
<td>HbgA1c</td>
<td>5.7±1.3</td>
<td>5.6±1.2</td>
<td>0.42</td>
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</tbody>
</table>


**Oral hypoglycemic agents in pregnancy**

- Glyburide versus Insulin
- Women treated after organogenesis
- Rates of anomalies similar in both groups
- Similar degrees of glycemic control
- Similar perinatal outcomes

Glyburide is an effective alternative to insulin in women with gestational diabetes

Since the study by Langer et al., there has been an increased interest in using oral hypoglycemic agents in patients with gestational diabetes.

- Metformin (Glucophage)
- Sulfonylurea (Glipizide, Glyburide)
- Glycovance (Glyburide and Glucophage)
- (Acarbose)

Oral hypoglycemic agents in pregnancy

Metformin

- Enhances the sensitivity of both hepatic and peripheral tissues to insulin
- Inhibits hepatic gluconeogenesis
- Also enhances muscle sensitivity
- No weight gain associated with medication
- FDA pregnancy category B
### Oral hypoglycemic agents in pregnancy

**Metformin**
- Start at 500 mg BID—take with breakfast and with dinner
- Dosage increased by 500 mg every 1-2 weeks until reaching maximum dose of 2000 mg/day
- Can result in the reduction of insulin doses by 40-50%
- FBS will start to decrease after 3-5 days

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**Glyburide**
- Start at 1.25 -2.5 mg once or twice daily
- Effect on maternal blood sugar within 2-3 days
- Increase as needed, max 20 mg daily (10 mg BID)
- Does not or minimally cross the placenta
- No known fetal teratogenic effect, BUT
- FDA pregnancy Category C
Oral hypoglycemic agents in pregnancy

Glipizide

- Second line therapy, not studied as extensively as Glyburide
- Occasionally used in pregestational DM in conjunction with insulin
- FDA pregnancy category C
- Don’t use after 36 weeks, associated with fetal hyperinsulinemia and hypoglycemia

Acarbose

- Is an alpha-glucosidase inhibitor
- Pregnancy Category B
- Competitively inhibits enzymes in small bowel to break down complex carbohydrates into mono-saccharides
- Delays absorption of carbohydrates
- Primarily affects postprandial glucose levels
  - Start at 25 mg daily or twice daily
  - Increase by 25 mg every 1-3 weeks
  - The maximum dosage is 75-100 mg BID
- Rarely used, significant side effects
  - Diarrhea, flatulence
## Management of GDM

### Target Plasma Glucose Levels in Pregnancy

- FBS – 60-90 mg/dl
- Preprandial – 60-105 mg/dl
- 1 hour postprandial - < 140 mg/dl
- 2 hours postprandial - < 120 mg/dl
- 2 am – 6 am - >60 mg/dl

## Management of GDM

- Insulin should be used to control glucose in GDM when diet and exercise alone are inadequate
- When insulin availability or use area problem oral therapy is justified; in very mild GDM oral therapy is increasingly becoming first line therapy
- The value of oral drugs in combination with insulin appears to be the greatest
  - Benefits in both gestational and pre-gestational diabetes
Management of GDM

- Class A2 GDM: follow with daily FBS and post-prandialglucoses (not pre-prandialglucoses*) *remember the definition of GDM – CHO Intolerance

- Goals in management of A2 GDM:
  - Reduction of macrosomia
    - Goals: FBS < 90 mg/dl
      1 hour < 120mg/dl
  - Reduction of stillbirths
    - Goals: FBS < 105 mg/dl
      1 hour < 140 mg/dl

Management of GDM

Macrosomia

- FBS < 105 mg/dl and 1 hour < 140 mg/dl
  - Rate of macrosomia is 24%
- FBS < 90 mg/dl and 1 hour < 120 mg/dl
  - Rate of macrosomia is 9%
Management of class A2 GDM

After Diagnosis:
- All initial interventions same as A1 GDM
- BS review every 1(-2) weeks by member of care team
- APFHRT at 32 weeks, or when medical therapy started
- US for EFW at 36-38 weeks
- Delivery 39-40 weeks if well controlled
- Delivery <40 weeks if HTN, prior stillbirth, poor compliance etc
- If EFW > 4500g consider cesarean section
- 75 g 2 hour OGTT or FBS 6-12 weeks postpartum

Management of class A2 GDM
TIMELINE

Timing Tests

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<td>Delivery</td>
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Management of overt Diabetes mellitus

Macrosomia

Management of Diabetes
What does ACOG say?

- ACOG Practice Bulletin #60, March 2005, reaffirmed 2010
- Pregnancy: insulin resistance and decreased sensitivity due to placental hormones (estrogen, hPL, progesterone, prolactin, pGH, cortisol
- Insulin demands increase throughout gestation
  - 0.7-0.8 units/kg/d first trimester
  - 0.8-1.0 units/kg/d second trimester
  - 0.9-1.2 units/kg/d third trimester
- HgbA1c should be as close to normal as possible ~<6.5%
Management of Diabetes
What does ACOG say?

- Maternal morbidity
  - Retinopathy – may worsen
  - Nephropathy in 5-10% of pregnancies
    - Poor obstetric outcome of >39 proteinuria, creatinine>1.5 mg/dl
  - CHTN in 5-10% on pregnancies
    - Increases risk for preeclampsia, stillbirth, IUGR
    - Often involves treatment with ACE inhibitors, contra-indicated in pregnancy!
- Heart disease, coronary artery disease
  - Potentially life threatening
  - Increasingly encountered due to long standing type II DM in younger women
- Neuropathy
  - Not well-studied
  - Apparent in gastroparesis

Management of pre-gestational DM

- Current strategies are aimed at:
  - Augmentation of insulin supply
    - Insulin
    - Sulfonylurea
  - Amelioration of insulin resistance
    - Exercise
    - Weight loss
    - Metformin
  - Limitation of postprandial hyperglycemia
    - Carbohydrate restriction
    - Acarbose
Management of pre-gestational DM

Pre-conception counseling!

Pre-conception evaluation includes:
• history, physical and laboratory evaluation

Emphasis: glucose control!
• Pre-pregnancy glucose control reduces rate of congenital anomalies

Pre-pregnancy OR early pregnancy exam includes:
• retinal exam & photos
• EKG
• TFT’s
• 24 hour urine (or microalbumin)
• HbA1c
• Crea, BUN, LFT’s, (baseline PIH labs), electrolytes

Management of pre-gestational DM

RATE OF CONGENITAL ANOMALIES

Normoglycemia at conception – 2-3%

Hyperglycemia at conception – 6-12%

HbA1c > 8.5% in the 1st trimester – 22.4%

HbA1c < 8.5% in the 1st trimester – 3.4%

Class A, B and C DM – 3.1-4.5%

Class D, F, R, H DM – 10.7-11.8%

Overt DM with vascular disease – 6.8%

Overt DM without vascular disease – 1.6%
Management of pre-gestational DM

CONGENITAL ANOMALIES

Most common anomalies include:

- Cardiac (transposition, VSD)
- CNS (neural tube defects)
- Renal anomalies
  - “Diabetic embryopathy” – cluster of anomalies
    - Congenital anomalies can account for up to 40% of the perinatal loss in IDDM
    - Pathognomonic – but rare: Caudal regression syndrome

Management of pre-gestational DM
(or poorly controlled A2 GDM)

After Diagnosis:

- All A1 and A2 GDM interventions, plus:
- Referral to perinatology for consult or ongoing management
- Additional end-organ lab evaluations (see separate slide)
- BS review every 1(-2) weeks
- APFHRT 32 weeks or earlier (see separate slide)
- Serial US for fetal growth after 28 weeks
- Third trimester labs: repeat HgbA1c, TSH
- Delivery 39 weeks, no later than 40 weeks if well controlled.
- Delivery <39 weeks if HTN, prior stillbirth, poor compliance etc after amniocentesis for fetal lung maturity
- If EFW > 4500g consider cesarean section
- If third trimester Hgb A1c > 6.5%, early postpartum follow up in primary care ~4 weeks postpartum.
Management of pre-gestational DM

TIMELINE

Timing Tests

Initial Exam  Baseline PIH labs, TFT’s, 24 hour urine, HgbA1c, retinal exam, EKG, U/S for viability
12 weeks  NT ultrasound (cardiac defect screening)
16-18 weeks  U/S to r/o anomalies
22-24 weeks  Screening Fetal Echo (no pediatric cardiology)
26-28 weeks  Fetal kick counts
28-30 weeks  U/S for growth
(28) 32-delivery Antepartum FHR Testing
36-38 weeks  U/S for EFW
38-40 weeks  Delivery (+/- amniocentesis for FLM)

Management of pre-gestational DM

Additional Risks in pre-gestational DM:

- Hypoglycemia
  - fetal effects unclear in regard to teratogenesis
  - effects of hypoglycemia on FHR tracing include: decreased variability, bradycardia, tachycardia
- Diabetic Ketoacidosis
  - most serious complication of DM in pregnancy
  - associated with a fetal loss rate of 30-40%
  - incidence ranges from 1.73% to 7.1%
  - Ketoacidosis defined as:
    - pH <7.30, HCO3 <15 mEq/ml, Hyperglycemia (glucose > 200 mg/dl), Ketosis
    - rarely can have DKA with glucose < 200 mg/dl
Management of pre-gestational DM

- Somogyi Response
  - hypoglycemic response at night with rebound fasting hyperglycemia

- Dawn Phenomenon
  - increasing night time blood glucose with fasting hyperglycemia
    - need to check 2-3 am glucose value to determine cause of fasting hyperglycemia

Management of GDM & DM

Antenatal Surveillance

- Class A1 GDM 40 weeks
- Class A2 GDM 32-34 weeks
- Class B,C,D DM 32-34 weeks
- Any vascular disease 28 weeks
- DM with associated HTN 28 weeks
- DM with previous SB 28 weeks
**Management of pre-gestational DM**

**Timing of delivery**

- ~38 weeks
- **Cervical Exam**
  - Not favorable
    - Good control
      - Compliant
      - Reactive NST
    - FHR testing until 40 weeks
  - Favorable
    - Poor control
      - Non-compliant
      - Non-reactive NST
    - U/S + amnio for FLM
    - immature
    - mature
    - DELIVER

**Management of GDM & DM**

**FIGURE 1**

Infant death and stillbirth rates in women with and without GDM

Comparing gestational age-specific rates of stillbirth and infant death in women with and without GDM.

GDM: gestational diabetes mellitus.

Management of pre-gestational DM

Route of Delivery
- C/S Rate approaches 40-45% in IDDM patients
- Elective C/S for macrosomia when EFW>4500 gram (AD-BPD ratio?)
  - 25% of IDDM patient with macrosomic infants have shoulder dystocia when 2\textsuperscript{nd} stage prolonged
  - risk for shoulder dystocia with EFW > 4000 gram ~30%
  - 443 c/s performed to prevent 1 shoulder dystocia

Management of pre-gestational DM

Type I DM – use of insulin pumps:
- Increasingly used for improved glucose control
- Typical regimen includes increasing insulin to carbohydrate ratio 1:15 in first trimester to ~1:8 in third trimester
- Multiple split basal rates with frequent boluses with meals
- Requires perinatal and endocrine involvement
Management of pre-gestational DM

Intrapartum Glucose Control

- management of glucose levels during labor, delivery, and postpartum is challenging and important
- plays a major role in the well-being of the neonate
- maternal hyperglycemia is the major cause of neonatal hypoglycemia
- incidence of neonatal hypoglycemia directly related to level of maternal glycemia maintained during labor

Intrapartum Glucose Control

- Goal of management during labor:
  - achieve and maintain normoglycemia
  - maintain glucose levels between 70 and 140 mg/dl
  - Continuous infusion of glucose & insulin proven most effective for controlling maternal glucose levels during labor

- IV Insulin Infusion
  - Add 50 units regular insulin to 500 cc NS
  - Flush line with 25 cc of IV solution
  - Option: add 5 cc of 25% albumin
  - 10 cc = 1 unit
### Intrapartum Glucose Control

<table>
<thead>
<tr>
<th>Fluids</th>
<th>Blood Glucose (mg/dl)</th>
<th>Insulin Dosage units/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>D5NS</td>
<td>&lt; 100 mg/dl</td>
<td>0</td>
</tr>
<tr>
<td>NS</td>
<td>100-140 mg/dl</td>
<td>0</td>
</tr>
<tr>
<td>D5NS</td>
<td>141-180 mg/dl</td>
<td>1.0</td>
</tr>
<tr>
<td>D5NS</td>
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</tr>
<tr>
<td>D5NS</td>
<td>&gt; 220 mg/dl</td>
<td>2.0</td>
</tr>
</tbody>
</table>

**Once in active labor**

**Postpartum Management**

- Following delivery, immediate decrease in insulin requirements due to:
  - loss of placenta
  - loss of peptide and steroid hormones produced by placenta
  - loss of insulin degrading enzymes
- No need for tight control for several days after delivery (exception: surgical wound healing!)
- Glucose values < 180 mg/dl acceptable short term


**Postpartum Management**

Class A1 GDM
- no need for continued glucose monitoring or diet
- Needs 6-12 week postpartum 2 hour GTT

Class A2 GDM
- May check FBS & postprandial if significant insulin needs; none if very low dose therapy
- If FBS > 110mg/dl or postprandial > 180 mg/dl, patient may need continued therapy
- Use 1/3 of pre-delivery insulin dose, continue HGM for 1-2 weeks
- Needs 6-12 week postpartum 2 hour GTT

**Postpartum Management**

For IDDM
- consider insulin drip x 24 hours
- once patient is tolerating ADAdiet, give 1/3 pre-delivery dose or 1/2 of pre-pregnancy dose as split doses or even single NPH dose (dependent on severity of disease)

For NIDDM
- Place patient back on oral agents after delivery
Postpartum Management

Risk profile of women with GDM

- Future pregnancies:
  - INCREASED risk for GDM, almost 80% will have GDM again

- Life time risk of diabetes:
  - 2-5fold increase over the general population
  - Increases after first decade after pregnancy
  - 20 years later, almost 60-80% will have type II DM (population dependent) compared to 7-10% to the general population

Recommended follow up: screening for DM q 1-3 years.

Summary

- Diabetes in pregnancy has increasing impact on maternal and fetal health
- Universal screening for DM/GDM may be beneficial
- Different screening strategies are available. ACOG does not currently endorse the new HAPO/old WHO screening criteria for GDM
- Perinatal mortality and morbidity are decreased in treated GDM
Summary

- Long term benefit of treatment of GDM remains unclear
- Carbohydrate restriction and exercise are the most effective treatment strategies
- Insulin and Glyburide are equally effective in treating GDM. Metformin is safe and may be beneficial in treating type II DM in pregnancy.
- Perinatal mortality and morbidity are significantly increased in overt DM in pregnancy

Summary

- Pre-conception care and BS control are the most effective in preventing adverse pregnancy outcome in DM
- Pre-gestational DM require close maternal and fetal observation