Learning Objectives

• Describe Maternal-Fetal Metabolism in Normal and Diabetic Pregnancy
• Discuss Counseling of overt diabetics
• Review guidelines and treatment for Gestational Diabetes

OUTLINE

• Pregnancy in the overt diabetic
  • Rx recommendations
  • Diagnosis and treatment GDM

Normal Changes with Pregnancy

• Increased levels of hormones cause beta cell hyperplasia
• Increase in maternal hypoglycemia between meals and at night due to fetus use of glucose
• Increase peripheral utilization of glucose further decrease maternal glucose levels
• Results in
  • lower fasting by 11 mg/dl
  • Unchanged post prandials
Continued changes

• Increased use of maternal fat stores are utilized for energy
• Levels of diabetogenic hormones rise during second and third trimesters causing increasing tissue resistance to maternal insulin
• If mother unable to increase and utilize insulin results in maternal and then fetal hyperglycemia

Elevation of Post Parandial levels

• Promotes storage of excess nutrients causing macrosomia
• Drives catabolism of the oversupply of fuel using energy and depleting fetal oxygen stores
• Episodic fetal hypoxia leads to outpouring of adrenal catecholamines
• This may cause fetal cardiac hypertrophy, stimulation of erythropoietin, increased hematocrit levels
• High hematocrits in turn lead to poor circulation and postnatal hyperbilirubinemia (jaundice)

Target Blood Sugars (ACOG)

• Fasting 60-90 mg/dl
• Preprandial 60-105 mg/dl
• 2 h postprandial < 120 (1h < 130-140)
• 2 am- 6 am 60-90mg/dl
• Relative hypoglycemia may cause IUGR (intrauterine growth restriction)
• Ideal mean glucose for 7x/day testing: 87-104*

IDDM Effects on Pregnancy
- Abortion
- Congenital Malformations
- Macrosomia
- Growth Retardation
- Perinatal Mortality
- Perinatal Morbidity

Complications of IDDM
- Retinopathy
- Nephropathy
- Hypertension
- Atherosclerotic heart disease
- DKA

Diabetic Retinopathy
- Leading cause blindness women 24-64 yo.
- Severity & duration DM best predicts progression risk.
- 1/2 progress with pregnancy
- Related to disease duration
- All partially regress postpartum
Retinopathy: Management
- Good control prior to pregnancy
- Early opthalmology exam
- Minimum yearly
- If early disease: q3-6 mos
- Advanced disease: monthly
- Prompt laser proliferative changes
- Reduces progression to blindness 50%
- Vitreous hemorrhage
- Valsalva may cause retinal detachment
- Limit second stage with forceps

Nephropathy
- > 500 mg protein or > 300 mg albumin 24 hrs
- Microangiopathic renal disease leading cause death and disability
  - Causes 30% deaths if onset < 31 yo
  - Incidence: 40-45% of IDDM
  - Related to control

Nephropathy
- Pregnancy may worsen mod-severe disease
  - Partial regression post partum
  - Second trimester improve
Nephropathy
- Third trimester worsen
- Difficult to identify preeclampsia
- Preeclampsia leading cause Preterm delivery
- Poor prognostic signs
  - BP med 1 tri
  - Serum Cr > 1.5
  - 24hr U Prot > 3 gm 1 trimester

Preeclampsia
- Disorder unique to pregnancy
- Characterized by poor perfusion of vital organs both of baby (vasospasm of placenta) and mother (headache, liver enzyme elevation, edema)
- These symptoms reversible with delivery
- Symptoms include: hypertension (B/P>140/90), proteinuria>300mg in 24 hour urine

Abortion
- Risk increases with elevation of HbA1C
- If well controlled no increase
- Theories of loss include: altered arachidonic acid levels, fetal hyperglycemia case formation of oxygen radicals in mitochondria of fetal tissues
Congenital Anomalies

• Most common cause Perinatal Morbidity (50%)
• No increase
  • Offspring diabetic fathers
  • True GDM
• Mechanism
  • Oxygen free radicals
    • Reece 1997: Rx with antioxidants decreases congenital malformation in diabetic animals
  • Yolk sac damage
  • Glycosylation of fetal tissues

Congenital Anomalies

• Increased by 2-3x
  • correlates with HbA1C
• CNS (Central Nervous System) most common
  • spina bifida
  • anencephaly
• Congenital Heart Defect 1%
  • Fetal echocardiogram
• Sacral agenesis (Caudal regression syndrome), type of hypoplastic development lower spine

Perinatal Morbidity

• ↑ Pre Term Delivery due to complications
• ↑ Respiratory Distress Syndrome
  • maturity delayed from mean 34 wk. to 38 wk..
• Polycythemia
  • increased erythropoietin
• Hyperglycemia
• hyperinsulinemia
• ↑ hypocalcemia
• hyperbilirubinemia
• Hypertrophic and congestive cardiomyopathy
Perinatal Mortality
- 2x increases non-diabetic
- 50% from Congenital Malformation
- Unexplained IUFD (Intrauterine fetal demise)
  - Hyperglycemia and hyperinsulinemia lead to progressive hypoxia, acidosis and death
  - Respiratory distress
  - Slower to achieve mature phospholipids

History of GDM
- 1979 First International Workshop on GDM
  - Def: Glucose intolerance with recognition of onset during pregnancy
- 1985 Second Workshop
  - Universal 50 gm screening with 140
  - Postpartum testing with 75 gm
  - Antepartum surveillance for poorly controlled patients
  - Increased obesity and IGT in offspring

History of GDM
- 1991 Third Workshop
  - Lowering 50 gm cut off increases sensitivity and decreases specificity
  - One abnormal 3 h GTT value may need Rx
  - Evidence of lg abdominal circum on ultrasound lead to more aggressive treatment
  - long-term implications GDM to child
History of GDM
- 1997 Fourth Workshop
  - Long term consequences GDM
    - Mother
    - Fetus
  - Strategies to prevent long term consequences

History of GDM
- 2007 Fifth Workshop
  - All women with dx have 75 gram 2 hour GTT postpartum
  - Encourage women to breastfeed
  - May use oral agents to Treat (Glyburide)

Guidelines in a Nutshell
- Universal screening with 50 gm
- Coustan & Carpenter’s 3 h GTT
- Diabetes Educator consult
- Medical Nutrition Therapy
  - Adjusted for BMI
- Home Glucose Monitoring for all GDM
- Insulin Therapy
- Intrapartum/Delivery Management
- Postpartum Follow-up
Coustan vs. O'Sullivan

- O'Sullivan: whole blood using Somogyi-Nelson technique
- Plasma levels: 14% > than whole blood
- Enzymatic methods: 5 mg/dl < than Somogyi-Nelson
- Coustan: converted O'Sullivan and rounded to nearest 5 mg

Why Switch?

- More accurate conversion
- Coustan identifies 50% more GDM
- GDM by Coustan alone vs. O'Sullivan
  - Same proportion need insulin¹
  - Same outcome as O'Sullivan²
  - Same proportion of macrosomia (25%)³
  - Same long term risk of overt diabetes⁴

<table>
<thead>
<tr>
<th>Time</th>
<th>O'Sullivan</th>
<th>Coustan</th>
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<tbody>
<tr>
<td>Fasting</td>
<td>&lt;105</td>
<td>&lt;95</td>
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<tr>
<td>1 hr pp</td>
<td>&lt;190</td>
<td>&lt;180</td>
</tr>
<tr>
<td>2 hr pp</td>
<td>&lt;165</td>
<td>&lt;155</td>
</tr>
<tr>
<td>3 hr pp</td>
<td>&lt;145</td>
<td>&lt;140</td>
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Pathogenesis Gestational Diabetes
• Delayed and blunted secretion of insulin
• Increased peripheral resistance
• Similar to Type II Diabetes
• Post receptor processing

Treating GDM is Important
• Decreased perinatal morbidity related to macrosomia
• Improve health-related quality of life
• Treatment with insulin in GDM reduces morbidity from macrosomia
• Improved glycemic control is associated with
  • Reduced rates of preeclampsia, gestational hypertension
  • Reduced cesarean delivery
• Less weight gain after dx with treatment

Other Treatment Options
• New studies indication efficacy of treatment with Glyburide
• Start with 2.5mg 1-2x day with increase to 20mg
• Unable to control with oral medication will need insulin
• Outcomes similar

Risk of Type 2 Diabetes

• 30-70% depending on length of f/u and population
• 70% incidence Prediabetes or DM over 12 years\(^1\)
• 30-50% over 3-5 years\(^2\)
• 60-100% after 12-18 years\(^2\)


Recurrence Risk GDM

• 30-50% recurrence
• If no recurrence, decreased risk Type 2 DM
• 3% vs. 30% over 16 years in Australia
• Each subsequent pregnancy with GDM increases risk of Type 2 DM


Early Screening 12-16 weeks

• Obesity
• > 40 yo
• Hypertension
• Prior History of Insulin Requiring Gestational
• 3-4+ glycosuria
• Strong family history DM
• Repeat at 24-28 weeks if negative
• If positive consider undiagnosed pregestational DM and Rx accordingly
Effects of Carbohydrate Intolerance Don't Follow Cut Offs

- ↑ intolerance = ↑ adverse outcome
- ↑ abnl or 2nd value > 1st on O’Sullivan
- ↑ Preeclampsia, macrosomia, c/s, jaundice
- With no dx GDM, as 2nd value ↑:
  - ↑ macrosomia, preeclampsia and cesarean section
  - 2nd value 120-164:
    - 27.5% macrosomia
    - 40% combined Preeclampsia or c/s


1 abnormal by Coustan’s Criteria

- Re-test 4 weeks later
- 34% will have 2 abnormal values


Starting Insulin

- ACOG criteria
  - Fasting > 105
  - 2 hours > 120
- State NH Guidelines
  - More than 2 abnormal values in 1 week
  - >20% out of target range
- Experience
  - Wait a few days after starting diet
  - See if patient can identify cause of hyperglycemia
  - Follow weight closely
Antenatal Testing

- Diet controlled gestational start 2x weekly Non Stress Testing at 40 weeks
- Insulin requiring gestational 2x weekly Non Stress Testing at 32 weeks
  - or if hypertension
  - or if prior still birth
- Fetal Movement Count for all at 28 weeks

Delivery

- Must do an amniocentesis if prior to 39 weeks
- Consider amnio and delivery if poor control
- Diet controlled gestational may deliver at term
- Increased risk of shoulder dystocia due to atypical adipose distribution
- Consider c/s if estimated fetal weight > 4500gms

Postpartum

- Random blood sugar Postpartum day #2 or #2
  - (< 200 is normal)
- Discuss risk of type 2 DM
- Educate regarding prevention
- Educate S/Sx of diabetes
- Recommend visit diabetes educator
- 75 Gm at 6 -12 weeks postpartum
- Annual fasting

Postpartum testing

- Who to test
  - All patients with diagnosis
  - Much recent work on different testing strategies
  - FBS lacks sensitivity
  - Recommend 75gm 2 hour GTT 6-12 weeks postpartum


Postpartum Screening Criteria

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Fasting glucose</th>
<th>Casual glucose</th>
<th>75 g 2-hour OGTT</th>
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<tbody>
<tr>
<td>IGT</td>
<td>≥ 110 and &lt; 126</td>
<td>≥ 140 and &lt; 200</td>
<td></td>
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<tr>
<td>Diabetes</td>
<td>≥ 126</td>
<td>≥ 200 + symptoms</td>
<td>≥ 200</td>
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Long Term Surveillance

- All patient both diet and medication requiring
- Annual fasting glucose
- Average age onset 50-60 yo, so 20-30 yrs surveillance