Care of Women With Gestational Diabetes: A Collaborative Model of Care

Kim Sakovich, MS, RN-C, WHNP-C, C-EFM
Disclosure Statement

• As it pertains to this presentation I do not have any disclosures

• Off-label use of diabetic medications will be discussed.
Objectives

At the end of this session the learner will be able to:

• Explain the physiology of gestational diabetes, the kidney and pancreas, and review medical nutrition therapy (MNT).

• Outline the mechanism of action (MOA) and pharmacokinetics and fetal side effect profile of medical therapy, when to initiate insulin, calculation, titration and evaluation of medical therapy in conjunction with MNT.

• Identify barriers to insulin therapy, determine appropriate fetal surveillance, effectively manage hyperglycemia, hypoglycemia, sick day guidelines, risks for neonatal hypoglycemia, diabetic ketoacidosis and appropriate referral.
Pancreatic Physiology

• 2 functions
  - β-cell produces insulin- Lower BS
  - Alpha cell produces glycogen- Raise BS
• Stress hormones- Raise BS
  - Epinephrine
  - Cortisol
  - Growth hormone
• Purpose is to preserve glucose
Physiology of Pregnancy

- Diabetogenic condition
- Insulin sensitivity ↓ by 80%
- ↓ insulin sensitivity in periphery
  - Insulin resistance begins in the 1st trimester
- Fasting hypoglycemia
- Postprandial (PP) hyperglycemia
- 1st half of pregnancy - anabolic state
  - Glucose uptake promotion
  - Risk of hypoglycemia in 1st trimester
- 2nd half of pregnancy - catabolic state
  - Maternal lipolysis ↑ (breakdown of fat stores)
  - BS and FFA concentrations ↑
  - Maternal fuel (lipids) sparing glucose for fetus
- Prolonged fasting exaggerates these alterations and ketonemia rapidly occurs
- Insulin resistance greatest in 3rd trimester
Gestational Diabetes (GDM)

- “Carbohydrate intolerance of variable severity with onset or first recognition during pregnancy” (ACOG, 2018)
- DM complicates 7% of pregnancies
- 86% are GDM
- Prevalence varies in direct proportion of DM2
- ↑ prevalence in Hispanic, AA, Native Americans, Asian, Pacific Islander, low SES
- Risk for GDM
  - 2 X > with overweight
  - 4 X > with obesity
  - 8 X > in the severely obese
- Greater prevalence in obesity and sedentary lifestyles
- Increasing globally
- GDM varies by season with more DX in summer than winter
Physiology of GDM

**Chronic Insulin Resistance**
- Cells no longer respond to insulin
- Failed insulin signaling => inadequate plasma membrane translocation of glucose transporter 4 (GLUT4)
- 1° transporter responsible for bringing glucose into the cell for energy use
- Rate of insulin-stimulated glucose uptake is reduced by 54% in GDM

**Beta Cell Dysfunction**
- 1° function- store and secrete insulin in response to glucose load
- Inability to sense BG concentration or release sufficient insulin
- Results from prolonged, excessive insulin production in response to chronic fuel excess
- Exacerbated by insulin resistance
- ↓ insulin-stimulated glucose uptake further contributes to hyperglycemia
- Cells are over-burdened and have to produce additional insulin in response
Gestational Diabetes Impact

- 80% of GDM results from β-cell dysfunction
- Affected women have a greater degree of insulin resistance than healthy pregnant women =>
  - Further reductions in glucose utilization
- Most β-cell impairment exists prior to pregnancy => ↑ risk of DM2
- According to the International Diabetes Federation Atlas (IDFA) from 2017, 16.2% of pregnancies experience a CHO disorder- 75-90% are GDM
- 2015 1st meta-analysis proved that CHO disorders may have a negative impact on offspring development:
  - Children by age 1-2 had a 41% lower mental development
  - 31% worse mental development
  - Up to 78% lower IQ

Processing of Ketones in Pregnancy

- Ketogenesis- starvation adaptation
- Ketones are metabolites of FA oxidation (β-hydroxybutyrate)
- Pregnant women produce 3X more ketones during nights
- Fat cells continue to release fats continuing production of ketones in liver R/T lack of insulin => excess ketones
- Favorable condition for ketogenesis
- Ketoneuria diagnosed after fasting
- Ketones pass freely across placenta
- Connection between mother’s ketonemia (β-hydroxybutyrate) and the mental development of their offspring
  - Lower IQ
  - May be linked to behavioral problems in later in life

Monitoring and Treatment Plan

- Glucose monitoring
- Dietary modifications
- Food diary review
- Morning ketones
- Daily exercise-activity - (10,000 steps)
- Follow-up weekly

- Pregnancy hormones fluctuate during nights
- Keep breakfast CHO low
- Spread CHO throughout the day
- 3 meals plus 3 snacks
- Insulin/oral agents
Blood Sugar Goals

- FBS ≤95
  - Check before 0800
- Preprandial <100
- 1 hr PP <140
- 2 hr PP <120
- 0200-0600 >60
- PP BS peaks at 90 minutes
- 2 hr PP BS checks are most accurate
- 1st week 6X /day
- 2nd week 4X /day
Medical Nutritional Therapy
Why is MNT Important?

- Primary treatment
  - Achieve euglycemia
  - Prevent ketosis
  - Adequate weight gain
  - Appropriate fetal growth and development
  - Prevention of fetal macrosomia
  - Prevent stillbirth
- Management of GDM by dietary counseling is beneficial, however, no one dietary therapy is more effective than another
- Low glycemic index (GI) foods
Importance of Monitoring

• Provides feedback
• Ensures adequate nutritional intake
• Monitors any changes in condition
• Identifies hyperglycemia
• Identifies hypoglycemia
• Identifies “Trigger foods”
• Patient reliability
• Identifies barriers to therapy
Carbohydrates

• Carbs matter most
• Majority of maternal/fetal energy
• Fetus needs uninterrupted fuel supply
• Maternal hypoglycemic state
• Withholding food => ↑ FFAs => ketones
• Biggest impact on postprandial BS
• Evening snack encouraged
• Food sources include milk, fruit, starchy vegetables, grains, legumes
• 175 gm minimum total CHO/day (33-40%)
• Diets composed of 50-60% CHO => excessive weight gain and hyperglycemia (ACOG, 2018)
Carbohydrate Distribution

- Breakfast: 2 Carbs + 1 Protein
- 3 Snacks: 1 Carb + protein at HS
- Lunch: 3 Carbs + 1 Protein + 1 Vegetable
- Dinner: 3 Carbs + 1 Protein + 1 Vegetable
- 15 gm = 1 CHO
- ½ cup = 1 CHO
- In GDM CHO in vegetables and proteins not counted (unless breaded)
- HS snack consumed before 2230-2300
Dietary Restrictions

• No fruit juice
• No simple sugars
• Limit enriched flour products
• Avoid milk and fruit for breakfast
• Aspartame (Equal, NutraSweet, Natra Taste), Acesulfame K (Sunett) and sucralose (Splenda) are approved safe in pregnancy
• Nutrition information when eating out
• Read labels
# Case Studies

## Food Diary/ Glucose Log

<table>
<thead>
<tr>
<th>Date</th>
<th>Morning glucose:</th>
<th>Glucose readings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast</td>
<td>Carbs (g)</td>
<td>Time</td>
</tr>
<tr>
<td>Lunch</td>
<td>Carbs (g)</td>
<td>Time</td>
</tr>
<tr>
<td>Dinner</td>
<td>Carbs (g)</td>
<td>Time</td>
</tr>
<tr>
<td>Snack 1:</td>
<td>Carbs:</td>
<td>Exercise:</td>
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<tr>
<td>Snack 2:</td>
<td>Carbs:</td>
<td>NOTES:</td>
</tr>
<tr>
<td>Snack 3:</td>
<td>Carbs:</td>
<td></td>
</tr>
<tr>
<td>Bedtime glucose:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
MB

- G1 P0
- 31 yo
- BL weight 138
- BMI 25.9
- GDM class at 30w 6d
MB Week 1

- FBS 78
- Breakfast 144
  - 3 buttermilk pancakes with light syrup
  - Coffee w sweetener and a little bit of milk
- Snack 81
  - 12 almonds and water
- Lunch 177
  - Potatoes with chorizo and bean burrito
  - Light Greek yogurt

- Snack 98
  - 1 orange
  - 1 banana
- Dinner 91
  - Chicken salad with lettuce, tomatoes, carrots, 3 chips
- Snack
  - None

Plan of care (POC)?
# MB Week 2

- **FBS**: 73  
- **Breakfast**: 103  
  - Sandwich of ham and 2 egg whites  
- **Snack**: 79  
  - 1 orange  
- **Lunch**: 116  
  - 1 quesadilla  
  - 1 orange  
- **Snack**: 70  
  - 1/2 banana  

- **Dinner**: 119  
  - Cactus with red chili and potatoes  
  - Beans  
  - Corn tortilla  

- **Snack**:  
  - ½ mini whole wheat bagel with strawberry cream cheese

**Plan of Care?**
Continue food documentation  
BS checks bid alternating between B/L/D with daily FBS
BK

- G3 P1102
- 40 yo
- BL weight 182
- BMI 34.1
- Risk factors
  - AMA
  - Late presentation
  - Obesity Class 1
- 28w 2d GDM class
### BK Week 1

#### Day 1
- **FBS**: 113
- **Breakfast**: 118
  - 2 bacon/egg/cheese breakfast burritos
- **Snack**: 104
  - 20 baby carrots w Ranch
- **Lunch**: 111
  - Turkey club sandwich
  - ½ bag of chips
- **Snack**: 107
  - Greek yogurt
- **Dinner**: 115
  - Spaghetti w meatballs w whole grain pasta
  - 1 bread stick
  - Salad
- **Snack**: None

#### Day 2
- **FBS**: 104
- **Breakfast**: 109
  - 2 wheat pancakes
  - Bacon and 2 eggs
- **Snack**: 100
  - Banana muffin
- **Lunch**: 112
  - 2 thin crust pepperoni pizza slices
  - Salad
- **Snack**: 98
  - Celery sticks with PB and raisins
- **Dinner**: 117
  - Beef fajitas with 3 tortillas
  - ½ c rice
- **Snack**: None

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**Care of Women with Gestational Diabetes**  
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BK Week 2

- FBS 82
- Breakfast 111
  - 2 toasts
  - 2 eggs w ham
- Snack 78
  - Apple
- Lunch 103
  - Cobb salad w chicken and croutons
  - Blueberries
  - Wheat crackers

- Snack 99
  - 1/3 cup hummus with crackers
- Dinner 117
  - Grilled salmon with steamed veggies
  - 1 breadstick
  - Orange slices
- Snack
  - 3 cups popcorn
  - Salami
## CD Week 1

### Day 1
- FBS: 98
- Breakfast:
  - 2 pancakes
  - 1 sausage
- Snack: 72
  - Bread with turkey
- Lunch:
  - Whole wheat tortilla
  - Cheese and turkey
- Snack: 72
  - Waffle with PB
- Dinner:
  - 2 pancakes
  - 2 sausages
- Snack: 133
  - PB

### Day 2
- FBS: 104
- Breakfast:
  - Pancakes
- Snack: 98
  - Waffle with PB
- Lunch:
  - Burrito w beans & cheese
  - Tortilla
- Snack: 104
  - Bread
- Dinner:
  - 7 chicken nuggets
- Snack: 152
  - Waffle with PB
CD Week 2

**Day 6**
- FBS 94
- Breakfast 108
  - Egg bowl with bacon sausage and cheese
- Snack 82
  - 2 Graham crackers
- Lunch 112
  - Turkey and cheese sandwich
  - Apple
- Snack 76
  - PB crackers
- Dinner 118
  - 1 cup pasta
  - Ground beef w tomatoes
  - ½ cup corn
- Snack
  - Grapes w cheese

**Day 7**
- FBS 87
- Breakfast 110
- Snack 73
  - PB crackers
- Lunch 115
  - Amy’s® bowl w corn, black beans, corn tortilla
- Snack 81
  - Raisins
- Dinner 116
  - Pork chop
  - ½ cup mac & cheese
  - ½ cup potatoes
  - Green beans
- Snack
  - Waffle w PB
LM

- 28 yo Hispanic
- G3/P2/LC2
- BL weight 215
- BMI 40.6
- DM class at 29 w 1d
- Risk factors: morbid obesity Class 3
LM week 1 30w 1d

• No BS readings as pt dropped her glucometer in water and had to get a new one
• No food diary
• Ketones negative
LM Week 2

• No food diary
• No BS readings
• Very busy with other kids and extra curricular activities
• “I don’t have time to check BS and I don’t have time to write everything down”
• Ketones negative
LM Week 3

- BS log with 3-4 sporadic readings
- Food diary with no foods documented
- “I have 4 kids, between school, volunteering, getting kids to extracurricular activities, this is just too hard and I cannot do it”
- Ketones negative
LM Week 2 33w 3d

- FBS 100
- Breakfast 100
  - 2 toasts
  - 2 eggs
- Snack
  - Fruit
- Lunch 99
  - Turkey sandwich
- Snack
  - Pretzels
- Dinner 100
  - Chicken wrap
- Snack
  - Raisins
KT

- G2 P1
- BL weight 240 BMI
- 46.3
- Risk factors
  - Morbid obesity Class 3
  - Mild CHTN
- DM class at 32 w 3d
- Sono: AC running behind
  - EFW 22%
  - AFI 11cm
  - Umbilical doppler WNL
  - BPP 8/8
<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>• FBS 104</td>
<td>• FBS 120</td>
</tr>
<tr>
<td>• Breakfast 112</td>
<td>• Breakfast 112</td>
</tr>
<tr>
<td>- 1 toast w cheese</td>
<td>- Cheddar/sausage biscuit</td>
</tr>
<tr>
<td>- 1 avocado</td>
<td>• Snack 114</td>
</tr>
<tr>
<td>• Snack 108</td>
<td>- Tortilla chips</td>
</tr>
<tr>
<td>- Pretzels</td>
<td>• Lunch 121</td>
</tr>
<tr>
<td>• Lunch 135</td>
<td>- Grilled chicken Cesar salad</td>
</tr>
<tr>
<td>- Turkey sandwich w mayo &amp; tomatoes</td>
<td>- Spicy dill pickle</td>
</tr>
<tr>
<td>• Snack 101</td>
<td>• Dinner 177</td>
</tr>
<tr>
<td>- Chicken tacos w cheese and sour cream</td>
<td>- Grilled chicken salad wrap</td>
</tr>
<tr>
<td>• Snack 101</td>
<td>(WW)</td>
</tr>
<tr>
<td>- Grilled zucchini</td>
<td>- 4 pita chips</td>
</tr>
<tr>
<td>• Dinner 101</td>
<td>• Snack 101</td>
</tr>
<tr>
<td>- ½ order bacon fries</td>
<td>- Jello</td>
</tr>
</tbody>
</table>
Night Shift CHO Distribution

- Breakfast now becomes your lunch or dinner
- 3 carbs +1 protein +1 vegetable
- Snack- 1 carb
- Your lunch is still your middle meal
- 3 carbs +1 protein +1 vegetable
- Snack- 1 carb
- Dinner now becomes your breakfast
- 2 carbs +1 protein
- After midnight no milk or fruit
- Bedtime snack- 1 carb + 1 protein
- Check your blood sugar before your snack
- This essentially becomes your **fasting** blood sugar level
## KT Week 2- Day Shift

### Day 1
- **FBS** 81
- **Breakfast** 90
  - 2 toasts & 2 eggs
- **Snack** 82
  - Apple
- **Lunch** 118
  - Turkey sandwich w chips
- **Snack** 98
  - Green grapes
- **Dinner** 121
  - Mushroom Swiss burger
  - French fries
- **Snack**
  - Jello w fruit and PB

### Day 2
- **FBS** 90
- **Breakfast** 112
  - Sausage biscuit
- **Snack** 85
  - Baked potato chips
- **Lunch** 100
  - Grilled chicken Cesar salad w croutons
  - Apple slices w milk
- **Snack** 79
  - ½ banana
- **Dinner** 117
  - 2 shrimp tostados with beans
- **Snack**
  - Bread w PB
## KT Week 3-Night Shift

### Day 1
- **Before lunch**: 92
  - Before lunch
- **Lunch**: 116
  - Chicken salad sandwich
  - Milk
- **Snack**: 97
  - 1 orange
- **Dinner**: 112
  - Baked chicken w pinto beans
  - Mashed potatoes
  - 1 tortilla
  - Green beans

### Snack:
- ½ banana

### Breakfast:
- ½ whole wheat bagel with cream cheese

### FBS:
- 89
  - Cheese and crackers
Medical Management of Gestational Diabetes
Pharmacological Therapy

- Failed MNT
- Excessive fetal growth
- Polyhydramnios
- Used in conjunction with MNT
- 20-60% of patients
- Linear relationship between adverse maternal/fetal outcomes and hyperglycemia
  - Elevated FBS associated with ↑ rates of unexplained stillbirths similar to those with overt DM
  - FBS >105 associated ↑ risk of fetal death in final 4-8 weeks of pregnancy
  - This increasing risk with progressive hyperglycemia prompted the IADPSG to emphasize the importance of identifying women with evidence of preexisting DM early in pregnancy

Physiology of Kidney in Pregnancy

• GFR increases 50%
• Renal plasma flow (RPF) ↑ up to 80%
• Clearance is ↑
• Tubular function and handling of nutrients, wastes, water and electrolytes is altered
• Glucose is freely filtered at glomerulus and reabsorbed in the proximal tubule
• In pregnancy there is less effective reabsorption of glucose and variability in glucose excretion
• Glycosuria occurs
  - Repetitive glycosuria- screen for GDM
Pharmacokinetics in pregnancy

• Drug must reach target tissue
• Physiological and biochemical changes
  - Absorption
  - Distribution
  - Metabolism
  - Elimination
  - Transport
• Dosage adjustments
Absorption

- Movement of drug from site of administration into systemic circulation
- Orally- greatest variability
- Absorption and bioavailability may be affected by:
  - N&V may ↓ amount of available drug
  - Gastric acid production is ↓
  - Mucous secretion ↑
  - Both lead to ↑ gastric pH
  - Slower intestinal motility
  - ↑ CO and intestinal blood flow may allow for ↑ drug absorption
- Data suggests that the GI changes in pregnancy have an overall minimal effect on the bioavailability and therapeutic effect of most oral drugs especially with repeated doses
Distribution

• Indicates how extensively a systemic dose of medication is ultimately dispersed throughout the body

• Influenced by:
  - Tissue perfusion
  - Tissue binding
  - Lipid solubility
  - Plasma protein binding

• Plasma volume, extracellular volume and total body water ↑ by 42%
  - ↑ volume of distribution of hydrophobic => increased plasma concentrations

• Maternal fat expands by about 4kg ↑ volume of distribution for lipophylic drugs

• Plasma binding of drugs ↓ during pregnancy R/T reduced concentrations of both albumin and alpha 1-acid glycoprotein
  - ↓ protein binding => higher concentrations of free drug

• Small-molecular-weight and lipophilic drugs readily cross placenta

• The fetus and amniotic fluid can act as additional compartments => ↑ drug accumulation and an apparent ↑ in volume of distribution of certain drugs
Metabolism

- Drugs are chemically modified => loss of drug activity
- Liver metabolizes vast majority of drugs
- Phase I (oxidation)
  - Reactions mainly carried out by the CYP450 family of enzymes that are ↑ in pregnancy => ↑ metabolism of drugs
  - CYP3A4 - Glyburide, nifedipine may need increased or more frequent dosing
  - May need higher or more frequent dosing
- Phase II (conjugation) favor excretion into urine or bile
- Metabolic activity can change when certain medications are co-administered
  - For example with 17 OH a modestly ↑ in activity of CYP2C19 such as tricyclic antidepressants, PPI and propranolol and may need to be ↑
Elimination

- Renal drug excretion depends on GFR, tubular secretion and reabsorption
- GFR ↑ by 50% by end of 1\textsuperscript{st} trimester and continues to ↑ until end of pregnancy
- If a drug is solely excreted by GFR, its renal clearance is expected to parallel changes in GFR
- Cefazolin and clindamycin exhibit an ↑ renal elimination
Oral and Insulin Therapies
Oral therapies

- Metformin/Glyburide
- Remain controversial
- Not recommended by the U.S. Food and Drug Administration
- Insulin remains ADA/ACOG recommended first-line therapy
Oral therapies

- ACOG does recognize metformin as a *reasonable* alternative to insulin and is safe for use in pregnancy
- Women who decline insulin therapy
- Concerns that the woman cannot safely administer insulin
- For those who cannot afford insulin
Metformin- Biguanides

- Decreases hepatic glucose production
- Stimulates glucose uptake in the periphery
- Stimulate insulin secretion
- ↓ intestinal absorption
- ↑ peripheral glucose uptake
- Improves insulin insensitivity
- ↓ fasting glycemia
- Hypoglycemia generally not associated
- GI discomforts
Metformin Dosing

• Considered category B
• Start at 500 mg/Max 2550 mg/day (ACOG, 2018)
• Can titrate up if GI discomforts
• Can give with insulin
• Absorbed slowly
• Immediate-release peaks 1-3 hours
• Extended-release peaks 4-8 hours
• Not metabolized but cleared by tubular secretion
Metformin vs Insulin

- Glycemic control comparable
- Maternal hypoglycemia not associated
- GI side effects with Metformin
- Decreased maternal weight gain with metformin
  - May reduce maternal/fetal adverse outcomes as many pts are obese
  - Metformin helps prevent macrosomia in lean to moderate overweight who develop GDM late in pregnancy
- Up 26-46% failure rate
  - Insulin doses lower when combined with insulin
- Similar rates of perinatal morbidity
  - Slight increase in PTD with metformin
- Lower rates of severe NNH with metformin
- May need higher doses of metformin R/T increase clearance

Pujara et al, 2017; Pryia & Kalra, 2018; Farrar et al, 2017; Hyer et al, 2018
Fetal-neonatal outcomes-Metformin

- Fetal concentrations may reach up to 50% of maternal concentrations.
- Metformin cord blood levels ranged from non-detectable to 1263ng/ml.
- Metformin not retained in placenta.
- Metformin does not affect placental uptake and transport of glucose.
- Fetal-to-maternal transfer higher than maternal-to-fetal transfer.
- Effect on infant metabolically is unknown.
- Long-term CV risks for infant are uncertain with metformin.
- Concerns for increased risk of childhood obesity and DM2.
  - However, many outcomes have not been statistically significant.
  - Poor trial quality.

Glyburide-2\textsuperscript{nd} Generation Sulfonylurea

- Enhances insulin secretion
- Decreases hepatic glucose production
- ↑ insulin secretion and insulin sensitivity peripherally
- Sulfur-based
- Rapid onset
- Has a short elimination life
- Metabolizes in liver and excreted in bile and urine equally
Glyburide Dosing

• Start at 2.5 mg- Max 20 mg/day in divided doses
• Daily doses up to 30mg may be necessary to achieve adequate control (ACOG, 2018)
• Peaks at 4 hours
• 4% - 16% of women needed insulin
• Failure rate of Glyburide increases when FBS >110-115
Maternal Outcomes:

• No significant difference in primary maternal outcomes in maternal glycemic control and preterm birth

• Slightly lower maternal weight gain with Glyburide

• Insulin decreases FBS better than Glyburide
Fetal Outcomes: Glyburide

- Very little placental transfer of Glyburide possibly R/T high protein-binding and short elimination life
- Slightly higher risk of macrosomia, LGA, nursery and NICU admissions with Glyburide vs insulin
- Higher incidence of NNH with Glyburide
- Significantly higher rates of severe NNH with Glyburide than insulin
- Unsure of neonatal risks
  - However, many outcomes have not been statistically significant
  - Poor trial quality

Pujara et al, 2017; Senat et al, 2018; Song et al, 2017; Pryia & Kalra, 2018
• Pujara & Kalra and Senat et al studies failed to justify Glyburide as a 1st line treatment
• “Metformin may be preferred over Glyburide as metformin increases insulin sensitivity, reduces hepatic gluconeogenesis and enhances peripheral glucose uptake resulting in lowering of blood glucose with minimal risk of hypoglycemia and weight gain. Therefore metformin is considered first-line over Glyburide." (Song et al, 2016)
Insulin Therapies

• Does not cross placenta
• Tight glycemic control can be achieved
• Regular and NPH only 2 recognized by FDA
• **All** insulin starting dose is based on gestation and maternal weight
  - 0.7u/kg: 1-18 weeks
  - 0.8u/kg: 18-26 weeks
  - 0.9u/kg: 26-36 weeks
  - 1.0u/kg: 36-40 weeks
Short/Intermediate

Regular
- Synthesized in *E. coli*.
- Onset \( \sim 30 \text{ min} \)
  - Range 10-75 min
- Peak 2-3 hours
  - Range 20 min-7 hrs
- Duration 4-6 hours
  - Up to 8 hrs
- Possible need to delay eating 30-45 minutes after injection
- Administer in abdomen for faster peak

NPH
- Synthesized in *E. coli*.
- Onset 1-2 hours
  - Range 4-8 hrs
- Peak 4 hrs
  - Range 4-8 hrs
- Duration 10-20 hours
- Administer thighs, hips
- Not recommended for panhyperglycemia
- NPH for elevated FBS only
Insulin Therapies

• Rapid and detemir analogues- ACOG encourages rapid and detemir due to the mimicking of normal insulin function

• Experience with rapid and detemir analogues with GDM is limited

• Studies were unable to demonstrate a benefit compared with conventional insulins (ACOG, 2018)
Rapid Acting

- Humalog
  - Produced in *E. coli*
  - Onset 10-15 min
  - Peak 30-90 min
  - Duration 3-4 hrs
  - Abdomen

- Novolog
  - Produced in *S. cerevisiae* (yeast)
  - Potential site reaction w yeast allergy
  - Onset 5-10 min
  - Peak 40-50 min
  - Duration 3-5 hrs
  - Less hypoglycemia than Regular
Long-acting

• detemir
• Basal insulin
• Mimics normal physiologic insulin secretion better than NPH
• Produced in *S. cerevisiae* (yeast)
• Potential site reaction w yeast allergy
• Administer in thigh
• Onset 1-2 hours
• Lacks defined peak
• Duration up to 20 hrs
• Less incidences of hypoglycemia than NPH
Calculation of Insulin in Pregnancy

• Calculate total daily insulin dose (wt/2.2 = kg)
• About 2/3 of total dose is given in the morning (33% rapid/66% long or intermediate acting)
• 1/3 in evening evenly divided in half for rapid/long or intermediate acting
• Example:
  - Calculate kg: 171 lbs/2.2 = 78kg
  - Gestation 33w 4d
  - Multiply 78kg by 0.9u (dose per gestation) = 70 total units per day
  - Divide 70 by 3 = 23 units in PM
  - Divide 23 by 2 = 11.5 units of rapid and long in evening
  - 46 units in AM
  - Divide 46 by 3 = 15 units of rapid at breakfast and 30 units long acting in AM

www.obfocus.com/calculators/insulin.htm
Barriers to insulin therapy

- Perception of failing MNT
- Fear
- Pain
- Ineffectiveness of insulin
- Inconvenience
- Fear of “addiction”
- Weight gain
- Expensive
- Demanding

- Skilled handling
- Insufficient education
- Lack of knowledge
- Low health literacy
- Low numeracy skills
- Language barriers
- Cultural
Review

- Evaluate all BS levels
- Food diary review
- Evening snacks
- Timing of insulin
- Appropriate use
- Return demonstration
- Rapid acting 0-10 min prior to meal
- Short acting 30-45 min before meal
- Rotate sites
Fetal Assessment

- Fetal surveillance may be beneficial for GDM poorly controlled and for women medically treated
- Usually begins at 32 weeks
- No consensus regarding AP fetal testing in well-controlled A1GDM
- Antenatal testing may not be necessary in well-controlled A1GDM prior to 40 weeks gestation
- Since polyhydramnios can result from fetal hyperglycemia serial AFI measures is common
- Fetal kick counts
- Specific test and frequency may be chosen according to local practice
Hypoglycemia
Signs and Symptoms

• In pregnancy defined as <60
• Mild hypoglycemia S&S:
  - Sweating
  - Trembling
  - Difficulty concentrating
  - Lightheadedness
  - Lack of coordination
  - Relieved quickly by food or drinks with CHO
  - Sweating
  - Shaky/jittery
  - Sleepy
  - Agitated
Causes of Hypoglycemia

- Medications
- Inappropriate CHO intake
- Missed meals and snacks
- Increased physical activity
- Missed meals/snacks
- Simple CHO
- Progesterone surges
Treatment of Hypoglycemia

15X15 Rule

- 15 gm fast-acting CHO (1 gm increases BS about 3-4 mg)
- 3-4 glucose tabs
- 2 tbsp raisins
- 1 piece of fruit
- 1 cup low-fat milk
- No simple sugars
- Beware liquid drinks
- Use premeasured items
- Keep within reach—bedside, purse, car

- Check BS 15-20 min later
- If <70 repeat
- BS>70 add low-fat protein
- Avoid high fat proteins as they decrease the absorption of glucose
- Avoid rebound hypoglycemia
- BS will increase before symptoms subside
Sick-Day Rules

• Do not stop insulin
• Seek treatment for illness and treatment for infections
• Try to eat normal diet-if you cannot, replace with fluids such as milk, sports drinks, broth
• Drink plenty of water: 5-7 pints/day. Sip throughout the day
• Frequent BS checks- every 2-4 hours
• Test urine for ketones at least 4 times daily
• Rest as exercise can make ketoacidosis worse
Seek Help If:

- Ketones are present
- BS remains very high
- Vomiting and unable to keep anything down
- No quick improvement
- You are worried
- BS are very low
- If flushed, persistent vomiting, deep rapid breathing, drowsiness report to ER immediately
Case studies
EP

- G2 P1
- 25 yo Hispanic
- BL weight 175
- BMI 32.9
- Risk Factors
  - Obese
  - Prior GDM
  - Previous delivery with shoulder dystocia
  - GDM class at 27w 3d
## EP Week 1 27w 3d

### Day 1
- FBS 184
- Breakfast 184
  - 2 eggs and 2 breads
- Snack 205
  - Pretzels
- Lunch 172
  - Turkey sandwich
  - Sun chips
  - Lemonade
- Snack 160
  - None
- Dinner 120
  - None
- Snack 160
  - None

### Day 2
- FBS 133
- Breakfast 140
  - Turkey sandwich
- Snack 120
  - Jello
- Lunch 164
  - Pork chop
  - 2 tortillas
- Snack 164
  - Apple
- Dinner 164
  - Sandwich
- Snack 164
  - None
EP Week 2 28w 4d

Day 1
- FBS 126
- Breakfast 157
  - Eggs/sausage
  - 2 wheat tortillas
- Snack 139
  - 1 cup melon
- Lunch 142
  - Turkey sandwich
  - Apple
- Snack 140
  - 3 cups popcorn
- Dinner 157
  - Pork chop w veggies
  - 2 tortillas and ½ c rice
- Snack
  - 3 cups popcorn
  - Cheese stick

Days 2-6
- FBS 92-129
- Breakfast 110-161 X 6
- Lunch 91-123 X 5
- Dinner 94-161 X 5

POC?
EP

• Insulin Initiation
• Weight- 210
• Gestation 29w 4d
• S>D
• Calculation
  - AM detemir 39u/PM detemir 14u
  - Breakfast rapid 19u/dinner rapid14u
EP Week 3 Insulin 29w 4d

- FBS 87-106 X6
- Breakfast 106-140 X4
- Lunch 92-129 X2
- Dinner 88-130 X4
- Insulin dose?
## EP

### Week 3 30w 4d
- FBS: 87-106 X6
- Breakfast: 106-140 X4
- Lunch: 92-129 X2
- Dinner: 88-130 X4
- Insulin dose?

### Week 4 31w 3d
- FBS: 83-102
- Breakfast: 101-126 X2
- Lunch: 113-198 X2
- Dinner: 103-165 X2
- Insulin dose?
BK

- G3 P1102
- 40 yo
- BL weight 182
- BMI 34.1
- Risk factors
  - AMA
  - Late presentation
  - Obesity Class 1
- EDC 4/12/19
- 28w 2d GDM class
<table>
<thead>
<tr>
<th>Day 1</th>
<th></th>
<th>Day 2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>BK week 1 28w 5d</td>
<td></td>
<td>BK week 1 28w 5d</td>
<td></td>
</tr>
<tr>
<td><strong>FBS</strong></td>
<td>113</td>
<td><strong>FBS</strong></td>
<td>104</td>
</tr>
<tr>
<td><strong>Breakfast</strong></td>
<td>118</td>
<td><strong>Breakfast</strong></td>
<td>109</td>
</tr>
<tr>
<td>- 2 bacon/egg/cheese breakfast burritos</td>
<td></td>
<td>- 2 wheat pancakes</td>
<td></td>
</tr>
<tr>
<td><strong>Snack</strong></td>
<td>104</td>
<td><strong>Snack</strong></td>
<td>100</td>
</tr>
<tr>
<td>- 20 baby carrots w Ranch</td>
<td></td>
<td>- Banana muffin</td>
<td></td>
</tr>
<tr>
<td><strong>Lunch</strong></td>
<td>111</td>
<td><strong>Lunch</strong></td>
<td>112</td>
</tr>
<tr>
<td>- Turkey club sandwich</td>
<td></td>
<td>- 2 thin crust pepperoni pizza slices</td>
<td></td>
</tr>
<tr>
<td>- ½ bag of chips</td>
<td></td>
<td>- Salad</td>
<td></td>
</tr>
<tr>
<td><strong>Snack</strong></td>
<td>107</td>
<td><strong>Snack</strong></td>
<td>98</td>
</tr>
<tr>
<td>- Greek yogurt</td>
<td></td>
<td>- Celery sticks with PB and raisins</td>
<td></td>
</tr>
<tr>
<td><strong>Dinner</strong></td>
<td>115</td>
<td><strong>Dinner</strong></td>
<td>117</td>
</tr>
<tr>
<td>- Spaghetti w/ meatballs w/ whole grain pasta</td>
<td></td>
<td>- Beef fajitas with 3 tortillas</td>
<td></td>
</tr>
<tr>
<td>- 1 bread stick</td>
<td></td>
<td>- ½ c rice</td>
<td></td>
</tr>
<tr>
<td>- Salad</td>
<td></td>
<td><strong>Snack</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Snack</strong></td>
<td></td>
<td>- None</td>
<td></td>
</tr>
<tr>
<td>- None</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
BK Week 2

- FBS 82
- Breakfast 111
  - 2 toasts
  - 2 eggs w ham
- Snack 78
  - Apple
- Lunch 103
  - Cobb salad w chicken and croutons
  - Blueberries
  - Wheat crackers
- Snack 99
  - 1/3 cup hummus with crackers
- Dinner 117
  - Grilled salmon with steamed veggies
  - 1 bread stick
  - Orange slices
- Snack
  - 3 cups popcorn
  - Salami
<table>
<thead>
<tr>
<th>Scenario 1</th>
<th>Scenario 2</th>
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</thead>
<tbody>
<tr>
<td><strong>FBS</strong></td>
<td><strong>FBS</strong></td>
</tr>
<tr>
<td>89-102 X5</td>
<td>102-113</td>
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<tr>
<td><strong>Breakfast</strong></td>
<td><strong>Breakfast</strong></td>
</tr>
<tr>
<td>107-111</td>
<td>110-119</td>
</tr>
<tr>
<td><strong>Lunch</strong></td>
<td><strong>Lunch</strong></td>
</tr>
<tr>
<td>103-110</td>
<td>116-121 X2</td>
</tr>
<tr>
<td><strong>Dinner</strong></td>
<td><strong>Dinner</strong></td>
</tr>
<tr>
<td>109-114</td>
<td>118-123 X3</td>
</tr>
</tbody>
</table>
KD

- G 2 P0
- 25 yo Indian Asian
- BL weight 122
- BMI 25.2
- GDM class at 31w 6d
- Sono
  - EFW 48%
  - AFI 17 cm
  - BPP 8/8
- Risk factors
- 1 hr GTT 203
KD Week 1 33weeks

- FBS: 111-141
- Breakfast: No readings
- Snack
- Lunch: 108-156 X4
- Snack
- Dinner: 139-179 Missing 3 readings
- Snack
- Sono: EFW 68%/AFI 14cm/BPP 8/8
- Only 2 days with foods documented
- Knowledge deficit
KD Week 3 34w 1d

- FBS 116-130
- Breakfast 125-143
- Lunch 99-138 X4
- Dinner 119-148 X6
- Food diary appropriate
- Insulin initiation
- Weight 141
- Insulin dose?
  - AM detemir 26u/PM detemir 10u
  - Breakfast rapid 13u/Dinner rapid 10u
KD After Visit via Phone

- States due to high insurance deductible which has not been met cannot afford detemir or rapid
- NPH/Regular OTC
- Still cannot afford
- Metformin 500mg BID
KD Week 5 35w 1d

- FBS  96-121
- Breakfast  109-131 X3
- Lunch  91-113
- Dinner  98-123 X4
- Sono: s=d/AFI 15/BPP 8/8
- Consult
- Options?
- Metformin increased
  - 1000mg HS
  - 500mg in AM
  - 500mg 2 hrs before dinner
KT

• G2 P1
• BL weight 240 BMI
• 46.3
• Risk factors
  - Morbid obesity Class 3
  - Mild CHTN
• DM class at 32 w 3d
• Sono: AC running behind
  - EFW 22%
  - AFI 11cm
  - Umbilical doppler WNL
  - BPP 8/8
### KT Week 1 33w 4d

#### Day 1
- **FBS** 104
- **Breakfast** 112
  - 1 toast w cheese
  - 1 avocado
- **Snack** 108
  - Pretzels
- **Lunch** 135
  - Turkey sandwich w mayo & tomatoes
- **Snack** 101
- **Dinner**
  - Chicken tacos w cheese and sour cream
  - Grilled zucchini
- **Snack**
  - ½ order bacon fries

#### Day 2
- **FBS** 120
- **Breakfast** 112
  - Cheddar/sausage biscuit
- **Snack** 114
  - Tortilla chips
- **Lunch** 121
  - Grilled chicken Cesar salad
- **Snack**
  - Spicy dill pickle
- **Dinner** 177
  - Grilled chicken salad wrap (WW)
  - 4 pita chips
- **Snack**
  - Jello
Night Shift CHO Distribution

- Breakfast now becomes your lunch or dinner
- 3 carbs + 1 protein + 1 vegetable
- Snack - 1 carb
- Your lunch is still your middle meal
- 3 carbs + 1 protein + 1 vegetable
- Snack - 1 carb
- Dinner now becomes your breakfast
- 2 carbs + 1 protein
- After midnight no milk or fruit
- Bedtime snack - 1 carb + 1 protein
- Check your blood sugar before your snack
- This essentially becomes your **fasting** blood sugar level
## KT Week 2 Day Shift

### Day 1
- FBS 81
- Breakfast 90
  - 2 toasts & 2 eggs
- Snack 82
- Apple
- Lunch 118
  - Turkey sandwich w chips
- Snack 98
  - Green grapes
- Dinner 121
  - Mushroom Swiss burger
  - French fries
- Snack
  - Jello w fruit and PB

### Day 2
- FBS 90
- Breakfast 112
  - Sausage biscuit
- Snack 85
  - Baked potato chips
- Lunch 100
  - Grilled chicken Cesar salad w croutons
  - Apple slices w milk
- Snack 79
  - ½ banana
- Dinner 117
  - 2 shrimp tostados with beans
- Snack
  - Bread w PB
KT Day 3-Night Shift Scenario 2

- Before lunch 92
- Lunch 116
  - Chicken salad sandwich
  - Milk
- Snack 97
  - 1 orange
- Dinner 112
  - Baked chicken w pinto beans
  - Mashed potatoes
  - 1 tortilla
  - Green beans

- Snack 89
  - ½ banana
- Breakfast 102
  - ½ whole wheat bagel with cream cheese
- FBS 110
  - Cheese and crackers

POC?
Postpartum Follow-up

- Up to 1/3 of women with GDM will have diabetes or impaired glucose metabolism postpartum
- Between 15%-70% will develop diabetes (DM2) later in life
- Women with previous history of GDM may have a 7-fold increased risk of developing diabetes than those without a history
- Screening is recommended for all women 4-12 weeks postpartum for all women
- 2hr fasting GTT is recommended as A1c may be impacted
- OGTT more sensitive at detecting glucose intolerance, prediabetes and diabetes
- GDM associated with an increased life-time maternal risk for DM testing should occur every 1-3 years
Diabetic Ketoacidosis
Definition

• State of relative or absolute insulin deficiency =>
  - Major shifts in metabolism
  - ↑ glucose production
  - ↓ peripheral uptake
  - Protein catabolism
  - Lipolysis

• Characterized by:
  - ↑ BS levels
  - Ketosis
  - ↑ anion gap metabolic acidosis
Statistics

• Can complicate DM1, DM2 and GDM
• Occurs in about 5-10% of all pregnancies
• Incidence expected to ↑ as GDM and DM2
↑ as a result of changes in pregnant women’s demographics and rising rate of pregnancies in women over 35
Physiology of DKP

• Incidence of DKP higher in pregnancy
• Buffering capacity is impaired
  – Bicarbonate ↓ to compensate for the pregnancy-associated hyperventilation and respiratory alkalosis
• Excess levels of hPL, cortisol, progesterone, and prolactin ↓ insulin sensitivity
• Enhanced lypolysis and ↑ fatty acids ↓ the threshold for ketogenesis
DKA in pregnancy-DKP

• Usually happens at lower or even normal blood glucose levels (>179 biggest concern)
• Progresses rapidly
• Morbidity and mortality may affect both woman and fetus
• DKP – associated fetal mortality ranges from 9-35%
• Maternal mortality <1%
Euglycemic DKP

- Plasma glucose level that is lower than usually associated with DKA
- Related to:
  - Significant glucose usage by fetoplacental unit
  - Glycosuria R/T ↑ GFR
  - ↑ glucose utilization by effects of estrogen and progesterone
  - Expanded plasma volume R/T dilution
- Accelerated starvation => lipolysis and ketosis along with depleted glycogen stores and impaired glucose production
- Baagar et al., 2017 cited the 2 most common precipitating factors of DKP
  - Excessive vomiting (55%)
  - Insulin non-compliance (45%)
- Patients tend to forget the “sick day rule” reflecting lack of proper diabetes education R/T stopping their insulin
Presentation

• Abdominal pain
• N&V
• Altered sensorium
• Kussmal respirations
• Tachycardia
• Lethargy
• Dehydration
• Hypotension
Risk factors

- New onset DM
- Protracted vomiting
- Hyperemesis gravidum
- Infections (influenza/UTI)
- Poor patient compliance
- Insulin pump failure
- Treatment with β-mimetic tocolytic medications
- Antenatal corticosteroids for lung maturity
JH

• G7/T2/P1/AB4/LC3
• Hispanic
• Presented to ER for kidney infection where she was diagnosed as pregnant
• Discharged with ABX for UTI
• Sono in office shows 5-6 week GS
• HbA1c 9.4
• BMI 32.9
• Has not been checking BS at all
• Current meds Januvia, Lantus, Novolog, cephalexin
• Glucometer given and pt attended DM class
• Klebsiella- Macrobid- Nitrite positive
JH Week 1

• Sono now shows viable IUP
• FBS 221-243
• Breakfast 55-167
• Lunch 128-188
• Dinner 176-222
• Pt has been drinking milk at 0330
• Pt not eating breakfast
• Missing meals and snacks
• Insulin Dose: Novolog B/L/D 14u HS Lantus 44u
• Klebsiella- Macrobid not therapeutic- Rocephin
JH at 29 weeks

- FBS and breakfast levels good
- Continues to be non-compliant with GDM diet
- 10 lb weight loss
- 3+ ketones
- L&D 120-130
- Insulin adjusted
- Nitrite positive—Keflex- Macrodantin suppression
- What do you notice?
JH at 31 weeks

- Begins to C/O of N&V on occasion
- Medications called in for N&V
- BS stable and euglycemic
- What do you think?
JH at 32 weeks

- Beginning to have a little more N&V/GERD
- Medications changed
- Not eating as she should
- BS are stable
- 4+ ketones
- Ranitidine called in for heartburn
- Sono ordered for next visit
- Pt seen by another provider
JH 32 w 3d

- Severe GERD
- Having trouble holding down liquids
- 4+ ketones
- Ranitidine not therapeutic
- Encouraged hydration, sports drinks
- Pt reports BS are all good with one elevation at 150 R/T not taking her insulin
- Pt seen by another provider
JH 33 weeks 1 day

- Sono s=d AFI 13 EFW 86%
- N&V since last Wednesday which stopped on Monday
- Diarrhea since last night
- Went to ER 4 days ago for N&V-dehydration-IV fluids
- Not eating
- Cannot keep foods or liquids down
- Sports drink ineffective
- Not doing insulin
- BS readings range from hypoglycemic to hyperglycemic with highest levels 160-180
- Pt does not feel well; does not look well
- Dyspnea
- 4+ ketones
- Rapid, shallow respirations (Kussmaul)
- Sent to ER and admitted for two days and released
JH 2 days after discharge

- Presented to L&D in labor
- PTD 33-34 weeks
- Placenta very friable
- Placenta and fluid odorous
References


Gestational diabetes mellitus. Practice Bulletin No 190. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2018; 131 (2); e49-64


