DIABETES AND PREGNANCY
DIABETES IN PREGNANCY
INTRODUCTION
Fellowship Trained OB/GYN Subspecialist
AKA “Perinatology” or “High-Risk OB”
Historical Roots: Management of Pregestational DM
Current Scope of Subspecialty
- Maternal medical conditions
- Critical care obstetrics (additional fellowship)
- Fetology
  - Fetal imaging
  - Prenatal diagnosis
  - Fetal therapy
  - Reproductive genetics (additional fellowship)
Personal
- Maternal medical conditions (especially DM)
- Intrapartum obstetrics (especially operative OB)
HISTORY
HISTORICAL PERSPECTIVE

- Pre-insulin Era
  - Type I DM: Women did not live to conceive
  - Type II DM: Rare, but occasional pregnancies with substantial morbidity/mortality

- Insulin (1920’s)
  - High Perinatal Morbidity/Mortality
  - High Maternal Morbidity/Mortality

- Present Day
  - Expectation of perinatal/maternal outcome similar to general OB population
  - Factors
    - Recognition that perinatal outcome is directly proportional to glycemic control
    - Modern NICU care
FUTURE

- Pregnant Women are Older
- Pregnant Women are Sicker (e.g. Type I DM with nephropathy)
- Explosion of Obesity and with it, Type II DM
- Role of Assisted Reproductive Technologies
- Lack of Research Involving Pregnant Women
  - Pharmaceutical advances
  - Device advances
    - Clinicians with knowledge about devices do not know pregnancy
    - Clinicians who know pregnancy lack knowledge about devices
RISKS

- Prevalence
- Pathophysiology
- Counseling
Pregestational Diabetes Complicates 1-2% of Pregnancies

In Reproductive-Age Women, Type II DM is Now More Prevalent Than Type I DM in Most Populations

Gestational DM Complicates 6-7% (range 1-25%) of Pregnancies
Pregnancy Leads to Insulin Resistance, Which Is Needed to provide CHO Fuel Substrate to the Fetus/Placenta

Placental “Diabetogenic” Hormones

- Growth Hormone
- Corticotropin-Releasing Hormone
- Placental Lactogen
- Progesterone

Maternal Pancreatic Function

- Absent (Type I)
- Insufficient (Type II or GDM)

Result: Wide Glucose Swings, Lower DKA Threshold, Microvascular Complications (Including Placental Insufficiency)
PEDERSEN HYPOTHESIS (1952)

Mother  Placenta  Fetus

Glucose  Insulin  Glucose

Insulin

Macrosomia/Fetopathy

Functional Immaturity
PRECONCEPTION COUNSELING

- Emphasize Need for Very Tight Glycemic Control
  - A1c <6.5% (ADA), generally requires 6 months
  - FBS 80-110, 2 hr. PP <120-140
  - Risk of hypoglycemia, recognition, treatment (glucagon kit)
  - Risk of DKA, need to check ketones for glucose >200
  - For many women, very high psychological cost
- Full Medical Evaluation of DM and non-DM Medical Comorbidities, with Optimization
- Full Recognition of the Myriad Fetal, Neonatal, and Maternal Risks
- “Pre” Conception is Ideal, as Hyperglycemia During First Trimester (Organogenesis) Markedly Increases the Risk of Congenital Defects
MATERNAL DISEASE BURDEN

- Obstetric
  - Miscarriage: Spontaneous pregnancy loss <20 weeks (2-3X)
  - Placentally-Mediated hypertension (pre-eclampsia), associated with microvascular disease (3-4X)
  - Hydramnios (excessive amniotic fluid)
  - Preterm delivery: Spontaneous (16 vs. 11%) and iatrogenic (22 vs. 3%)
  - Cesarean delivery and traumatic vaginal delivery

- Medical
  - Severe hypoglycemia (lower targets, hyperemesis), DKA
  - Exacerbation of preexisting DM complications
  - Retinopathy
    - Pregnancy is an independent risk factor for worsening proliferative disease
    - Rapid tightening of glycemic control
Nephropathy
- Mild albuminuria with normal function may have transient increase in protein.
- HTN or Cr >1.5 or protein >3gm/24 hr. are at significant risk of permanent loss of function including ESRD.
- ADA: Cr >3 or CrCl <50, >40% will have permanent worsening of renal function

Recommended Viewing: Steel Magnolias, 1989

Cardiovascular Disease
- Macrovascular: CAD, Heart Failure, Stroke, Peripheral Vascular Disease
- Microvascular: Angiopathy, autonomic neuropathy
- Autonomic neuropathy: Gastroparesis, hypoglycemia unawareness, orthostasis. Severe gastroparesis is extremely difficult to manage and is associated with hypoglycemia, weight loss, and multiple hospitalizations
Congenital Malformations

- Directly proportional to A1c
- 2.9-12.3%
- Baseline OB population = 2%
- Most common:
  - Conotruncal Cardiac Defects
  - Neural Tube Defects
FETAL DISEASE BURDEN

- **Macrosomia**
  - Birth Weight >4000 to >4500g (40-60%)  
  - Morbidity: Brachial Plexus injury  
  - Birth Depression  
  - Cardiomyopathy

- **SGA (<3rd percentile)**
  - Associated with microvascular disease, HTN. (6-10X)
FETAL DISEASE BURDEN

- NICU Admission
  - Metabolic Derangements
  - Prematurity
  - Birth Depression
  - Separates the maternal-infant pair
FETAL DISEASE BURDEN

- Macrosomia
  - Cardiomegaly
  - Birth Trauma
  - Birth Depression

- Metabolic Derangement
  - Hypoglycemia
  - Mag, Ca deficits

- Perinatal Mortality
PERINATAL MORTALITY

- Fetal/Neonatal Death from 24 weeks GA to 28 days of life
- General US OB Population 0.4%
- For A1c > 6.9%: 3-4%
- Even with optimal glycemic and risk factor control, there is an excess of PNM
CHILDHOOD DISEASE BURDEN

- Permanent Erb-Duchenne Palsy
  - Continuous risk relationship with Birth Weight
  - ACOG recommends cesarean birth if EFW >4500g

- Obesity, Metabolic Syndrome
  - In utero programming and alteration of gene expression
ANTENATAL CARE

- Monitoring
- Glycemic Control
- OB Care
SELF GLUCOSE MONITORING

- ACOG and ADA Targets
  - Fasting < 95
  - 1 hour PP < 140
  - 2 hour PP < 120

- Treatment Adjustment > 1/3 Values Above Target

- Diet Logs

- Urine Ketones
Ideally Every 1-2 Weeks, Remotely

Office Flow
- Designated RN to Collect Patient Data and Make Adjustments
- Management Algorithm, MD Immediate Contact for Outliers
- MD Approval for Documentation

Communication
- Fax
- Telephone
- EHR Patient Portal (Requires Web Access and App Functionality)
- E-Mail/SMS Are Not Secure

Remote Evaluation Requires Huge Time Commitment
Alternative is Patient Visits
COORDINATION OF CARE

- No “One Size Fits All” Approach
- Variables
  - OB management by OB, metabolic management by MFM or Endocrinology
  - Most patients have comorbidities
  - Visit burden for patients
- Co-management Schemes Are Most Common
  - Key factor is the need for glucose values to be evaluated every 1-2 weeks.
  - Monthly glucose evaluations are not optimal
Registered Dietitian, Ideally CDE

Goals of Therapy
- Glucose values at target
- Avoid ketosis/ketonuria
- Adequate maternal weight gain per IOM recommendations
- Fetal well being: Conflicting evidence that MNT affects birth weight

Little Evidence That Supports One MNT Regimen as Superior

Two Components
- Calories
- Carbohydrates

Ketones: Limited information suggests ketosis/ketonuria may be associated with suboptimal fetal neurodevelopmental outcome.
### CALORIES AND CHO

<table>
<thead>
<tr>
<th>Actual Maternal Body Weight</th>
<th>Kcal/kg/day</th>
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<tbody>
<tr>
<td>Normal</td>
<td>30</td>
</tr>
<tr>
<td>Overweight</td>
<td>22-25</td>
</tr>
<tr>
<td>Obese</td>
<td>12-14 (minimum 1800)</td>
</tr>
<tr>
<td>Underweight</td>
<td>40</td>
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</tbody>
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ADA recommends a minimum of 175 g CHO/day in pregnant women.

<table>
<thead>
<tr>
<th>Meal</th>
<th>B</th>
<th>Snack</th>
<th>L</th>
<th>Snack</th>
<th>D</th>
<th>Snack</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHO (g)</td>
<td>15</td>
<td>15-30</td>
<td>45</td>
<td>15-30</td>
<td>45-60</td>
<td>15-30</td>
</tr>
</tbody>
</table>

As a practical tip, patients can adjust CHO intake at particular meals if they are exceeding glucose targets, up to a point.
INSULIN

- Type II Patients on Oral Hypoglycemics, Transition to Insulin
  - No good evidence to support oral agents in pre-existing DM in pregnancy
  - Insulin has a proven “track record” of improving all prenatal outcomes.
- No Particular Regimen (or CSII) Has Been Shown to be Superior to Another
  - Typically, if the patient is on an intensive insulin regimen prenatally, I keep the patient on that (i.e. Basal Lantus/Levemir, Meal Novolog/Humalog/Apidra)
  - My personal preference is to avoid mixed insulin, NPH, Regular. I believe analog insulins provide superior pharmacokinetics.
  - CSII patients generally self-manage, with “gentle” suggestions. Avoid starting CSII during pregnancy
  - All patients must realize that insulin needs will increase throughout pregnancy, typically will max out at total dose 70% greater than before pregnancy.
OBSTETRICAL MANAGEMENT

- Standard OB Management and Testing
- Assessment of Comorbidities
  - A1c: If >6.5% add fetal echocardiogram
  - TSH: 40% incidence of thyroid abnormality in women with Type I DM
  - EKG/Echo if history of cardiovascular symptoms or hypertension
  - Retinal exam by Ophthalmologist, follow-up as her recommendation
- First Trimester USN to accurately date the pregnancy, as many of these patients will have scheduled delivery.
- Management of Medical Comorbidities (with liberal subspecialty consultation) as They Develop
- Generally Patients Will be Seen Every 2 Weeks Until 36 weeks, then Weekly.
- Particular Attention to Clinical Suspicion of Pre-eclampsia and Preterm Labor.
No Good Evidence Exists That Supports the Superiority of any Particular Testing Scheme.

- Timing
- Frequency

However, DM is Associated With a Risk of Stillbirth Proportional to Glucose Control

Testing Scheme

- Test women based upon disease severity
- Test women based upon co-morbidities

Patient Compliance is an Important Factor
ANTENATAL TESTING SCHEMES

- Unencumbered By Data
- Weekly BPP Starting at 32 Weeks
- Twice Weekly NST Starting at 32 Weeks
- Twice Weekly NST With Weekly Amniotic Fluid Assessment Starting at 32 Weeks
- Other Centers Use Weekly NST Starting At 32 Weeks at Twice Weekly NST Starting at 36 Weeks
- Take Home: Some Type of Testing is Better Than None
FETAL GROWTH SURVEILLANCE

- Goal: To Identify Fetuses With Growth Acceleration
  - Intensify Therapy if Suspected Growth Acceleration
  - Plan for Timing of Delivery
  - Plan for Route of Delivery
- Macrosomia: EFW >4500 g
- Consensus: EFW Assessment at Some Point After 36 Weeks, Mainly to Help With Timing/Route of Delivery.
- USN Before This if Abnormal Growth Suspected
USN Technology is Not Particularly Sensitive/Specific for Detection of Macrosomia.
- Technically challenging patients to scan
- EFW formulas are multiple regressions of data sets in which most fetuses were of normal birth weight.

USN Performs Better in DM Pregnancies Due to Higher Prevalence of Macrosomia.
- Better at identifying normal sized fetuses than macrosomic ones
- If EFW < 4500g, 80+ percent chance correct
- If EFW > 4500g, 50 percent chance correct
ACOG Recommendation: Offer Cesarean Delivery if EFW >4500gm, Based Upon Risk of Permanent Erb’s Palsy

Timing: Current Emphasis on Good Glycemic Control Has Influenced Recommended Timing of Delivery

Induction Before 39 weeks For “Impending Macrosomia” is Not Supported by Evidence.

In General, Induction of Labor at 39 Weeks if the Cervix is Favorable, 40 weeks if Cervix Unfavorable.

Induction of Labor Before 39 Weeks Should Only be Done if Risks of Continuing the Pregnancy Exceed the Risk of Respiratory Distress Syndrome.
INTRAPARTUM MANAGEMENT
In General, Goal is for Maternal Glucose Values 70-110 to Minimize the Risk of Neonatal Hyperglycemia

Typical Labor Management Scheme:

- Baseline glucose infusion of Dextrose 5%/0.45% NaCl at 100ml hour with IV insulin infusion starting at 0.1 U/kg/hr. Dextrose 10%/0.45% NaCl if patient has fluid restriction (i.e. pre-eclampsia)
- Hourly glucose checks to adjust either insulin or glucose infusions
- Tendency for insulin requirement to drop as labor progresses; however women with Type I DM will always require some insulin, especially if they have not taken basal insulin within 24 hours

CSII Patients Typically Can Avoid IV Insulin Infusion and Self Manage by Adjusting Basal Infusion

The Pediatric Team Generally Will Have a Management Algorithm with the Goal of Detecting Hypoglycemia and Keeping the Maternal-Infant Pair Together
POSTPARTUM MANAGEMENT
IMMEDIATE POSTPARTUM

- With Delivery of the Placenta, Insulin Requirements Will Dramatically
  - CSII: Decrease all basals 50-60%, meal boluses to 1U/10-15gm CHO
  - Other Patients, Similar Adjustments
    - Decrease HS basal to 50-60% of current dose
    - Meal insulin bolus generally simple, i.e. 4U short acting insulin with each meal
- Transition Care Back to Endocrinology or Refer if Patient Does Not Have an Endocrinologist
- 1-2 Week Follow-Up to Evaluate Glucose Homeostasis. Glucose Targets Can Return to Prepregnancy Values.
- Discussion About Contraception
- Actively Encourage Breastfeeding.