DIABETES AND PREGNANCY

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DIABETES IN PREGNANCY

- ✓ Introduction
- ✓ History
- ✓ Risks
- ✓ Counseling
- ✓ Antepartum
- ✓ Intrapartum
- ✓ Postpartum

INTRODUCTION

- ✓ Maternal-Fetal Medicine

MATERNAL-FETAL MEDICINE

- 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
- ✓ Patho-physiology
- ✓ Counseling

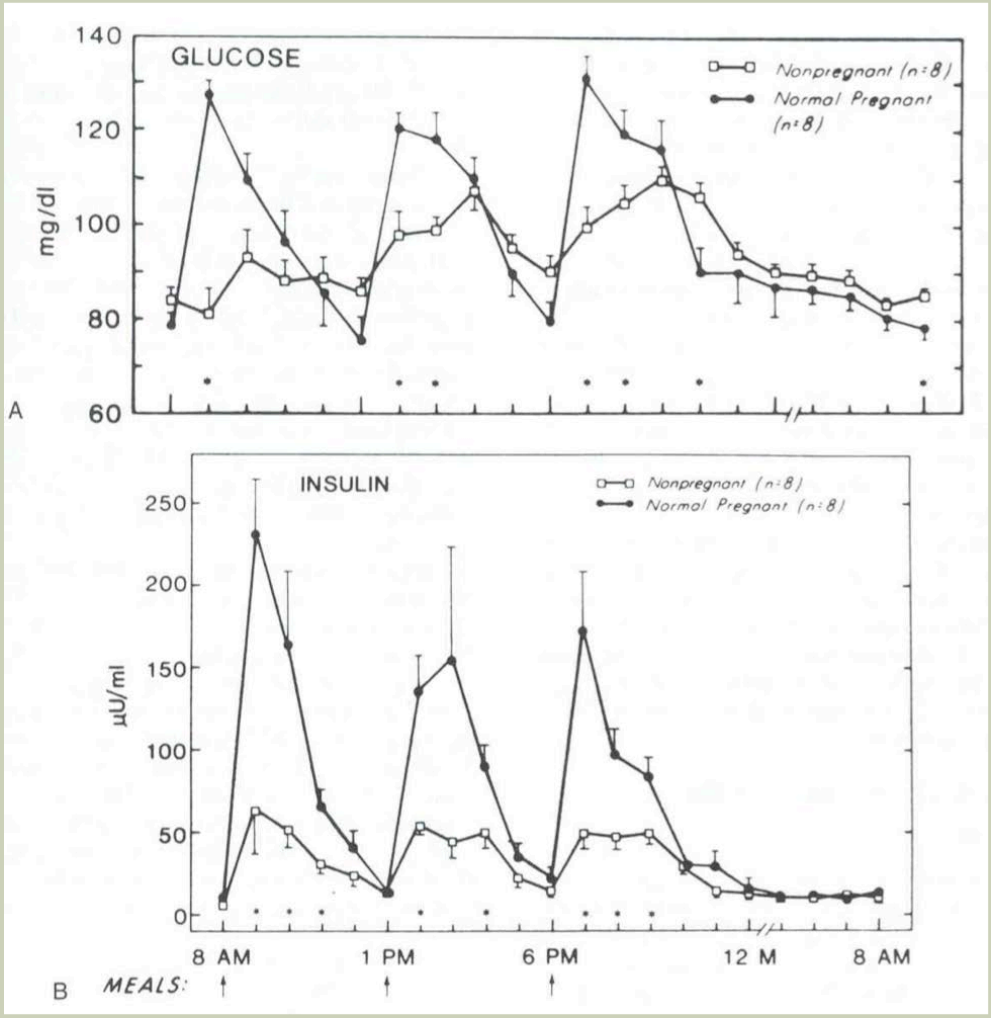
PREVALENCE

- 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

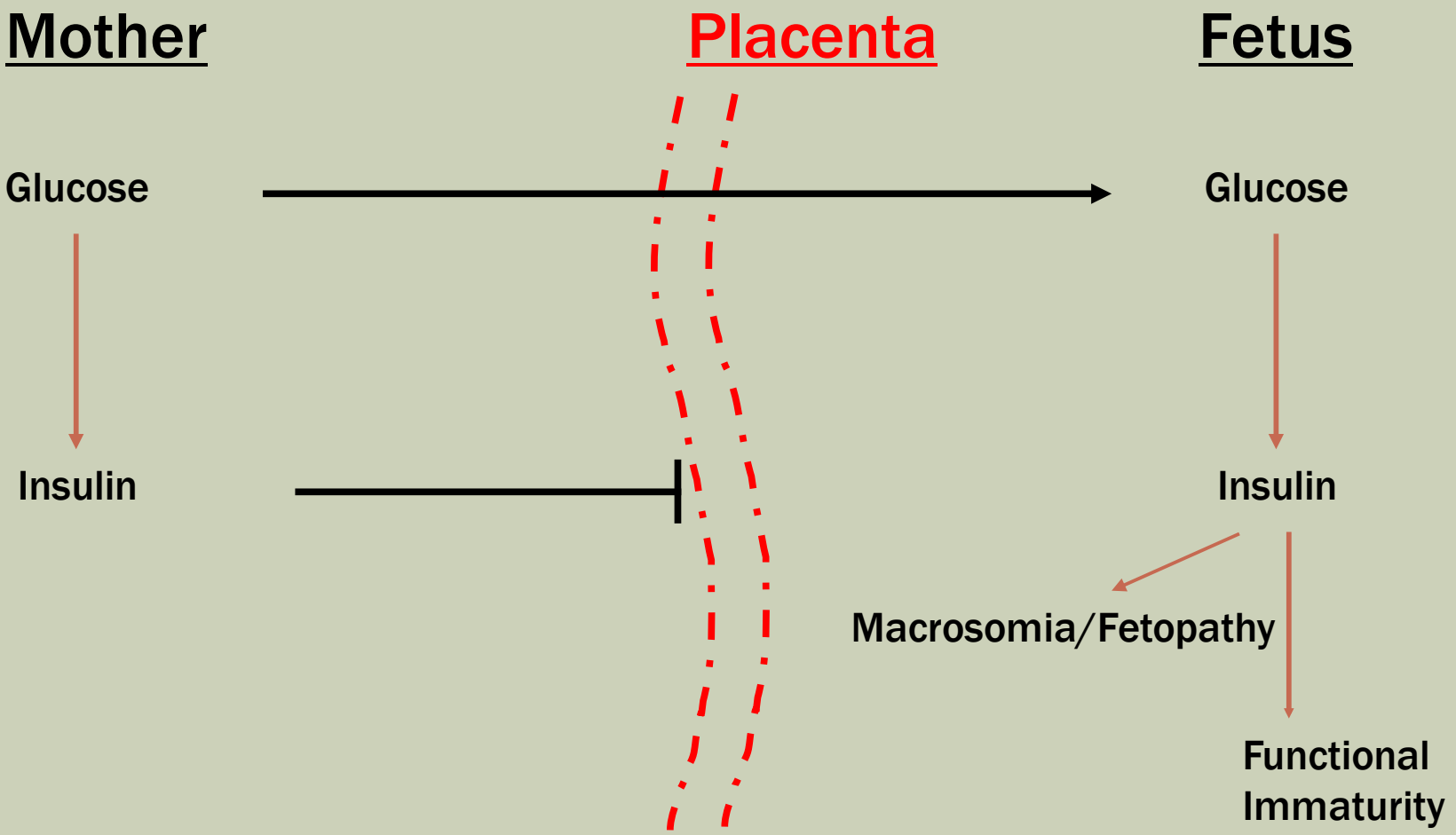
BASIC PATHOPHYSIOLOGY

- 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)

INSULIN RESISTANCE



PEDERSEN HYPOTHESIS (1952)



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

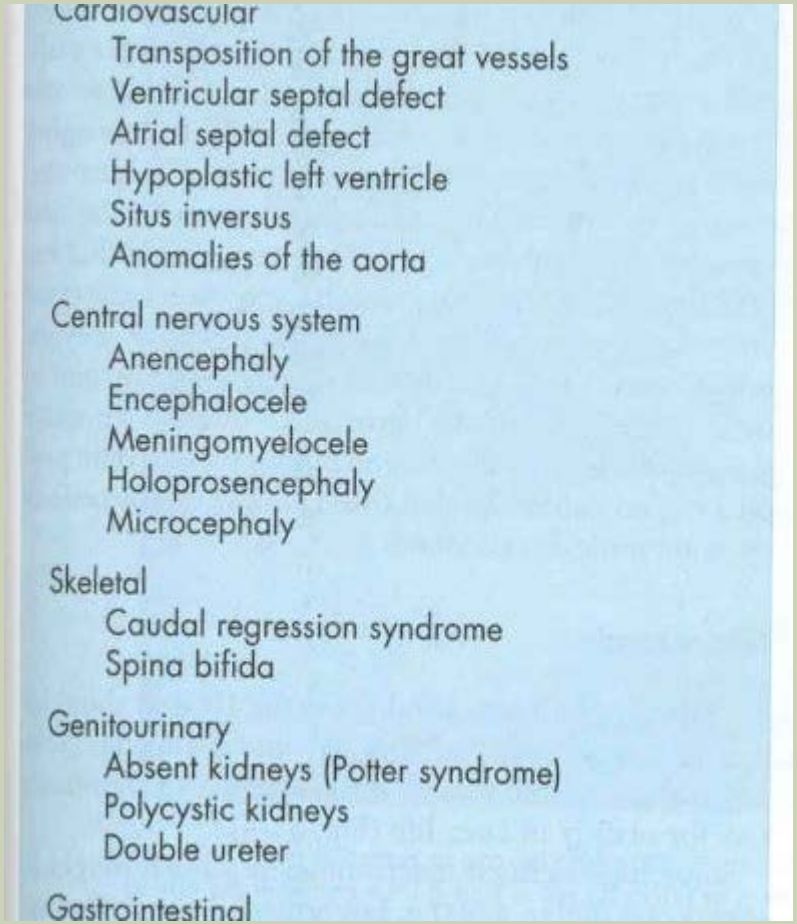
- Obstetric
  - Miscarriage: Spontaneous pregnancy loss <20 weeks (2-3X)
  - Placentally-Mediated hypertension (pre-eclampsia), associated with microvascular disease (3-4X)
  - Hydramnios (excessive amniotic fluid)
  - Preterm delivery: Spontaneous (16 vs. 11%) and iatrogenic (22 vs. 3%)
  - Cesarean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

MATERNAL DISEASE BURDEN

- 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

FETAL DISEASE BURDEN

- Congenital Malformations
  - Directly proportional to A1c
  - 2.9-12.3%
  - Baseline OB population =2%
  - Most common:
    - Conotrucal Cardiac Defects
    - Neural Tube Defects


Cardiovascular
Transposition of the great vessels
Ventricular septal defect
Atrial septal defect
Hypoplastic left ventricle
Situs inversus
Anomalies of the aorta

Central nervous system
Anencephaly
Encephalocele
Meningomyelocele
Holoprosencephaly
Microcephaly

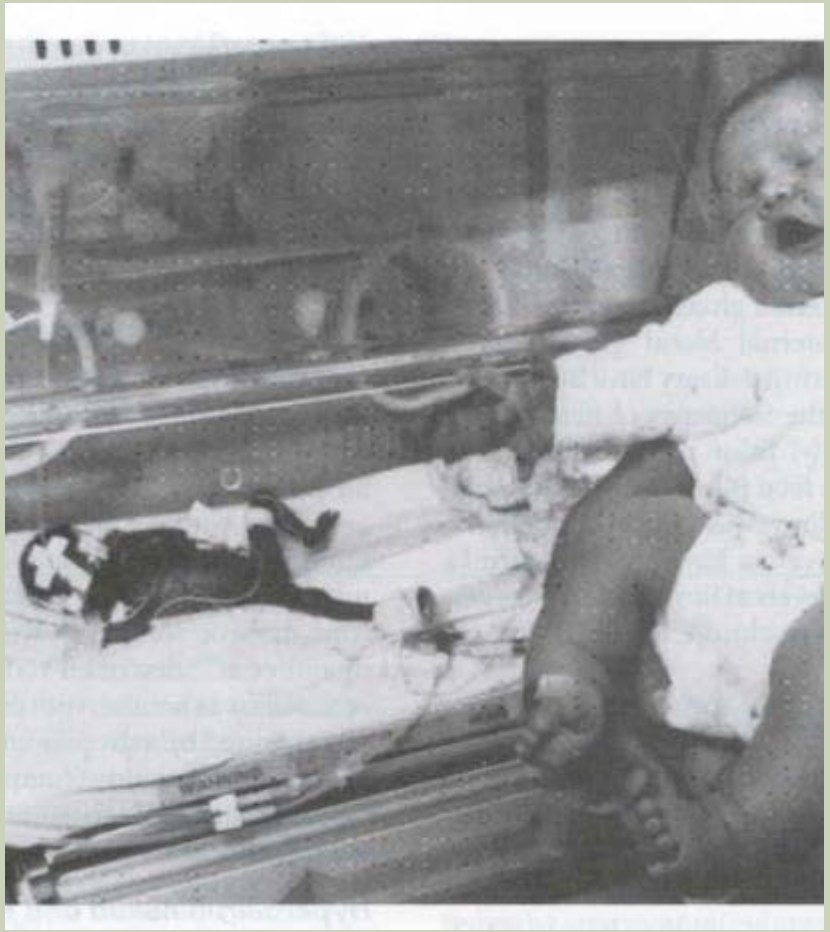
Skeletal
Caudal regression syndrome
Spina bifida

Genitourinary
Absent kidneys (Potter syndrome)
Polycystic kidneys
Double ureter

Gastrointestinal

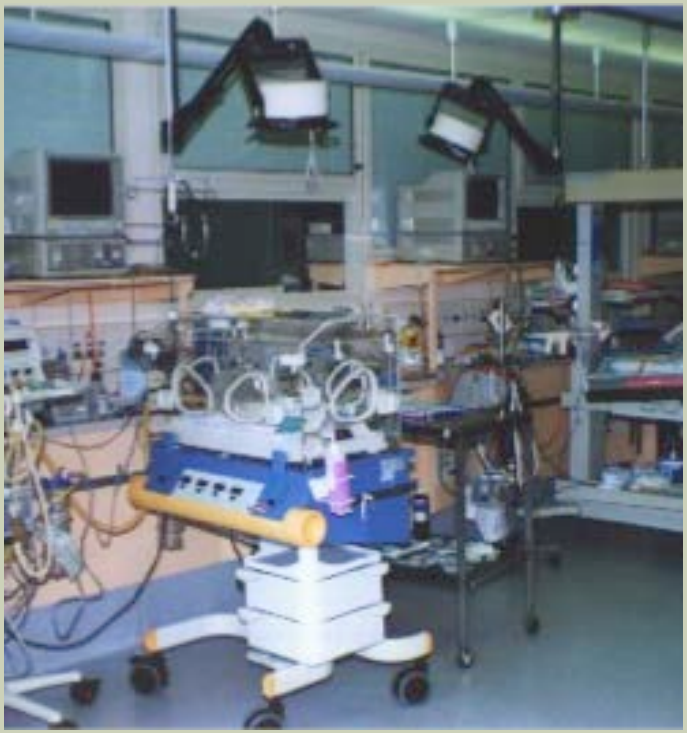
FETAL DISEASE BURDEN

- 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)



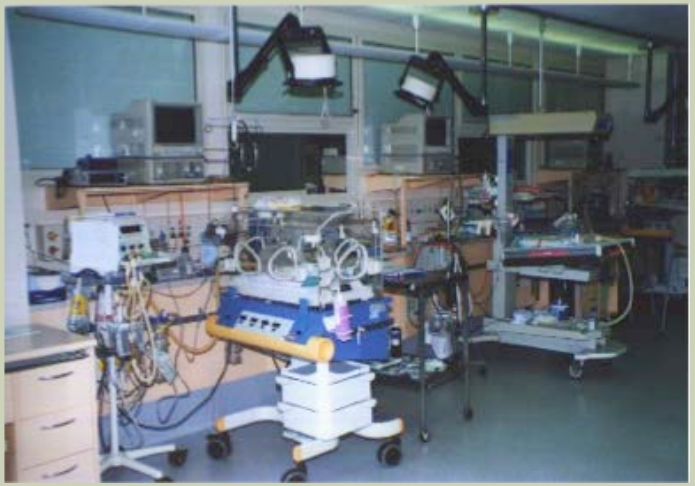
FETAL DISEASE BURDEN

- 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

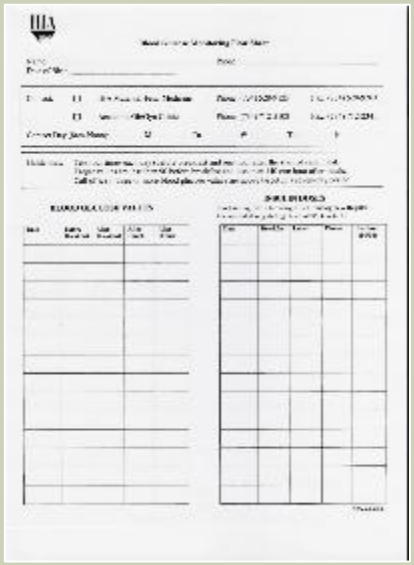
- Permanent Erb-Duchenne Palsy
  - Continuous risk relationship with Birth Weight
  - ACOG recommends cesarean birth if EFW >4500g

- 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

PHYSICIAN EVALUATION

- 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

MEDICAL NUTRITION THERAPY

- 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

Actual Maternal Body Weight	Kcal/kg/day
Normal	30
Overweight	22-25
Obese	12-14 (minimum 1800)
Underweight	40

ADA recommends a minimum of 175 g CHO/day in pregnant women.

Meal	B	Snack	L	Snack	D	Snack
CHO (g)	15	15-30	45	15-30	45-60	15-30

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.

ANTENATAL FETAL TESTING

- 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

ESTIMATED FETAL WEIGHT

- 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

DELIVERY IN DM PREGNANCIES

- 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

LABOR 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.