Nutrition in Pregnancy: Lessons from Gestational Diabetes

Teri L. Hernandez, PhD, RN

Associate Professor of Medicine and Nursing
University of Colorado Anschutz Medical Campus
Pediatric Nurse Scientist | Children’s Hospital Colorado
March 3, 2018

CWHR Women’s Health Symposium
Objectives

1. Describe the powerful influence of nutrition in pregnancy on glucose, lipids, and infant adiposity
2. Articulate the case for complex carbohydrates in nutrition therapy for GDM
Nutrition in Pregnancy: A Powerful Influence

“Implications of maternal fuels...go far beyond diabetes in pregnancy...”

-Dr. Norbert Freinkel
Banting Lecture, 1980
Intrauterine environment:
“Incubation medium”

Mother

Placenta

Fetus

Overnutrition
Insulin Resistance
Insulin Deficiency

↑↑ Glucose
↑↑ Fat
↑↑ Protein

Glucose

Concentration Gradient

Lipase

FFA

TG

Na+ dependent transporters

AA

FFA

FFA

FFA

FFA

Glucose

↑Glucose

↑Insulin

↑Amniotic Fluid insulin

↑Growth

↑Insulin Resistance

↑Overnutrition

Fetal Overgrowth

Pedersen, 1952; Freinkel, 1980, Diabetes, 29(12):1023

19 lbs/8600g
# Nutrition in Pregnancy: Overall Goals

## Dietary Reference Intakes (RDA)

<table>
<thead>
<tr>
<th></th>
<th>Carbohydrate</th>
<th>Fiber</th>
<th>Total Fat</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant</td>
<td>175g</td>
<td>28g</td>
<td>‘Not Determined’</td>
<td>71g</td>
</tr>
<tr>
<td>Non-Pregnant</td>
<td>130g</td>
<td>25g</td>
<td>‘Not Determined’</td>
<td>45g</td>
</tr>
<tr>
<td>% of total calories</td>
<td>45-65%</td>
<td>20-35%</td>
<td>10-35%</td>
<td></td>
</tr>
</tbody>
</table>

## Energy Intake Adjustments for Pregnancy

- **Pregnancy**
  - Estimated Energy Requirement (kcal/day) = Nonpregnant EER + Pregnancy Energy Deposition
  - 1st trimester: EER = Nonpregnant EER + 0
  - 2nd trimester: EER = Nonpregnant EER + 340
  - 3rd trimester: EER = Nonpregnant EER + 452

---

Otten JJ, Institute of Medicine, 2006, http://www.nap.edu
Goal for Glucose Management: “Good” Glycemic Control by mimicking Normoglycemia

Suggested Postprandial Targets based on +1SD from weighted means:
1-hour: <122 mg/dL
2-hour: <110 mg/dL

FBG from HAPO: 80.9±6.9 mg/dL

- 2011: In nearly 50 years of research, only n=255 women
  - NW to OW, BMI range 22-28 kg/m²
  - Pre-pregnancy BMI vs. BMI at time of study unclear
  - Only 1 study had characterized glycemia in obese pregnant women (n=15)

Hernandez TL, 2011, Diabetes Care, 34(7): 1660
Freinkel N, 1980, Diabetes, 29(12):1023
Hernandez TL, 2015, Curr Diab Rep, 15: 565
More than Maternal Glucose: Maternal Lipids Matter for Fetal Growth

Normalizing Metabolism in Diabetic Pregnancy: Is It Time to Target Lipids?

Diabetes Care 2014;37:1484-1493 | DOI: 10.2337/dc13-1934


Slide credit: Linda Barbour, MD

Infant Body Fat (%)

Continuous Glucose Profiles in Obese and Normal-Weight Pregnant Women on a Controlled Diet

Harmon K, Hernandez T, Bessesen D, Barbour L Diab Care 2011;34:2198
Meal-Driven Triglycerides Drive Infant Adiposity

Measures after 3 d controlled diet; Liquid meal, blood sampled at 10 points over 4 hrs at ~14 and ~28 wks

OB Early ~ NW Late

Fasting & 1-hr PPTG at 14 wks predict infant %Fat in obesity
Obesity has changed the Landscape of Pregnancy:

High Potential for Nutrition Therapy in GDM

- Nutrition therapy: the original and most potent approach to treatment of diabetes (Joslin diet was 2% carbohydrate)\(^1,2\)
- **Recognized as the cornerstone to treatment of GDM\(^3\)**
- Pioneers in obstetrics and diabetes recognized that in-utero environmental conditions are shaped by maternal nutrition\(^4\)
- Diet therapy has the potential to effectively treat GDM without medication and ↑fetal surveillance\(^5\)
- **Nutrition therapy is the single treatment component that will reach every woman with the diagnosis independent of diagnostic criteria and GDM phenotype\(^6\)**

4. Freinkel, 1980, Diabetes, 29(12):1023
Nutrition Therapy in GDM: Doomed from the Start? The Denver Experience: Anxiety, Rigid Adherence, and Unintended Consequences

Until GDM diagnosis, pregnancy was “normal”...

- Suddenly: High risk pregnancy label, “diet”, ↑rigid control of glucose, ↑surveillance, medications
- Anxiety, fear, depression

Psychology related to nutrition therapy in GDM

- Focus: rigid restriction of carbohydrate
- Rapid adaptation in late pregnancy is challenging; food selection is mentally taxing
- Infringement on cultural/social beliefs
- Feel confined by the diet
  - Narrow range of “acceptable foods,” limited food choices
- Rigid diet control: the most difficult component to treatment
  - Unintended consequences: ↑↑fat intake

Lawson EJ, 1994, Social Health Illn, 16(4):536
Hui AL, 2014, Diabetes Educ, 40(5): 668

University of Colorado Hospital, circa 2002
A Clinical Paradox

• Does the conventional carbohydrate-restricted diet worsen maternal insulin resistance in women with GDM?

... resulting in increased substrate delivery and fetal growth?

Funded in 2010
R21 DK 088324:

Role of Macronutrient Diet Composition on Maternal and Infant Metabolic Outcomes in Gestational Diabetes
Nutrition Therapy is the Cornerstone to GDM Treatment

- **Choosing Healthy Options In Carbohydrate**
  - **Energy = CHOICE™**
    - High Complex Carb/Low-Fat (HCC/LF)
    - 60% carb, mostly complex
    - 25% fat
    - 15% protein
  - ‘Conventional Diet’
    - Low-Carb/Conventional (LC/CONV)
    - 40% carb
    - 45% fat
    - 15% protein
  - Both diets
    - SFA- 35-45%; MUFA- 35-45%; PUFA- 15-20%
    - Simple Sugars: fixed at 70±5g in both diets
    - Carbs are ‘complex,’ low-moderate glycemic index
    - Fiber is similar (~24g/day in LC, ~29g/day in CHOICE)

R01 DK 101659
Randomized, Crossover Study:
Similar 24-hour Glycemia

- Similar patterns
- No difference in nocturnal or FBG
- No difference in mean glucose

Hernandez, TL, 2014, Diabetes Care, 37(5):125
Average Post-Meal Glucose is within Treatment Targets

*Data from Continuous Glucose Monitoring x3 days

Higher Insulin Excursion on CHOICE™

*post-breakfast plasma data

Similar Postprandial TG on both Diets

*post-breakfast plasma data

Higher FFA on the Conventional Diet

![Graph showing FFA levels over time with a 19% difference.]

*post-breakfast plasma data

What does FFA response to the Atkin’s Diet look like?

- Atkin’s diet (20g carb/day) vs. 55% Carb after 6 weeks of weight loss

**Non-pregnant humans**

Hernandez TL, 2010, AJCN, 91(3):578

Also: Hernandez, TL, 2016, Diabetes Spectr, 29(2), 82
Lower Fasting Glucose on CHOICE™ after 6-7 weeks

Weight Gain over 6-7 wks: 2.6kg 2.3kg

Hernandez, TL, 2016, Diabetes Care, 39(1), 39
Lower Fasting Insulin on CHOICE™ after 6-7 weeks

Hernandez, TL (2013), Preliminary data, R21DK 088324

*p=0.06
Greater insulin-suppression of Lipolysis on CHOICE™ after 6-7 weeks

Week 37 Adipose tissue biopsies

Hernandez, TL, 2016, Diabetes Care, 39(1), 39
# Lower Infant Adiposity with CHOICE Exposure

<table>
<thead>
<tr>
<th></th>
<th>LC/CONV</th>
<th>CHOICE</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>C-section</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>2/4</td>
<td>3/3</td>
</tr>
<tr>
<td>Gest Age, weeks</td>
<td>39.2±0.4</td>
<td>40.5±0.5</td>
</tr>
<tr>
<td>Birth Weight, g</td>
<td>3421±186</td>
<td>3273±104</td>
</tr>
<tr>
<td>Adiposity, PeaPod, 2wks</td>
<td>12.6±2.0</td>
<td>10.1±1.4</td>
</tr>
</tbody>
</table>

Mean±SEM

Hernandez, TL, 2016, Diabetes Care, 39(1), 39

![Graph showing % body fat, PeaPod](image)
Maternal insulin resistance at 37 weeks predicts neonatal adiposity

Maternal Fasting insulin, Week 37 Vs. Infant Adiposity
r=0.694, p=0.03

Can maternal insulin action be targeted with nutrition therapy in pregnancy and GDM?

Hernandez, TL, 2016, Diabetes Care, 39(1), 39
Evidence from 19 trials: different types of dietary advice for women with GDM suggests no clear differences in outcomes and secondary outcomes assessed using GRADE, except for a possible reduction in caesarean section for women receiving a DASH diet compared with a control diet. Few differences were observed for secondary outcomes.

Current evidence is limited by the small number of trials in each comparison, small sample sizes, and variable methodological quality.

**Approaches reviewed across trials:**
- Glycemic Index (Low, Moderate, Higher) ~ Energy-restricted ~ Dietary Approaches to Stop Hypertension (DASH) ~ Low vs. Higher Carbohydrate ~ High vs Low Unsaturated Fat ~ Higher vs. Standard Fiber ~ Diet recommendations + behavior advice ~ Soy-protein enrichment ~ Ethnic-specific
Suggestions of Benefit: The Case for Higher Quality Complex Carbs instead of pure Carb Restriction

**Improved**
- Maternal glucose control, equal to or superior to carbohydrate restriction
- Fasting glucose
- Response to OGTT
- A1C
- Insulin action, insulin resistance index
- Systolic BP

**Decreased**
- Total, LDL cholesterol
- Fasting, postprandial lipemia

**Vascular Benefits**
- ↑total glutathione/anti-oxidant capacity

**Appropriate GWG when calories not in excess**
- Less C-section delivery
- Less macrosomia, lower birth weights

References on last slide
Nutrition in GDM and Pregnancy: Evidence-Based Advice for Moving Forward

Prevention of GDM starts long before pregnancy

Pre-pregnancy interventions can include:
- Good nutrition focused on ↑diet quality, healthy eating patterns
- Return to normal body weight before conception
- Attention on psychological factors such as anxiety, depression, and dysfunctional eating patterns

Nutrition Implications for all pregnant women, children and families:
- Focus on increasing diet quality and reinforcing healthy eating patterns: ↑fruits, vegetables, legumes, whole grains
- Avoidance of simple sugars: contribute to hyperglycemia
- Fats in moderation: high total and increased saturated fats contribute to insulin resistance

Higher Patterns of 24-hr Glycemia in OB vs. NW Women Across Gestation

24-hr glucose AUC ~ total potential fetal glucose exposure

Arrows show meal start times

NW, n=24
Ob, n=22

Barbour LA, R01DK78645
Hernandez TL...Barbour LA, 2018, data in preparation
Nutrition Principles for GDM may extend to Overweight/Obesity without GDM

Who are we treating???

N= 4 GDM at diagnosis before treatment

Barbour LA, R01DK78645
Nutrition in GDM is Nutrition for all Pregnancy

Similar Glucose and Lipid Exposure: Nutrition-Treated GDM and Obesity

Hernandez TL & Barbour LA, 2018, in-press
It takes a Village...

- Linda A. Barbour, MD, MSPH
- Jacob E. Friedman, PhD
- Rachael E. Van Pelt, PhD
- Nicole Hirsch, MS, CLC
- Sarah Farabi, PhD, RN
- Libby Haugen, BA, Nursing Student
- Emily Zans, MS, RD, CDE
- Laurie Moss, MS
- Nancy Krebs, MD
- Dan Frank, PhD
- Theresa Powell, PhD
- Becky DelaHoussaye, MS
- Kristy Heiss, BS
- Robert H. Eckel, MD
- CCTSI grant support
- R01 DK 078645
- Judith Regensteiner, PhD
- CU Center for Women’s Health Research
- CCTSI Adult/Pediatric Nursing Core
- R01 DK 101659