

Carbohydrate Content in the GDM Diet: Two Views

View 1: Nutrition Therapy in Gestational Diabetes: The Case for Complex Carbohydrates

Teri L. Hernandez

■ **IN BRIEF** Restriction of dietary carbohydrate has been the cornerstone for treatment of gestational diabetes mellitus (GDM). However, there is evidence that a balanced liberalization of complex carbohydrate as part of an overall eating plan in GDM meets treatment goals and may mitigate maternal adipose tissue insulin resistance, both of which may promote optimal metabolic outcomes for mother and offspring.

Nutrition therapy is the most formative approach to treating gestational diabetes mellitus (GDM). In pregnancy, a prevailing maternal metabolic adaptation is the shift in glucose metabolism from insulin sensitivity to insulin resistance, exemplified by higher circulating lipids, heightened postprandial glucose, and increased β -cell demand/response (1,2). These intriguing exacerbations of human physiology are recognized to be additive to the prepregnancy phenotype (3), now largely characterized by overweight and obesity (4). When women cannot adapt to the glycemic demands of pregnancy, hyperglycemia and glucose intolerance manifest by the late second trimester, and this is recognized as GDM (5). There is hope that optimal nutrition therapy can offer a lower-cost treatment strategy for the rising number of women with GDM, which is anticipated to encompass 18% of all pregnancies after new diagnostic criteria are adopted (6,7). A treatment approach that circumvents expensive medication, reduces intensified fetal surveillance, and favorably affects both maternal and infant health is crucial.

The conventional approach to nutrition therapy in GDM has focused on carbohydrate restriction

(8). Although effective based on clinical experience, this approach is perhaps the most challenging component to treatment adherence in GDM. Moreover, the paucity of evidence supporting carbohydrate restriction or any diet prescription in GDM has now been recognized. With carbohydrate restriction comes the potential for increased dietary fat intake, and mounting evidence supports a strong association between maternal lipids (i.e., triglycerides and free fatty acids [FFAs]) and excess fetal growth (9). Accordingly, in 2005, the American Diabetes Association withdrew nutrition therapy guidelines for GDM (10). To date, there is no consensus on the optimal diet for women with GDM, emphasizing the need for highly controlled randomized trials (10–12).

A more contemporary understanding of dietary complex carbohydrate has underscored a differential impact on postprandial glucose, wherein some polysaccharides and starches (primarily from whole grains, starchy vegetables, and legumes) tend to mitigate a sharp rise in postprandial glucose (13). This raises the possibility that nutrition therapy in GDM may safely include more complex, nutrient-dense carbohydrate than the conventional restrictive approach has

Department of Medicine, Division of Endocrinology, Metabolism, and Diabetes and College of Nursing, University of Colorado, Anschutz Medical Campus, Aurora, CO

Colorado Pediatric Nurse Scientist Program, Children's Hospital Colorado, Aurora, CO

Correspondence: Teri L. Hernandez, teri.hernandez@ucdenver.edu

DOI: 10.2337/diaspect.29.2.82

©2016 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See <http://creativecommons.org/licenses/by-nc-nd/3.0> for details.

allowed. The purpose of this article is to review the background, evidence, and rationale for a balanced liberalization of complex carbohydrate within nutrition therapy regimens for women with GDM.

Potential of Nutrition Therapy to Break a Relentless Cycle

A balanced, effective macronutrient diet composition in GDM could improve maternal glycemia, but simultaneously could prevent worsening of maternal metabolic parameters that lead to excessive fetal growth. GDM has the potential to create a relentless cycle of obesity and diabetes prevalence. Up to 50% of mothers with GDM will develop type 2 diabetes within 10–20 years of their pregnancy (14–17). Moreover, the offspring of women with GDM are at risk for being large for gestational age (LGA) (18), having increased adiposity (19,20), and developing impaired glucose tolerance (21,22), metabolic syndrome (23), and type 2 diabetes (15,16,24–26). Strong positive associations between infant birth weight and later BMI support that larger newborns are more likely to become obese adults (18,27), and females born LGA (≥ 90 th percentile) have a doubled risk for delivering an LGA infant themselves (28). Because the risk is attributed to in utero exposure to diabetes or GDM (26,29,30), women with GDM perpetuate a cycle of obesity and diabetes prevalence through generations when affected daughters become pregnant (31). Overweight and obesity currently affect up to 75% of young women in the United States (32), and, as GDM prevalence increases, the GDM intrauterine metabolic environment is expected to further fuel the risk of offspring obesity and glucose intolerance (33). Nutrition therapy holds great potential to effectively treat this growing population of mothers and offspring.

Stress, Anxiety, and Fear as Barriers to GDM Nutrition Therapy Treatment

A GDM diagnosis generates stress, anxiety, and fear, all of which may undermine any approach to nutrition therapy. Until the diagnosis at ~28 weeks' gestation, most women have experienced a "normal" pregnancy, during which the development of GDM has occurred asymptotically (34). The diagnosis suddenly necessitates a high-risk pregnancy label, adherence to nutrition therapy, and heightened surveillance. Anxiety and depression in these women may stem from self-blame (34), feelings of loss of control (35,36), fear of macrosomia or infant complications (36,37), feelings of being misunderstood by their partner (38), and fear of future type 2 diabetes (34), all of which are magnified by the confining high-risk pregnancy label and controlled or restrictive nature of nutrition therapy (36–38).

Women with GDM have expressed feeling an intense moral obligation to the health of their unborn child, motivating them to endure intensified management (38). Although they are motivated to modify their lifestyle, adherence to nutrition therapy has been identified as the most arduous, confining component of treatment (34,36,37). Nutrition therapy has been described as intrusive (34) and an infringement on cultural/social roles, beliefs, and diet practices (35,36,39). Quick adaptation to a new diet composition late in pregnancy is challenging (34,40). Many women do not understand food properties (i.e., types of carbohydrates and types of fats), making food choices mentally taxing (40). In our clinic, women with GDM were so fearful of macrosomia that they followed extreme carbohydrate-restricted diets, opting to replace calories from carbohydrates with calories from fat. Although this practice resulted in controlled glycemia, mounting evidence supports a potential deleterious intrauterine pro-

gramming effect of FFAs on aberrant fetal growth and long-term infant health outcomes (41,42).

Unintended Consequences of Carbohydrate Restriction in GDM?

Nutrition therapy is the first line of treatment for women with GDM. If effective, glycemia is controlled, and adequate weight gain and nutritional status are supported (12,43). Twenty years ago, it was reported based on clinical experience that a carbohydrate-restricted diet (40%) in GDM blunted postprandial glucose excursions (8). This observation fueled the focus on dietary carbohydrate and was corroborated when a strong association between maternal postprandial glycemia and infant size was reported (44,45). Although there is a rationale for carbohydrate restriction (i.e., glucose control), it also creates a context for unbalanced macronutrient intake. In obesogenic environments, a focus on carbohydrate restriction facilitates an increase in dietary fat due to the abundance and cost-effective availability of saturated fats and processed foods (46,47). A large increase in protein is unlikely because it is consumed consistently in humans (46). An unbalanced increase in protein (i.e., without appropriate micronutrient intake) within pregnancy diets has been linked to reduced birth weight (48).

A diet-induced worsening of maternal insulin resistance (49,50) could further increase nutrient delivery to the fetus and worsen fetal hyperinsulinemia (51). Emerging data in animal and nonhuman primate models support an intrauterine influence of dietary fat in promoting offspring adiposity, hepatic steatosis, and metabolic syndrome (42,52). In humans, maternal triglyceride and FFA levels may be stronger predictors of excess fetal fat accretion than maternal glucose (9,53), raising the question of whether glycemia should constitute the only focus for therapy in GDM (54).

TABLE 1. Comparison of Nutrition Therapy Recommendations for GDM From Professional Health Care Organizations*

Guidelines	Recommendations
ADA 5th International Workshop-Conference on GDM, 2005 (10)	Insufficient evidence; recommendations withdrawn
ADA Medical Nutrition Therapy Guidelines, 2013 (83) ^a	Inconclusive evidence; individualization needed
ACOG Guidelines, 2013 (5)	Carbohydrate 33–40% of total calories
The Endocrine Society Guidelines, 2013 (55)	Carbohydrate 35–45% of total calories
American Heart Association/American College of Cardiology (AHA/ACC) Guidelines, 2013 (57) ^{a,b}	Carbohydrate 55–59%, fat 26–27%, saturated fat 5–6%, and protein 15–18% of total calories

*For further comparison, recommendations from the ADA for diabetes outside of pregnancy and from the AHA/ACC for cardiometabolic health outside of pregnancy are included.

^aRecommendations for diabetes management outside of pregnancy.

^bLifestyle recommendations to reduce the risk of cardiovascular disease.

Consensus panels, recognizing the metabolic impact of dietary macronutrients beyond carbohydrate, have withheld specific diet recommendations because of insufficient evidence (10). Despite the lack of evidence, the American College of Obstetricians and Gynecologists (ACOG) (5) and the Endocrine Society (55) still refer to carbohydrate restriction (33–40% of total calories) as the approach to treatment. Mixed messages are conveyed to providers from consensus panels emphasizing glycemic and cardiometabolic health, within and outside of pregnancy (Table 1). Because women with GDM and their offspring are known to have heightened risk for type 2 diabetes and cardiovascular disease, overall glycemic and cardiovascular health are relevant considerations. For example, if a heart-healthy eating plan (56,57) can meet GDM management goals, it might also create an optimal intrauterine environment and a healthy long-term maternal postpartum nutritional pattern. Although limiting carbohydrate can control glycemia, the influence of a carbohydrate-restricted, higher-fat diet in obese women with pre-pregnancy insulin resistance may unintentionally promote intrauterine overnutrition.

Higher-Complex-Carbohydrate Diets in GDM: Challenging the Dogma

Restriction of dietary carbohydrate

has been the cornerstone of diabetes treatment for >100 years. Before insulin, a diet prescription of ~8% carbohydrate and ~70% fat nearly eliminated glycosuria (58). Early 20th century pioneers in diabetes management established that a low-carbohydrate diet prescription required individualization but is generally ≤40% of total calories (58). As early management protocols for diabetes in pregnancy emerged to focus on “good” glycemic control to reduce maternal and fetal complications (59,60), nutrition therapy for GDM evolved to focus on control of maternal glucose. Data from later, nonrandomized trials supported carbohydrate restriction (61) by demonstrating blunted insulin secretion in response to a meal high in saturated fatty acids (62) and less need for insulin therapy with a carbohydrate intake <42% (63). However, carbohydrate restriction to <39% has been linked to the highest infant birth weights (64). Most studies of nutrition therapy in GDM are riddled with confounding insulin use, lack of compliance, heterogeneity in outcome reporting, and the absence of reported infant outcomes (i.e., birth weight and body composition) (11,12).

Grounded in the concern about increased fat intake, we asked a question to challenge the dogma emphasizing carbohydrate restriction in GDM. What if nutrition

therapy in GDM focused on liberalization of complex carbohydrate instead of restriction of all carbohydrate? A salient finding across the few published randomized, controlled trials was that diets that were higher in complex carbohydrate and low-glycemic index foods (55–70% carbohydrate) were well tolerated (65–67). In fact, in GDM, diets higher in unrefined/complex carbohydrate have effectively blunted postprandial glycemia (65,68), reduced the need for insulin therapy (66), lowered fasting LDL cholesterol levels (65,69) and FFAs (65), and improved insulin sensitivity (70), A1C (69), and systolic blood pressure (69).

Thus, we developed a diet to challenge the low-carbohydrate diet for GDM (13). We have named this diet CHOICE (Choosing Healthy Options in Carbohydrate Energy), emphasizing an overall cardiometabolically healthy, nutrient-dense eating plan (57) that encourages choosing the right kinds of carbohydrate to control glycemia (unrefined/complex/nutrient-dense), instead of restricting total carbohydrate. Recently, we demonstrated in a controlled, randomized crossover study (all food provided, diet-controlled GDM), that, compared to a low-carbohydrate diet (40% carbohydrate/45% fat), the CHOICE diet (60% carbohydrate/25% fat) effectively controlled glycemia to

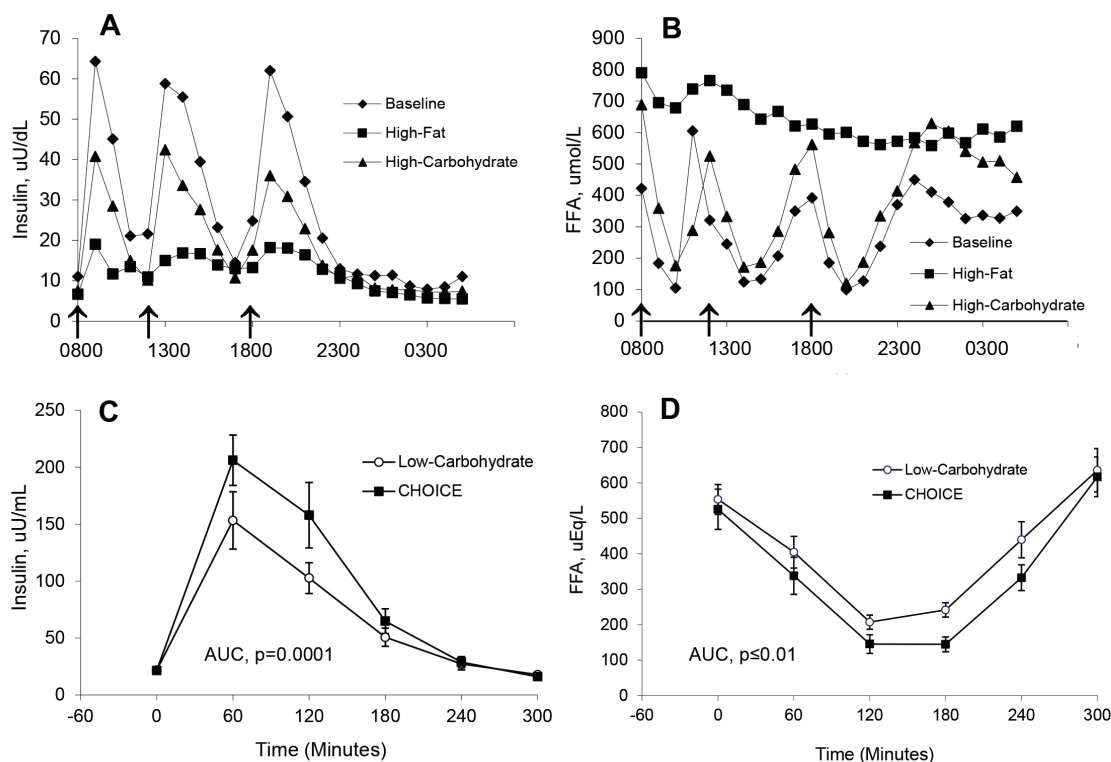


FIGURE 1. The case for complex carbohydrates in nutrition therapy for GDM: lessons from studies outside and within pregnancy. **A and B.** Thirty-two healthy, obese subjects were admitted to the Clinical Translational Research Center (CTRC) after a 12-hour fast for a 24-hour feeding study during which blood was drawn hourly and meals were administered at regimeted times (indicated by arrows; baseline diet composition 55% carbohydrate/30% fat). They were then randomly assigned to follow a carbohydrate-restricted, high-fat diet (20 g carbohydrate/day; $n = 16$) or a calorie-restricted, low-fat/high-carbohydrate diet (55% carbohydrate/30% fat; $n = 16$) for 6 weeks. The 24-hour feeding study was repeated 6 weeks later with meals matching the randomized diet composition. Figure 1A shows reduced insulin secretion on the low-carbohydrate diet, and Figure 1B shows the parallel lack of FFA suppression by insulin and sustained elevated FFAs over 24 hours on the low-carbohydrate diet. Copyright American Society of Nutrition, 2010. Reprinted with permission from ref. 81. **C and D.** In a randomized, crossover study, 16 women with diet-controlled GDM followed a conventional low-carbohydrate diet (40% carbohydrate/45% fat) and the CHOICE diet (60% carbohydrate/25% fat) in random order for 3 days each (gestational week 31, 100% of calories provided, 2.5-day washout period between diets). On the fourth day of each diet treatment, women reported to the CTCRC after an overnight fast. Baseline samples were collected, and a standardized breakfast test meal matching the randomized diet composition was consumed. Blood was drawn hourly for 5 hours. Figure 1C shows the postprandial insulin response on CHOICE, and Figure 1D shows a parallel better suppression of postprandial FFAs by CHOICE. The low-carbohydrate diet resulted in less insulin secretion (C) but worse suppression of lipolysis and increased postprandial FFAs (D). Copyright American Diabetes Association, 2014. Reprinted with permission from ref. 13.

within current treatment targets (13). Although more high-quality, randomized studies are needed, all of the evidence to date suggests that liberalization of complex carbohydrate in nutrition therapy for GDM meets management goals, may be effective in optimizing maternal and infant metabolic outcomes, and may help mitigate rising insulin resistance with advancing gestation in women with diet-controlled GDM.

Diet and Insulin Action: The Case for Complex Carbohydrates

Maternal insulin resistance is a key regulator of fetal nutrient exposure. Might it be possible to mitigate adipose tissue insulin resistance using nutrition therapy in GDM? If effective, this would result in optimal nutrient delivery and avoid the intrauterine overnutrition that programs aberrant growth patterns (42).

One of the greatest concerns in GDM is the risk for fetal LGA status and increased adiposity, historically linked to maternal hyperglycemia (25,71) and recently confirmed (72,73). Freinkel (51) described the intrauterine environment as an “incubation medium” shaped by all maternal nutrients—not only glucose. It is now understood that maternal glucose, lipids (triglycerides, FFAs), and amino acids are all potent fuels

for fetal growth. In normal late pregnancy, maternal insulin resistance increases to ensure rapidly increasing fetal-placental energy requirements and fetal growth. However, overweight and obese women who develop GDM enter pregnancy with chronic preexisting insulin resistance (74) and insufficient β -cell reserve (1,3). These women display worsened insulin resistance in skeletal muscle (75), liver, and adipose tissue (2,3,76,77) by the third trimester. Diets high in fat may promote insulin resistance in part through elevation of tumor necrosis factor α (78) and FFAs, resulting in impaired insulin signaling (76,79). Elevated FFAs may also promote a β -cell defect (76), and evidence suggests that higher pre- and early pregnancy intake of animal fats and cholesterol (80) are associated with increased risk for GDM, implicating an effect of dietary fat and cholesterol on exacerbation of insulin resistance. Thus, there is concern that a low-carbohydrate diet that facilitates an unbalanced increase in fat may actually worsen maternal insulin resistance in GDM, contributing to intrauterine overnutrition.

Insulin is a hormone with many functions beyond glucose control. It serves as a suppressor of FFA release (lipolysis) from stored triglyceride in adipose tissue. With better insulin action, there is better insulin suppression of lipolysis, less FFA exposure over time, and improved tissue sensitivity to insulin.

We have learned important lessons about diet and fuel metabolism from our controlled studies, both outside and within pregnancy. For example, after following a low-carbohydrate, high-fat diet (20 g carbohydrate/day) for 6 weeks, men and women secreted minimal insulin over 24 hours, resulting in an almost complete lack of FFA suppression by insulin (a marker of insulin resistance) and sustained elevated FFA levels over 24 hours (Figure 1A and B) (81). Our crossover study in diet-controlled GDM (13) showed that, after a controlled

breakfast on the CHOICE diet, there was a higher insulin response, resulting in lower postprandial FFAs. The low-carbohydrate diet resulted in less insulin secretion (as seen in our nonpregnant participants) and worse suppression of lipolysis/increased postprandial FFAs (Figure C and D).

Humans are postprandial much of the day, and if the patterns seen in Figures 1A and B were similar in mothers with GDM, there would be high fetoplacental lipid exposure over 24 hours on a low-carbohydrate diet. In diet-controlled GDM, if the responses in Figures 1C and D were similar across meals, the low-carbohydrate diet would result in nearly 20% more lipid exposure than with the CHOICE diet. Importantly, early evidence also showed that 6–7 weeks of therapy with the CHOICE diet resulted in lower fasting glucose and FFAs, better insulin suppression of FFAs in adipose tissue, less adipose tissue inflammation, and a trend for less neonatal adiposity, all of which suggest better insulin action despite the rising insulin resistance of pregnancy (82). The case for including complex carbohydrates in nutrition therapy for GDM, then, is that, *if* the degree of maternal insulin resistance is a key regulator in controlling maternal glucose, lipids, and amino acids to the fetal-placental unit, *and* it can be lessened by balanced liberalization of complex nutrient-dense carbohydrate and reduced dietary fat, *then* excessive fetal growth and potential programming effects could be strongly modifiable by nutrition therapy in GDM.

Conclusion

Adherence to a low-carbohydrate diet is one of the most challenging components to therapy for GDM. It is possible that a less restrictive approach to nutrition therapy will lessen feelings of confinement in GDM. Although more high-quality, randomized trials are needed, there is evidence that a balanced liberalization of complex carbohydrate as part of an

overall nutrient-dense eating plan in GDM meets treatment goals and may mitigate maternal adipose tissue insulin resistance, both of which may promote optimal metabolic outcomes for mothers and their offspring.

Acknowledgments

The author acknowledges the mentoring she has received from Linda A. Barbour, MD, Jacob (Jed) E. Friedman, PhD, and Robert H. Eckel, MD, and support received from the National Institutes of Health (NIH) National Center for Advancing Translational Sciences Colorado Clinical and Translational Research Institute (UL1 TR000154), the University of Colorado Center for Women's Health Research, the Colorado Program for Healthy Nutrition and Development, and the NIH National Institute for Diabetes and Digestive and Kidney Diseases (R01 DK101659).

Duality of Interest

No potential conflicts of interest relevant to this article were reported.

References

- Di Cianni G, Miccoli R, Volpe L, Lencioni C, Del Prato S. Intermediate metabolism in normal pregnancy and in gestational diabetes. *Diabetes Metab Res Rev* 2003;19:259–270
- Butte NF. Carbohydrate and lipid metabolism in pregnancy: normal compared with gestational diabetes mellitus. *Am J Clin Nutr* 2000;71:1256S–1261S
- Buchanan TA, Xiang AH. Gestational diabetes mellitus. *J Clin Invest* 2005;115:485–491
- Nicklas JM, Barbour LA. Optimizing weight for maternal and infant health: tenable, or too late? *Expert Rev Endocrinol Metab* 2015;10:227–242
- American College of Obstetricians and Gynecologists. Gestational diabetes mellitus (Practice Bulletin No. 137). *Obstet Gynecol* 2013;122:406–416
- Sacks DA, Hadden DR, Maresh M, et al. Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel-recommended criteria: the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. *Diabetes Care* 2012;35:526–528
- Metzger BE, Gabbe SG, Persson B, et al. International Association of Diabetes and Pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 2010;33:676–682
- Jovanovic-Peterson L, Peterson CM. Dietary manipulation as a primary treatment strategy for pregnancies complicated by diabetes. *J Am Coll Nutr* 1990;9:320–325

9. Schaefer-Graf UM, Graf K, Kulbacka I, et al. Maternal lipids as strong determinants of fetal environment and growth in pregnancies with gestational diabetes mellitus. *Diabetes Care* 2008;31:1858–1863
10. Metzger BE, Buchanan TA, Coustan D, et al. Summary and recommendations of the Fifth International Workshop—Conference on Gestational Diabetes Mellitus. *Diabetes Care* 2007;30(Suppl. 2):S251–S260
11. Han S, Crowther CA, Middleton P, Heatley E. Different types of dietary advice for women with gestational diabetes mellitus. *Cochrane Database Syst Rev* 2013;3:CD009275
12. Hernandez TL, Anderson MA, Chartier-Logan C, Friedman JE, Barbour LA. Strategies in the nutritional management of gestational diabetes. *Clin Obstet Gynecol* 2013;56:803–815
13. Hernandez TL, van Pelt RE, Anderson MA, et al. A higher-complex carbohydrate diet in gestational diabetes mellitus achieves glucose targets and lowers postprandial lipids: a randomized crossover study. *Diabetes Care* 2014;37:1254–1262
14. American Diabetes Association. Gestational diabetes mellitus. *Diabetes Care* 2004;27(Suppl. 1):S88–S90
15. Barbour LA. New concepts in insulin resistance of pregnancy and gestational diabetes: long-term implications for mother and offspring. *J Obstet Gynaecol* 2003;23:545–549
16. Ferrara A, Kahn HS, Quesenberry CP, Riley C, Hedderon MM. An increase in the incidence of gestational diabetes mellitus: Northern California, 1991–2000. *Obstet Gynecol* 2004;103:526–533
17. Lauenborg J, Hansen T, Jensen DM, et al. Increasing incidence of diabetes after gestational diabetes: a long-term follow-up in a Danish population. *Diabetes Care* 2004;27:1194–1199
18. Rogers I. The influence of birthweight and intrauterine environment on adiposity and fat distribution in later life. *Int J Obes Relat Metab Disord* 2003;27:755–777
19. Catalano PM, Thomas A, Huston-Presley L, Amini SB. Increased fetal adiposity: a very sensitive marker of abnormal in utero development. *Am J Obstet Gynecol* 2003;189:1698–1704
20. Vohr BR, McGarvey ST, Tucker R. Effects of maternal gestational diabetes on offspring adiposity at 4–7 years of age. *Diabetes Care* 1999;22:1284–1291
21. Silverman BL, Landsberg L, Metzger BE. Fetal hyperinsulinism in offspring of diabetic mothers: association with the subsequent development of childhood obesity. *Ann N Y Acad Sci* 1993;699:36–45
22. Silverman BL, Metzger BE, Cho NH, Loeb CA. Impaired glucose tolerance in adolescent offspring of diabetic mothers: relationship to fetal hyperinsulinism. *Diabetes Care* 1995;18:611–617
23. Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. *Pediatrics* 2005;115:e290–e296
24. Dabelea D, Mayer-Davis EJ, Lamichhane AP, et al. Association of intrauterine exposure to maternal diabetes and obesity with type 2 diabetes in youth: the SEARCH case-control study. *Diabetes Care* 2008;31:1422–1426
25. Jovanovic L. Gestational diabetes mellitus: the case for euglycemia. *Can J Diabetes* 2003;27:428–432
26. Silverman BL, Rizzo TA, Cho NH, Metzger BE. Long-term effects of the intrauterine environment: the Northwestern University Diabetes in Pregnancy Center. *Diabetes Care* 1998;21(Suppl. 2):B142–B149
27. Wells JC, Chomtho S, Fewtrell MS. Programming of body composition by early growth and nutrition. *Proc Nutr Soc* 2007;66:423–434
28. Ahlsson F, Gustafsson J, Tuvemo T, Lundgren M. Females born large for gestational age have a doubled risk of giving birth to large for gestational age infants. *Acta Paediatr* 2007;96:358–362
29. Dabelea D, Knowler WC, Pettitt DJ. Effect of diabetes in pregnancy on offspring: follow-up research in the Pima Indians. *J Matern Fetal Med* 2000;9:83–88
30. Dabelea D, Hanson RL, Lindsay RS, et al. Intrauterine exposure to diabetes conveys risks for type 2 diabetes and obesity: a study of discordant sibships. *Diabetes* 2000;49:2208–2211
31. Barbour LA. Changing perspectives in pre-existing diabetes in pregnancy and gestational diabetes: implications on maternal and infant short- and long-term outcomes. *Curr Opin Endocrinol Diabetes Obes* 2014;21:264–270
32. Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999–2010. *JAMA* 2012;307:491–497
33. Heerwagen MJ, Miller MR, Barbour LA, Friedman JE. Maternal obesity and fetal metabolic programming: a fertile epigenetic soil. *Am J Physiol Regul Integr Comp Physiol* 2010;299:R711–R722
34. Lawson EJ, Rajaram S. A transformed pregnancy: The psychosocial consequences of gestational diabetes. *Soc Health Illn* 1994;16:536–562
35. Devsam BU, Bogossian FE, Peacock AS. An interpretive review of women's experiences of gestational diabetes mellitus: proposing a framework to enhance midwifery assessment. *Women Birth* 2013;26:e69–e76
36. Hui AL, Sevenhuysen G, Harvey D, Salamon E. Stress and anxiety in women with gestational diabetes during dietary management. *Diabetes Educ* 2014;40:668–677
37. Lapolla A, Di Cianni G, Di Benedetto A, et al. Quality of life, wishes, and needs in women with gestational diabetes: Italian DAWN Pregnancy Study. *Int J Endocrinol* 2012;784726
38. Evans MK, O'Brien B. Gestational diabetes: the meaning of an at-risk pregnancy. *Qual Health Res* 2005;15:66–81
39. Smith-Morris CM. Diagnostic controversy: gestational diabetes and the meaning of risk for Pima Indian women. *Med Anthropol* 2005;24:145–177
40. Hui AL, Sevenhuysen G, Harvey D, Salamon E. Food choice decision-making by women with gestational diabetes. *Can J Diabetes* 2014;38:26–31
41. Innis SM. Metabolic programming of long-term outcomes due to fatty acid nutrition in early life. *Matern Child Nutr* 2011;7(Suppl. 2):112–123
42. Friedman JE. Obesity and gestational diabetes mellitus pathways for programming in mouse, monkey, and man: where do we go next? *Diabetes Care* 2015;38:1402–1411
43. Gunderson EP. Gestational diabetes and nutritional recommendations. *Curr Diab Rep* 2004;4:377–386
44. Combs CA, Gunderson E, Kitzmiller JL, Gavin LA, Main EK. Relationship of fetal macrosomia to maternal postprandial glucose control during pregnancy. *Diabetes Care* 1992;15:1251–1257
45. de Veciana M, Major CA, Morgan MA, et al. Postprandial versus preprandial blood glucose monitoring in women with gestational diabetes mellitus requiring insulin therapy. *N Engl J Med* 1995;333:1237–1241
46. Simpson SJ, Raubenheimer D. Obesity: the protein leverage hypothesis. *Obes Rev* 2005;6:133–142
47. Booth SL, Sallis JF, Ritenbaugh C, et al. Environmental and societal factors affect food choice and physical activity: rationale, influences, and leverage points. *Nutr Rev* 2001;59:S21–S39
48. Barker DJ, Thornburg KL. The obstetric origins of health for a lifetime. *Clin Obstet Gynecol* 2013;56:511–519
49. Lichtenstein AH, Schwab US. Relationship of dietary fat to glucose metabolism. *Atherosclerosis* 2000;150:227–243
50. Deer J, Koska J, Ozias M, Reaven P. Dietary models of insulin resistance. *Metabolism* 2015;64:163–171
51. Freinkel N. Banting Lecture 1980: Of pregnancy and progeny. *Diabetes* 1980;29:1023–1035
52. McCurdy CE, Bishop JM, Williams SM, et al. Maternal high-fat diet triggers lipotoxicity in the fetal livers of nonhuman primates. *J Clin Invest* 2009;119:323–335
53. Harmon KA, Gerard L, Jensen DR, et al. Continuous glucose profiles in obese and normal-weight pregnant women on a con-

- trolled diet: metabolic determinants of fetal growth. *Diabetes Care* 2011;34:2198–2204
54. Barrett HL, Dekker NM, McIntyre HD, Callaway LK. Normalizing metabolism in diabetic pregnancy: is it time to target lipids? *Diabetes Care* 2014;37:1484–1493
55. Blumer I, Hadar E, Hadden DR, et al. Diabetes and pregnancy: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2013;98:4227–4249
56. Eckel RH. Role of glycemic index in the context of an overall heart-healthy diet. *JAMA* 2014;312:2508–2509
57. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014;129(25 Suppl. 2):S76–S99
58. Westman EC, Yancy WS Jr, Humphreys M. Dietary treatment of diabetes mellitus in the pre-insulin era (1914–1922). *Perspect Biol Med* 2006;49:77–83
59. Mestman JH. Historical notes on diabetes and pregnancy. *Endocrinologist* 2002;12:224–242
60. Hernandez TL. Glycemic targets in pregnancies affected by diabetes: historical perspective and future directions. *Curr Diab Rep* 2015;15:565–576
61. Peterson CM, Jovanovic-Peterson L. Percentage of carbohydrate and glycemic response to breakfast, lunch, and dinner in women with gestational diabetes. *Diabetes* 1991;40(Suppl. 2):172–174
62. Ilic S, Jovanovic L, Pettitt DJ. Comparison of the effect of saturated and monounsaturated fat on postprandial plasma glucose and insulin concentration in women with gestational diabetes mellitus. *Am J Perinatol* 1999;16:489–495
63. Major CA, Henry MJ, de Veciana M, Morgan MA. The effects of carbohydrate restriction in patients with diet-controlled gestational diabetes. *Obstet Gynecol* 1998;91:600–604
64. Romon M, Nuttens MC, Vambergue A, et al. Higher carbohydrate intake is associated with decreased incidence of newborn macrosomia in women with gestational diabetes. *J Am Diet Assoc* 2001;101:897–902
65. Nolan CJ. Improved glucose tolerance in gestational diabetic women on a low fat, high unrefined carbohydrate diet. *Aust N Z J Obstet Gynaecol* 1984;24:174–177
66. Moses RG, Barker M, Winter M, Petocz P, Brand-Miller JC. Can a low-glycemic index diet reduce the need for insulin in gestational diabetes mellitus? A randomized trial. *Diabetes Care* 2009;32:996–1000
67. Louie JC, Markovic TP, Perera N, et al. A randomized controlled trial investigating the effects of a low-glycemic index diet on pregnancy outcomes in gestational diabetes mellitus. *Diabetes Care* 2011;34:2341–2346
68. Cypryk K, Kaminska P, Kosinski M, Pertynska-Marczewska M, Lewinski A. A comparison of the effectiveness, tolerability and safety of high and low carbohydrate diets in women with gestational diabetes. *Endokrynol Pol* 2007;58:314–319
69. Asemi Z, Tabassi Z, Samimi M, Fahiminejad T, Esmailzadeh A. Favourable effects of the Dietary Approaches to Stop Hypertension diet on glucose tolerance and lipid profiles in gestational diabetes: a randomised clinical trial. *Br J Nutr* 2013;109:2024–2030
70. Lauszus FF, Rasmussen OW, Henriksen JE, et al. Effect of a high monounsaturated fatty acid diet on blood pressure and glucose metabolism in women with gestational diabetes mellitus. *Eur J Clin Nutr* 2001;55:436–443
71. Jovanovic L. What is so bad about a big baby? *Diabetes Care* 2001;24:1317–1318
72. Metzger BE, Lowe LP, Dyer AR, et al. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med* 2008;358:1991–2002
73. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study Group. Associations with neonatal anthropometrics. *Diabetes* 2009;58:453–459
74. Catalano PM, Huston L, Amini SB, Kalhan SC. Longitudinal changes in glucose metabolism during pregnancy in obese women with normal glucose tolerance and gestational diabetes mellitus. *Am J Obstet Gynecol* 1999;180:903–916
75. Barbour LA, McCurdy CE, Hernandez TL, Friedman JE. Chronically increased S6K1 is associated with impaired IRS1 signaling in skeletal muscle of GDM women with impaired glucose tolerance postpartum. *J Clin Endocrinol Metab* 2011;96:1431–1441
76. Sivan E, Homko CJ, Whittaker PG, Reece EA, Chen X, Boden G. Free fatty acids and insulin resistance during pregnancy. *J Clin Endocrinol Metab* 1998;83:2338–2342
77. Sivan E, Chen X, Homko CJ, Reece EA, Boden G. Longitudinal study of carbohydrate metabolism in healthy obese pregnant women. *Diabetes Care* 1997;20:1470–1475
78. Kirwan JP, Hauguel-de Mouzon S, Lepercq J, et al. TNF-alpha is a predictor of insulin resistance in human pregnancy. *Diabetes* 2002;51:2207–2213
79. Barbour LA, McCurdy CE, Hernandez TL, Kirwan JP, Catalano PM, Friedman JE. Cellular mechanisms for insulin resistance in normal pregnancy and gestational diabetes. *Diabetes Care* 2007;30(Suppl. 2):S1–S8
80. Bowers K, Tobias DK, Yeung E, Hu FB, Zhang C. A prospective study of prepregnancy dietary fat intake and risk of gestational diabetes. *Am J Clin Nutr* 2012;95:446–453
81. Hernandez TL, Sutherland JP, Wolfe P, et al. Lack of suppression of circulating free fatty acids and hypercholesterolemia during weight loss on a high-fat, low-carbohydrate diet. *Am J Clin Nutr* 2010;91:578–585
82. Hernandez TL, van Pelt RE, Anderson MA, et al. Women with gestational diabetes randomized to a higher-complex carbohydrate/low-fat diet manifest lower adipose tissue insulin resistance, inflammation, glucose, and free fatty acids: a pilot study. *Diabetes Care* 2016;39:39–42
83. Evert AB, Boucher JL, Cypress M, et al. Nutrition therapy recommendations for the management of adults with diabetes. *Diabetes Care* 2013;36:3821–3842