Diabetes and Pregnancy
Before, During, & After Delivery

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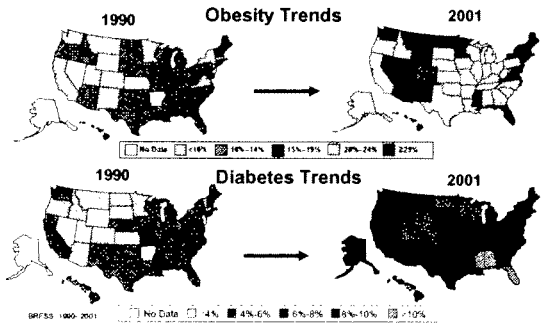
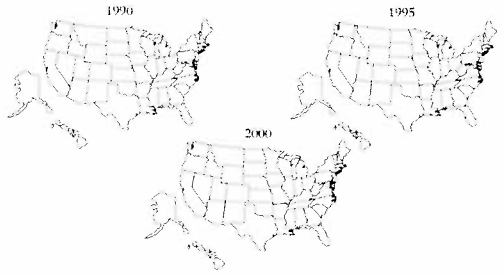
Diabetes Facts and Figures

- 18 million Americans afflicted (6% of population)
- 1 million with Type 1
- 15 million with Type 2
- 800,000 diagnosed annually
- Incidence of Type 1 and Type 2 increasing
- Diagnosed cases have risen by nearly half in 10 years and is expected to rise an additional 165% by 2050 to 29 million (CDC)

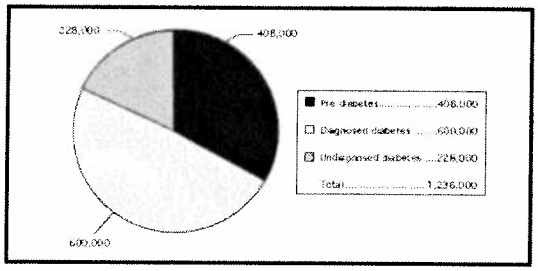


Diabetes and Gestational Diabetes Trends Among Adults in the U.S., BRFSS 1990, 1995 and 2000



Source: Mokdad et al., *Diabetes Care* 2000;23:1278-83; *J Am Med Assn* 2001;286(10).

Figure 6.
Estimated number of adults with some form of chronic hyperglycemia in N.C., 2006



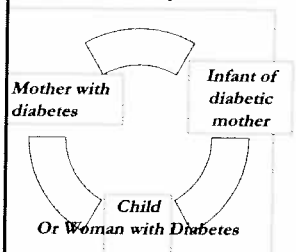
Data sources: Diagnosed diabetes is from NC BRFSS data;
Undiagnosed diabetes and pre-diabetes is from National Health and Nutrition Examination Survey III data.
Notes: All rounded to the nearest one thousand.

CDC Issues Warning June 2003

- Unless trends change, **1 out of every 3** children born in 2000 will become diabetic
- **1 out of every 2** Hispanic and Black children
- This means that 39% Caucasian girls, 53% of Hispanic girls, and 49% of African American girls now age 2-3 will develop diabetes
- This effects every medical provider

Children and Diabetes

- A vicious cycle



Approximately 151,000 people below the age of 20 years have diabetes. This number is growing

Birth weight and parental BMI predict overweight in children from mothers with gestational diabetes, by U.M. Schaefer-Graf and colleagues. Diabetes Care 28:1745-1750,2005

Fetal Origins Hypothesis

Taylor PD Exp Physiol 2007; 92:287

- **Metabolic factors in the intrauterine environment**

  (glucose, FFAs, TGs, inflammatory cytokines, insulin, hormones, growth factors), have a profound effect on prenatal development and enhances susceptibility to later chronic disease

Diabetes in Pregnancy

- Preexisting Diabetes
  - Type 1
  - Type 2
- Gestational Diabetes
  - Any diabetes diagnosed during pregnancy
  - Affects 3-5% of all pregnancies

Further Classification using the White Classification System

Diagnosis of Diabetes Mellitus in the Non–Pregnant State

- Plasma glucose level of 126 mg/dl on 2 occasions
- Casual plasma glucose >200 mg/dl

Diagnosis of GDM

- Two Step Approach
- Screening with 50g glucose load and a 1hr blood glucose
- >140 ⇨ 3hr. OGTT
- <140- No additional action taken

*For those at high risk, the 3hr. OGTT without screening may be more cost effective

Diagnostic Criteria- 100g OGTT Carpenter and Coustan

- FBG ≥95 mg/dl
- 1 hr ≥180 mg/dl
- 2 hr ≥155 mg/dl
- 3 hr ≥140 mg/dl

(2 or more values diagnostic)
* Until HAPO is accepted

- Thresholds selected due to their prediction of Type 2 DM in mom postpartum; **not neonatal outcomes!**

Risk Factors
Consider Early Screening

- Family history
- Previous child > 9 pounds
- Glycosuria
- Previous stillbirth – fetal anomalies - polyhydramnios
- Maternal age (>30)
- Non-Caucasian
- Obesity

Screening for gestational diabetes (GD): the effect of screening time

Time	Morning (0930–1200)	Afternoon (1205–1710)
Number screened	176	470
Age in years (mean ± SD)	31.2 ± 4.7	31.7 ± 5.0
Weight (mean ± SD)	59.4 ± 10.5 kg	60.8 kg ± 12.9 kg
Family history of diabetes	27	24
Positive result, 50 gm GTT	30 (17.0%)	146* (31.1%)

*$p < 0.001$

Med J Aust 1998;169:93-7

HAPO
(Hyperglycemia And Pregnancy Outcomes*)

Followed > 23,000 women after a 2-hour 75 gram GTT to determine whether there were glucose value thresholds that separated normal outcomes from complicated outcomes.

Women with FBS > 105 or 2-hr glucoses > 200 were unblinded.

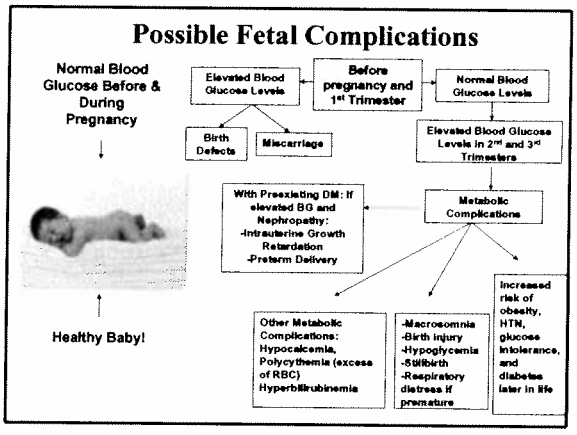
Followed for BW > 90th percentile, primary cesarean, neonatal hypoglycemia, cord-blood C-peptide > 90th percentile.

*NEJM 2008;358:1991-2002

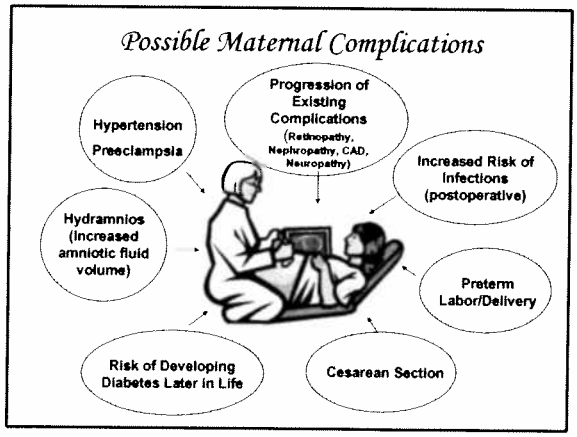
HAPO Conclusion

- Strong, continuous associations of maternal glucose levels below those diagnostic of GDM were seen with birth weight and increased cord-blood C-peptide levels.
- The current criteria for diagnosing and treating hyperglycemia during pregnancy needs to be re-evaluated.

Possible Fetal Complications

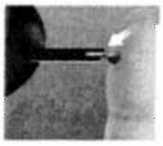


Possible Maternal Complications



Self-Monitoring of Blood Glucose (SMBG)

How do we know how and when to adjust treatment?



Blood Glucose Goals During Pregnancy

	Goals
▪ **Fasting**	**60-95**
▪ **Pre-meal**	**60-105**
▪ **2 hours after meal**	**<120**
▪ **1 hour after meal**	**<130 ***

•Note: Home blood glucose meters measure glucose in whole blood, however, most are plasma-calibrated. Glucose levels in plasma are 10-15% higher than whole blood.

Treat to What Target? Are We Missing the Mark?

- Evidence suggests that nondiabetic pregnant women averaged fasting BG's of 55-65 and 1hr postprandial BG's <105 mg/dl
  (Paretti et al.)

Current Recommendations:

Fasting: 70-105

1hr. Postprandial: <130-140

2hr. Postprandial: <120

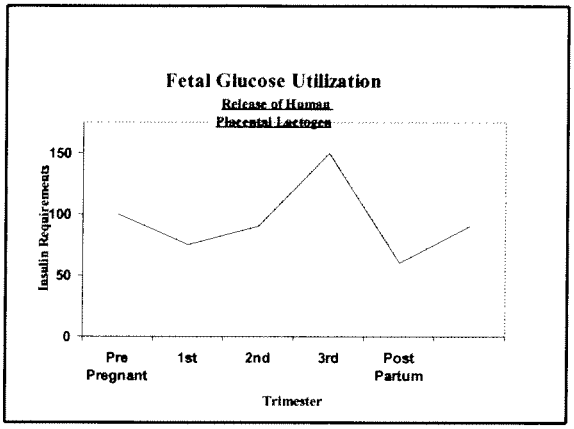
Continuous Glucose Monitoring (CGMS)

- FBG in normal pregnancy: **75 mg/dl**
- Peak postprandial: **110 mg/dl**
- Peak ~70-90 mins but differs with fat intake Yogev Y AJOG 2004
- Awaiting MFMU; FBG target likely to be lowered to ≤90

Tests of Glycemia in Diabetes

- Hb A1c (Reflects 2-3 months) (Recommended every trimester)
- Fructosamine- Glycated serum protein (14-25 days)
- Fasting or random blood glucose
- Urine test for glucose or ketones (Does not reflect overall control but may flag a possible problem)

Insulin Management



*Insulin Needs during Pregnancy

- 1st Trimester = .6 - .8 units/kg
- 2nd Trimester = .8 – 1.0 units/kg
- 3rd Trimester = .8 – 1.2 units/kg
- During labor and delivery = amount to maintain blood glucose 70-90 mg/dL
- Postpartum (after the baby is born) = ≤0.6 units/kg, need declines dramatically
- If breastfeeding = needs often are variable

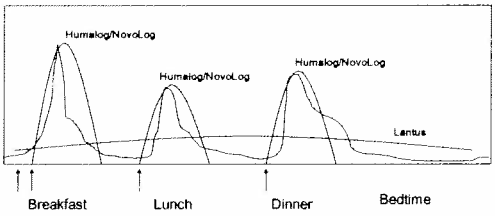
** Insulin amount is based on blood glucose monitoring results*

Insulin Regimens

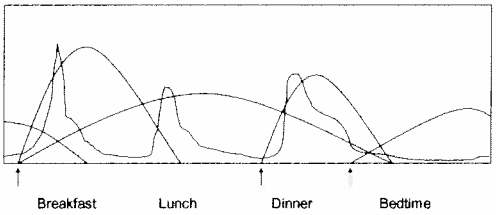
- Standard NPH/ Regular: BID
- R at each meal, NPH at bedtime
- NPH & Humalog or Novolog: TID or QID
- Lantus & Humalog or Novolog

Goal: To maintain tight control without severe hypoglycemia while preventing hyperglycemia and Diabetic Ketoacidosis

Four Injections Using Lantus and Humalog/NovoLog



Three Injections of NPH and/or Regular

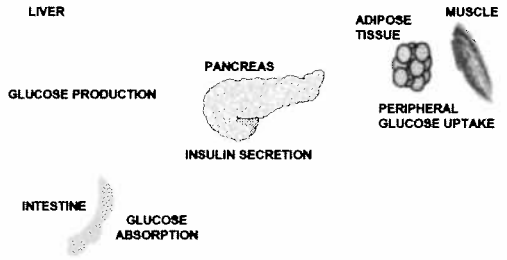


Advantages of Pump Therapy

- May improve glycemic control
- Provides easier dose adjustments
- Requires fewer injections
- Offers advanced programming
  - Multiple Basal Rates
  - Bolus and Correction calculator
  - Dual &Square Wave
  - Temporary Rate
  - Alarms/ Safety

New options for pump therapy

Overview in Diabetes Mellitus

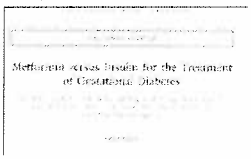


Glyburide

- Findings Suggest
  - Glyburide does not cross the placenta
  - May be useful adjunct to MNT
  - Cost Effective[1]
  - 20% failure rate (women dx prior to 25 weeks, marked hyperglycemia, and obesity
  - Rates of anomalies similar to insulin when given after organogenesis[2]

1 Goetzl, Wilkins Glyburide Compared to Insulin for the Treatment of Gestational Diabetes Mellitus: A Cost Analysis. Journal of Perinatology, 2002

2 Langer et al. A comparison of glyburide and insulin in women with gestational diabetes mellitus. N Engl J Med 2000 ;343:1134-1138



- 751 women with GDM randomized to Metformin vs Insulin (Auckland, New Zealand and Adelaide, Australia)
- 500 qd-bid to 2500 mg total dose
- Exclusions: Maternal liver or renal dz, fetal anomaly, gestational htn,
- preeclampsia, IUGR, ruptured membranes
- Trial designed to rule out 33% ↑ neonatal adverse composite outcomes

Conclusions

- 93% continued Metformin until delivery
- 46% required supplemental insulin
- No serious adverse events
- Women preferred Metformin to insulin
- Do not give to women with IUGR, placental insufficiency, preeclampsia
- What if Metformin increases insulin sensitivity in the fetus? Will they get fatter????

Nutritional Recommendations for Pregnancy

- Each plan is individualized
- Calorie level based on pre- pregnancy wt, physical activity, & recommended wt. gain
- Calories per kg:
  - 30-35 cal/kg (normal wt.)
  - 24cal/kg overweight
- IBW * 10, 15, or 20 (based on activity + 300)

What Diet Would You Recommend?

- Low Carb, Higher fat?
- High Carb, Lower fat?
- How many calories?
- How much weight gain?

Lower Carb Diets

- 40% carb diet demonstrated to blunt postprandial glucose excursion **Peterson, Jovanovic**
  Diabetes 1990; 40 suppl 2:172
- PP glucoses correlate best with macrosomia
  De Veciana M, NEJM, 1995
- Decreases the number of patients that require insulin

Carbohydrate Counting

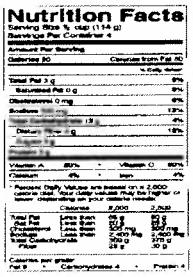
- Carbohydrate is the main factor affecting postprandial blood glucose
- Carbohydrate counting offers greater flexibility for all patients

- Various Methods
  - Gram counting (more accurate)
  - Counting servings or choices

What's Important on a Label?

Serving size

Total grams of carbohydrate



Weight Gain Recommendations

- BMI 20-26 wt: 25-35 lbs
- BMI 26.1-29.9: 15-25 lb
- BMI ≥30 At least 15 lbs
- No distinction between obese, severely, or morbidly obese e.g. ≥35 (Class II) and ≥40 (Class III)

Additional Considerations for Mothers With Diabetes

- Nausea/ Vomiting
- Extra vitamin supplementation???
- Gastroparesis or delayed gastric emptying
- Hypoglycemia & changes in awareness through pregnancy

Risks of Obesity

Weiss JL 2004 AJOG:190:1091; ACOG Committee Opinion #315, Sept 2005
Saravanakumar K 2006 Curr Opin Obstet Gynecol 18:631

- GDM 3 fold, Metabolic Syndrome, Insulin Resistance
- Hypertensive disorders, Preeclampsia (2-3 fold; 14%)
- Hypertriglyceridemia
- Cholelithiasis, Non-Alcoholic Fatty Liver Ds (NAFLD)
- Thromboembolism; Postpartum Hemorrhage
- Sleep Apnea (Pulm Htn, R Heart failure, inadequate O2 delivery to fetus)
- 50% C-section risk if BMI >35; failed IOL
- Post op wound infections
- Failed intubations and difficulties placing epidurals
- Difficulties with breastfeeding (latching)

Fetal Risks of Maternal Obesity

- ↑ 1st trim and recurrent miscarriage (3-fold)
- ↑ birth defects
- Neural tube (2-fold), cardiac (2-fold), GI (3-fold), orofacial clefts, CNS
- Inability to dx fetal anomalies (suboptimal in 37%)
- Macrosomia (18%)
- Shoulder dystocia with nerve palsies
- Meconium aspiration
- Perinatal mortality quadrupled
- Antepartum risk 3-fold; neonatal death 2-fold
- Insufficient oxygen for excess fetal growth

Krishnamoorthy U. BJOG 2006 113:1134; Yu CKH; BJOG 2006113:1117; King JC Ann Rev Nutr 2006 26:271; Catalano PM 2007 Obstet Gynecol 2007 109:

ACOG 2002 Recommendations For Exercise

- Mod exercise (3-5 METS), ≥30 mins or more per day on most, if not all days of week recommended for women with low risk pregnancies. Women at risk for preclampsia or GDM should be even more active
- Avoid in women at risk for placental insufficiency, IUGR
- Well hydrate, avoid excess temp, avoid high intensity later in pregnancy
- **Healthy, fit** age 20-29: **145-160 HR**
- Healthy fit age 30-39 140-155 HR
- Healthy, less fit 130-145

Breast feeding

- May reduce baby's risk for developing diabetes
- Hypoglycemia is common esp. within 1hr.
- Recalculate insulin requirements at .6 units/kg
- Can continue oral agents and insulin
- More prone to Mastitis if poorly controlled

Postpartum Care

- Preexisting Diabetes
  - Schedule appointment with Endocrinologist
  - Schedule eye exam
  - Assist with medication adjustment and prescriptions until care is transferred back to Endocrinologist
  - Emphasize the continuing need for diabetes management
  - Schedule appt. with educator to discuss birth control, weight loss, and other related issues

Postpartum Care

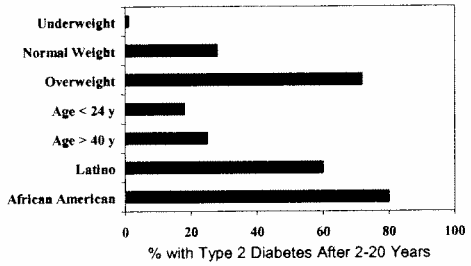
- Gestational Diabetes
  - Monitor BG after delivery to make sure euglycemia is restored (FBG<100, 2hr <140)
  - Some women may need to monitor periodically at home at different times. If values normal d/c testing
  - At 6-8 weeks following delivery, pt. should be reassessed by FBG and fructosamine level or by 75-g OGTT
  - Encourage healthy lifestyle

Postpartum Glucose Testing after GDM*

- **Retrospective cohort study of 344 women with GDM, 2001-2004**
- **Only 45% had postpartum glucose testing**
- **Of those, 36% had persistent abnormal glucose tolerance.**
- **Recommendations:**
  - **Improve attendance at postpartum visits**
  - **Improve continuity between antepartum and postpartum care**

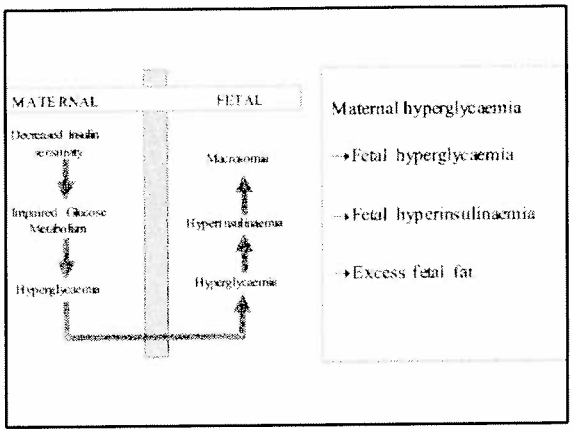
**Obstetrics & Gynecology* 2006;108:1456-1462

Emergence of Type 2 DM in Women with Previous GDM

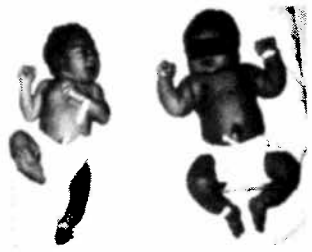


Mestman, Oats, Gestational Diabetes. Vienn: Springer-Verlag 1988

Developmental Origins of Disease



The Phenotype of Fetal Hyperinsulinemia



Type 2 or GDM; Obesity

Childhood Obesity and Diabetes Explosion

- Obesity has tripled in children in the last 2 decades (1/3 of kids ages 6-19 overweight)
- By 2010, 30% of girls 11-15 will be obese
- Type 2 diabetes up by> 300% in adolescents
- Decreased life expectancy

Summary

- GDM requiring medical treatment identifies a group of pregnant women at risk for multiple pregnancy complications and at increased long-term risk of type 2 diabetes.
- Lesser degrees of abnormal carbohydrate metabolism are also associated with an increased rate of pregnancy complications, but the threshold for treatment / non-treatment is not yet clear.
- Risks and complications of type 2 diabetes (and probably GDM) can be decreased by changes in lifestyle, particularly diet and exercise.

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